Nihon Schering K.K.

2.7.6　　個々の試験のまとめ

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試験の種類	試験相	試験番号 (報告書番号)	実施国	被験対象	生物薬剤学 /臨床薬理	有効性	安全性
健康被験者における PK 及び初期忍容性試験	第 I 相	010559 (B866)	日本	健康な閉経後日本人女性	●		●
(参考資料)	第 I 相	010560 (B867)	日本	健康な閉経後日本人女性	(参考資料)		(参考資料)
	第 I 相	010561 (B868)	日本	健康な閉経後日本人女性	●		●
(参考資料)	第 I 相	308560 (A20152)	ドイツ	健康な閉経後白人女性	(参考資料)		
内因性要因を検討した PK 試験 (参考資料)	第 I 相	305044 (A06581)	日本, ドイツ	健康な閉経後日本人女性及び白人女性	(参考資料)		(参考資料)
申請する適応症に関する 比較対照試験	後期第Ⅱ相	300107 (BC69)	日本	自然閉経後の更年期障害, 又は 両側卵巣摘出による卵巣欠落症状を有する患者		●	●
	後期第Ⅱ/Ⅲ相	300103 (A23185)	日本	自然閉経後又は両側卵巣摘出に伴う骨粗鬆症患者	(参考資料)		●
	前期第Ⅱ相 〈step1〉	010646 (B123)	日本	自然閉経後の更年期障害, 又は 両側卵巣摘出による卵巣欠落症状を有する患者		●	(参考資料)
その他の臨床試験 (参考 資料)	前期第Ⅱ相 〈step2〉	010730 (A02614)	日本	自然閉経後の更年期障害, 又は 両側卵巣摘出による卵巣欠落症状を有する患者		(参考資料)	(参考資料)
	前期第Ⅱ相 〈step2〉	010731 (A02103)	日本	自然閉経後の更年期障害, 又は 両側卵巣摘出により卵巣欠落症状を有する患者		(参考資料)	(参考資料)
	前期第Ⅱ相 〈step1〉	010568 (B006)	日本	女性の退行期骨粗鬆症患者, 又は 卵巣機能欠落に伴う骨量減少例			(参考資料)
	第Ⅱ相	[redacted]216 (A00403)	ハンガリー	更年期障害を有する閉経後女性患者		(参考資料)	(参考資料)
	第Ⅱ相	[redacted]216 (A06276)	ハンガリー	更年期障害を有する閉経後女性患者		(参考資料)	(参考資料)
	第Ⅲ相	[redacted]065 (A00404)	ハンガリー, チェコ	更年期障害を有する閉経後女性患者		(参考資料)	(参考資料)

2.7.6.1 健康被験者における PK 及び初期忍容性試験報告書

試験 No. 010559/報告書 No. B866

試験 No. 010560/報告書 No. B867 (参考資料)

試験 No. 010561/報告書 No. B868

試験 No. 308560/報告書 No. A20152 (参考資料)

試験 No.010559/報告書 No.B866

有効成分の名称:	エストラジオール（Estradiol：E2）/ レボノルゲストレル（Levonorgestrel：LNG）	
治験の標題:	第 I 相試験 単回投与試験（1）	
治験総括医師	[redacted]	
治験責任医師:	[redacted]	
実施医療機関:	[redacted]	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted]年[redacted]月[redacted]日 **終了日（最後の被験者が完了した日）：** 19[redacted]年[redacted]月[redacted]日	**治験の相:** I
目的:	健康な閉経後女性に E2，E2 及び LNG を単回経口投与した時の，安全性並びに薬物動態について検討した．	
方法:	E2 錠単剤（1.0mg，2.0mg）投与群と，E2 錠及び LNG 錠併用（E2 1.0mg＋LNG 40μg，E2 2.0mg＋LNG 80μg）投与群の各投与群に対し，それぞれ低用量から高用量の順に，被験者の安全性を確認しながら投与を行った．同一被験者への投薬は少なくとも 1 週間以上の休薬期間を設けた． 各投与群の被験者数はそれぞれ 12 例であり，この内 2 例はプラセボ錠を服用し，プラセボ対照二重盲検比較試験を行った．	
被験者数（計画時，解析時）：	計画被験者数：計 24 例（E2 単独投与群 12 例，E2/LNG 併用投与群 12 例） 解析被験者数：計 24 例（E2 単独投与群 12 例，E2/LNG 併用投与群 12 例）	
診断及び主要な選択基準:	被験者は本治験に先立ち投与前 1 ヶ月以内に健康診断を受け，その結果を治験担当医師が検討し，治験参加の適否を選択基準に従い判定する． [選択基準]　健康な閉経後日本人女性 1）本治験の目的及び内容をよく理解し，自由意志により書面で治験参加の同意を得た者 2）年齢 45 歳以上 64 歳以下の者 3）最終月経後 6 ヶ月以上経過している者 4）本治験の開始前 6 ヶ月以内にエストロゲン治療を受けていない者 5）本治験の開始前 1 ヶ月以内に本治験に影響を及ぼすと考えられる薬剤を使用していない者 6）本試験に不適当と考えられる既往歴がない者 7）薬物等に対するアレルギー症または特異体質のない者	
被験薬: **用量:** **投与方法:** **バッチ番号:**	SH T 546 KB　：1 錠中に E2 1.0mg を含有する錠剤 SH T 546 LA　：1 錠中に E2 2.0mg を含有する錠剤 SH T 594 F　：1 錠中に LNG 40μg を含有する錠剤 SH T 594 G　：1 錠中に LNG 80μg を含有する錠剤 E2 1.0mg：E2 1.0mg 錠，1 錠 E2 2.0mg：E2 2.0mg 錠，1 錠 E2 1.0mg+LNG 40μg：E2 1.0mg 錠及び LNG40μg 錠，各 1 錠（計 2 錠） E2 2.0mg+LNG 80μg：E2 2.0mg 錠及び LNG80μg 錠，各 1 錠（計 2 錠） 空腹時（午前 9 時）に少量の水とともに単回経口投与する． SH T 546 KB　：[redacted] SH T 546 LA　：T* SH T 594 F　：O* SH T 594 G　：Q*	
投与期間:	単回投与	
対照薬: **用量:** **投与方法:** **バッチ番号:**	SH T 546 PA　：プラセボ錠剤 有効成分なし E2 単剤投与群にはプラセボ錠 1 錠，E2 錠+LNG 錠併用投与群にはプラセボ錠 2 錠 空腹時（午前 9 時）に少量の水とともに単回経口投与する． SH T 546 PA　：U*	
投与期間:	単回投与	

評価基準:	試験の性質上，有効性の評価は行わない．ただし，薬物動態及び内分泌検査により，本治験薬の薬物動態的な特徴及び内分泌に及ぼす影響を検討する．安全性についても試験の性質上，概括的な安全性の評価は行わず，臨床症状，理学検査，臨床検査の各項目について安全性を確認する．
有効性:	該当なし
安全性:	グループ間の背景因子の均質性を検討する． 自覚症状（副作用）については詳細な情報を投与群別に集計し，また用量相関性を検討する． 理学検査，一般臨床検査並びに内分泌検査については，変動の推移とともに用量相関性を推測する．
薬物動態（適切な場合）:	薬物動態についてはコンパートメントモデル等を用いて薬物動態学的パラメーターを算出する．
薬力学（適切な場合）:	該当なし
統計手法:	治験終了後，治験総括医師並びにコントローラーは，各被験者の解析上の取り扱いを協議し決定する．また，治験総括医師が各被験者の検査結果が正しく症例記録用紙に記載されている事を確認した後，コントローラーは割り付け表の開封を行う．解析は日本シエーリング社 臨床解析課で行われ，上記のような検討を行う．

要約・結論

薬物動態・内分泌検査の結果:

血漿中 E2 濃度の測定は，通常行われているラジオイムノアッセイ（radio immunoassay：RIA 法）の測定で問題となる交差反応物資を除去した高感度測定法で行った．E2 を単回投与後約 2～4 時間で最大薬物濃度（maximum concentration：C_{max}）付近に達し，投与後 12 時間まではその濃度でほぼ定常状態を示した．C_{max} の平均濃度は E2 用量 1.0mg 投与時で 37.16±12.96pg/mL，E2 用量 2.0mg 投与時で 68.20±35.10pg/mL であり，閉経前の正常月経周期の卵胞期あるいは黄体期に匹敵する血中濃度が得られた．血漿中エストロン（Estrone：E1）は投与後約 2～4 時間で C_{max} 付近に達し，血漿中 E2 とほぼ同様な推移を示した．投与量の増加に伴う血漿中濃度の増加は，E2，E1，総エストロン（非抱合型及び抱合型）の全てに認められ，また，LNG 併用による影響は，E2 の平均滞留時間（mean residence time：MRT），E1 の最高血中濃度到達時間（time to reach maximum concentrations：t_{max}）に認められたが，症例誤差の影響が考えられた．

E2 を単回経口投与したときの尿中排泄に関して，総 E2，総 E1，LNG はいずれも，投与 24 時間後までにほとんどが排泄され，排泄量は投与量に対して，総 E2 が 6.4～8.4%，LNG が 0.00～0.05%であった．

内分泌検査では黄体化ホルモン（luteinizaing hormone：LH）と卵胞刺激ホルモン（follicle-stimulating hormone：FSH）が LNG の併用に関係なく，E2 の投与量に依存して低下したが，正常範囲内の低下であり，閉経後に上昇した LH，FSH が閉経前の状態となった結果であった．

安全性の結果:

臨床症状（自覚症状，視診，触診，聴・打診），理学検査，臨床検査に異常は全く認められなかった．

結論:

第Ⅰ相臨床試験＜単回投与試験（1）＞として，本剤を健康な閉経後日本人女性に単回投与した時の薬物動態的特徴及び安全性が確認された．

Nihon Schering K.K.

試験 No.010560/報告書 No.B867

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題:	第 I 相試験 単回投与試験(2): 食事の影響	
治験総括医師	[redacted]	
治験責任医師:	[redacted]	
実施医療機関:	[redacted]	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）:** 19[redacted]年[redacted]月[redacted]日 **終了日（最後の被験者が完了した日）:** 19[redacted]年[redacted]月[redacted]日	**治験の相:** I
目的:	健康な閉経後女性に E2 及び LNG を単回経口投与した時の，安全性並びに薬物動態に及ぼす食事の影響を検討した.	
方法:	1 用量のオープン試験 10 例の被験者に対して，E2 2.0mg と LNG 80μg を朝食後 30 分（午前 9 時）に投与し，安全性及び薬物動態を，本治験薬の単回投与試験(1)で行った空腹時に投与した結果と比較検討した.	
被験者数 （計画時，解析時）:	計画被験者数：10 例 解析被験者数：10 例	
診断及び主要な選択基準:	被験者は本治験に先立ち投与前 1 ヶ月以内に健康診断を受け，その結果を治験担当医師が検討し，治験参加の適否を選択基準に従い判定する. [選択基準] 健康な閉経後日本人女性 1) 本治験の目的及び内容をよく理解し，自由意志により書面で治験参加の同意を得た者 2) 年齢 45 歳以上 64 歳以下の者 3) 最終月経後 6 ヶ月以上経過している者 4) 本治験の開始前 6 ヶ月以内にエストロゲン治療を受けていない者 5) 本治験の開始前 1 ヶ月以内に本治験に影響を及ぼすと考えられる薬剤を使用していない者 6) 本試験に不適当と考えられる既往歴がない者 7) 薬物等に対するアレルギー症または特異体質のない者	
被験薬: **用量:** **投与方法:** **バッチ番号:**	SH T 546 LA : 1 錠中に E2 2.0mg を含有する錠剤 SH T 594 G : 1 錠中に LNG 80μg を含有する錠剤 E2 2.0mg 錠及び LNG 80μg 錠，各 1 錠（計 2 錠） 朝食後 30 分（午前 9 時）に少量の水とともに単回経口投与する. SH T 546 LA : T* SH T 594 G : Q*	
投与期間:	単回投与	
対照薬:	該当なし	
評価基準: **有効性:** **安全性:** **薬物動態（適切な場合）:** **薬力学（適切な場合）:**	試験の性質上，有効性の評価は行わない．ただし，薬物動態及び内分泌検査により，本治験薬の薬物動態的な特徴及び内分泌に及ぼす影響を検討する．また，食事による影響を空腹時に投与した単回投与試験（1）の結果と比較検討する．安全性についても試験の性質上，概括的な安全性の評価は行わず，臨床症状，理学検査，臨床検査の各項目について安全性を確認する. 該当なし 被験者の背景因子の集計を行うとともに，単回投与試験（1）の被験者の背景との均質性を検討する．自覚症状（副作用）については詳細な情報を集計し，また，薬剤との関連性を検討する．理学検査，一般臨床検査並びに内分泌検査については変動の推移とともに薬剤との関連性を推測する. 薬物動態ついてはコンパートメントモデル等を用いて薬物動態学的パラメーターを算出する．また，食事の影響を推測する. 該当なし	

＊新薬承認情報提供時に置き換え

統計手法:	治験終了後，治験総括医師並びにコントローラーは，各被験者の解析上の取扱いを協議し決定する．また，治験総括医師は各被験者の検査結果が正しく症例記録用紙に記載されている事を確認する．解析は日本シエーリング社 臨床解析課で行われ，上記のような検討を行う．なお，その際，食事の影響を検討するため，別途行われる単回投与試験(1)のデータを参考にする．

要約・結論

薬物動態・内分泌検査の結果:

血漿中 E2 濃度の測定は，通常行われている RIA 法の測定で問題となる交差反応物質を除去した高感度測定法で行った．空腹時投与に対して食後投与では，t_{max} が空腹時投与の平均 6.25 時間から食後投与の平均 9.20 時間と有意に延長した．MRT，C_{max} 及び投与 48 時間後までの薬物濃度-時間曲線下面積（area under the curve：AUC)には，食事の影響は認められなかった．血漿中 LNG についても，t_{max} が空腹時投与で平均 1.20 時間から食後投与で平均 2.10 時間と有意に延長したが，MRT，C_{max} 及び AUC(0-48h)については，食事の影響は認められなかった．血漿中 E1 は，食後投与の C_{max} が空腹時投与に対し約 40.7%低く，同様に AUC が 38.5%低かった．血漿中総 E1（非抱合型及び抱合型）に，食事の影響は認められなかった．

尿中排泄に関して，総 E2，総 E1，LNG は，いずれも投与 24 時間後までにほとんどが排泄され，排泄量は投与量に対して，総 E2 が 5.5%，LNG が 0.03%であった．内分泌検査では，LH と FSH が投与前に対して投与後にそれぞれ 28.8%，21.1%減少したが，正常範囲内の減少で，閉経後に上昇した LH，FSH を閉経前の状態にするものであった．尿中排泄及び内分泌検査での結果は，食事の影響は認められなかった．

安全性の結果:

臨床症状（自覚症状，視診，触診，聴・打診），理学検査，臨床検査に異常は全く認められなかった．

結論：

本剤の第Ⅰ相臨床試験＜単回投与試験(2)＞として，本剤を健康な閉経後日本人女性に食後 30 分に単回投与し，薬物動態的特徴を空腹時投与した単回投与試験(1)の結果と比較検討した．エストロゲンとして最も活性の高い E2 並びに LNG では t_{max} のわずかな延長が認められたが，MRT，C_{max} 及び AUC(0-48h)には食事の影響が認められなかった．t_{max} の延長は，食物摂取による胃腸管からの吸収遅延と考えられ，本剤を空腹時あるいは食後に投与しても MRT，C_{max} 及び AUC(0-48h)に変化は認められないことから，食事による影響は少ないと考えられる．血漿中 E1 は，空腹時投与に対し食後投与で C_{max} 及び AUC が低かった．E1 のエストロゲンレセプターに対する親和性は，E2 が 100 に対し 11 であり，一般的に E1 の生物活性は E2 より弱く，また，E1 の血中アルブミンへの結合率は E2 より高いことから，E2 と比較して E1 の生体への作用は弱いと考えられる．また，安全性においても異常が認められなかったことより，有効性及び安全性に関して本剤への食事の影響は少ないことが示唆された．

Nihon Schering K.K.

試験 No.010561/報告書 No.B868

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題:	第 I 相試験 反復投与試験	
治験総括医師	[redacted]	
治験責任医師:	[redacted]	
実施医療機関:	[redacted]	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted]年[redacted]月[redacted]日 **終了日（最後の被験者が完了した日）：** 19[redacted]年[redacted]月[redacted]日	**治験の相:** I
目的:	健康な閉経後女性に E2，E2 及び LNG を 28 日間反復経口投与した時の安全性並びに薬物動態について検討する．	
方法:	E2 錠単剤（1.0mg，2.0mg）投与群と，E2 錠及び LNG 錠併用（E2 1.0mg＋LNG 40μg，E2 2.0mg＋LNG 80μg）投与群の各投与群に対し，それぞれ低用量から高用量の順に，被験者の安全性を確認しながら投与を行った．同一被験者への投薬は少なくとも 4 週間以上の休薬期間をもうけた． 各投与群の被験者数はそれぞれ 12 例であり，この内 2 例はプラセボ錠を服用し，プラセボ対照二重盲検比較試験を行った．	
被験者数（計画時，解析時）：	計画被験者数：計 24 例（E2 単独投与群 12 例，E2/LNG 併用投与群 12 例） 解析被験者数：計 25 例（E2 単独投与群 13 例，E2/LNG 併用投与群 12 例*） *E2 単剤の 1.0mg 投与時に 1 例脱落したため，2.0mg 投与時に 1 例追加	
診断及び主要な選択基準:	被験者は本治験に先立ち投与前 1 ヶ月以内に健康診断を受け，その結果を治験担当医師が検討し，治験参加の適否を選択基準に従い判定する． [選択基準] 健康な閉経後日本人女性 1）本治験の目的及び内容をよく理解し，自由意志により書面で治験参加の同意を得た者 2）年齢 45 歳以上 64 歳以下の者 3）最終月経後 6 ヶ月以上経過している者 4）本治験の開始前 6 ヶ月以内にエストロゲン治療を受けていない者 5）本治験の開始前 1 ヶ月以内に本治験に影響を及ぼすと考えられる薬剤を使用していない者 6）本試験に不適当と考えられる既往歴がない者 7）薬物等に対するアレルギー症または特異体質のない者	
被験薬:	SH T 546 KB ：1 錠中に E2 1.0mg を含有する錠剤 SH T 546 LA ：1 錠中に E2 2.0mg を含有する錠剤 SH T 594 F ：1 錠中に LNG 40μg を含有する錠剤 SH T 594 G ：1 錠中に LNG 80μg を含有する錠剤	
用量:	E2 1.0mg：E2 1.0mg 錠，1 日 1 回 1 錠 E2 2.0mg：E2 2.0mg 錠，1 日 1 回 1 錠 E2 1.0mg+LNG 40μg：E2 1.0mg 錠及び LNG 40μg 錠，1 日 1 回各 1 錠（計 2 錠） E2 2.0mg+LNG 80μg：E2 2.0mg 錠及び LNG 80μg 錠，1 日 1 回各 1 錠（計 2 錠）	
投与方法:	一定時刻（午前 9 時）に少量の水とともに 28 日間経口投与する．	
バッチ番号:	SH T 546 KB ：[redacted] SH T 546 LA ：T# SH T 594 F ：O# SH T 594 G ：Q#	
投与期間:	28 日間	
対照薬:	SH T 546 PA ：プラセボ錠剤	
用量:	有効成分なし	
投与方法:	E2 単剤投与群にはプラセボ錠 1 錠，E2 錠+LNG 錠併用投与群にはプラセボ錠 2 錠を 1 日 1 回一定時刻（午前 9 時）に少量の水とともに 28 日間経口投与する．	
バッチ番号:	SH T 546 PA ：U*	
投与期間:	28 日間	

評価基準:	試験の性質上，有効性の評価は行わない．ただし，薬物動態及び内分泌検査により，本治験薬の薬物動態的な特徴及び内分泌に及ぼす影響を検討する．安全性についても試験の性質上，概括的な安全性の評価は行わず，臨床症状，理学検査，臨床検査の各項目について安全性を確認する．
有効性:	該当なし
安全性:	グループ間の背景因子の均質性を検討する． 自覚症状（副作用）については詳細な情報を投与群別に集計し，また用量相関性を検討する． 理学検査，一般臨床検査並びに内分泌検査については，変動の推移とともに用量相関性を推測する．
薬物動態（適切な場合）:	薬物動態についてはコンパートメントモデル等を用いて薬物動態学的パラメーターを算出する．
薬力学（適切な場合）:	該当なし
統計手法:	治験終了後，治験総括医師並びにコントローラーは，各被験者の解析上の取り扱いを協議し決定する．また，治験総括医師が各被験者の検査結果が正しく症例記録用紙に記載されている事を確認した後，コントローラーは割り付け表の開封を行う．解析は日本シエーリング社 臨床解析課で行われ，上記のような検討を行う．

要約・結論

薬物動態・内分泌検査の結果:

血漿中 E2 濃度は E2 単独投与群では投与 17 日目までにほぼ定常状態に達した．定常状態での平均トラフ濃度は，E2 1.0mg 単独投与で 27.5～31.3pg/mL，E2 2.0mg 単独投与で 54.4～71.0pg/mL であった．血漿中 E1 は血漿中 E2 とほぼ同様な推移を示した．

E2 単独投与群の尿中排泄に関して，総 E2（非抱合型及び抱合型），総 E1（非抱合型及び抱合型）は投与 1 日目及び投与 28 日目の両方において投与後 0～24 時間でほとんど排泄され，排泄量は投与量に対して，総 E2 が約 10%であった．

内分泌検査では LH，FSH，性ホルモン結合グロブリン（sex-hormone binding globulin：SHBG），遊離トリヨードサイロニン（triiodothyronine：T3），遊離サイロキシン（tyroxine：T4），サイロキシン結合グロブリン（thyroxine-binding globulin：TBG）に薬剤によると思われる変動が認められたが，いずれも正常範囲内の変動であった．

安全性の結果:

自覚症状として，下腹部膨満感，乳頭痛，帯下，腰痛，下肢浮腫，下肢倦怠感が認められ，いずれも重症度の判定は軽度であった．また，性器出血の消退出血が E2 単独投与群で 4 例に，E2/LNG 併用投与群で 13 例に認められ，不正出血は E2/LNG 併用投与群にのみ 3 例に認められたが，何ら処置の必要もなく速やかに消失し，また，子宮内膜細胞診でも異常は認められなかった．その他，理学検査，臨床検査には異常は認められなかった．

結論:

本剤を 28 日間反復投与した時の薬物動態的特徴及び安全性が確認された．

試験 No.308560/報告書 No.A20152

有効成分の名称:	エストラジオール（E2）	
治験の標題:	健康な閉経後女性 24 名に 190micro g E2(SH T04170F)を経口投与したときの E2 の生物学的利用性に対する食事の影響と，100micro g E2(SH T04170E)を経口投与したときの薬物動態を検討するオープンラベル，単回投与，ランダム化クロスオーバー試験	
治験責任医師:	[redacted]（ドイツ）	
実施医療機関:	[redacted] Berline, Germany	
公表文献:	なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 20[redacted]年[redacted]月[redacted]日 **終了日（最後の被験者が完了した日）：** 20[redacted]年[redacted]月[redacted]日	**治験の相:** I
目的:	健康な閉経後白人女性を対象に E2 0.19mg を単回経口投与したときの薬物動態に及ぼす食事の影響及び E2 0.19mg 又は E2 0.10mg を単回経口投与したときの E2 及びその代謝物でありエストロン（E1）及び E1 の硫酸抱合体の薬物動態を検討する.	
方法:	E2 0.19mg を空腹時及び食後に又は E2 0.10mg を空腹時に単回経口投与するクロスオーバー非盲検試験.	
被験者数（計画時，解析時）：	計画被験者数：計 24 例 解析被験者数：計 24 例	
診断及び主要な選択基準:	[選択基準] 1）健康な女性志願者 2）年齢 55 歳以上 75 歳以下の者 3）ボディマスインデックス 20kg/m^{2}以上 35kg/m^{2}以下の者 4）本治験の参加に文書により同意した者 5）最低 2 年以上閉経状態にあるもの	
被験薬: **用量:** **投与方法:** **バッチ番号:**	SH T04170E　：1 錠中に E2 0.10mg を含有する錠剤 SH T04170F　：1 錠中に E2 0.19mg を含有する錠剤 E2 0.10mg を単回投与 E2 0.19mg を単回投与 経口投与 [redacted]	
投与期間:	単回投与	
対照薬:	該当なし	
評価基準: **有効性:** **安全性:** **薬物動態（適切な場合）：** **薬力学（適切な場合）：**	 該当なし 有害事象，臨床検査 主要変数：E2 0.19mg 単回経口投与時の濃度曲線下面積 AUC(0-tlast)及び E2 の最高濃度（Cmax） 該当なし	
統計手法:	記述統計量，共分散分析，食事の影響検討のための相対的生物学的利用率の評価	

要約・結論

薬物動態の結果:

主要評価項目である E2 0.19mg 単回経口投与時の AUC(0-tlast)及び Cmax に関して，空腹時と食後投与時の AUC(0-tlast)の比は 100.4%（空腹時/食後）であり，比の 90%信頼区間は 94.2～100.7%，Cmax の比は 100.7%（空腹時/食後）であり，比の 90%信頼区間は 91.8%～110.5%であった.
AUC(0-tlast)及び Cmax の両者について，両側 90%信頼区間が事前に設定した基準（70%～143%）の範囲内であったことから，E2 の生物学的利用性に食事の影響はないことが示された.

E2 0.10mg 又は E2 0.19mg 単回経口投与したときのそれぞれの E2, E1 及び E1 の硫酸抱合体の AUC(0-tlast)及び Cmax を投与前のそれぞれの血清中濃度を減じて補正した補正後 AUC(0-tlast)及び補正後 Cmax を比較すると，E2 0.19mg 投与群で得られた値は，E2 0.10mg 群で得られた値の約 1.9 倍であった．この結果は E2 の薬物動態が用量比例的であることを示している．

安全性の結果:

本試験において死亡例及び重篤な有害事象は認めなかった．

合計 7 例に合計 11 件の有害事象を認めた（1 投与群あたり 3～4 例）．これらのうち 2 件の有害事象が治験薬の投与と関連あり（明らかに関連あり，おそらく関連あり，関連あるかもしれないを関連ありと分類した）と評価され，9 件は関連なし（関連なし，関連性は考えにくいを関連なしと分類した）と評価された．関連ありと評価された有害事象はいずれも頭痛であった．有害事象の程度に関して 3 件の有害事象は中等度と評価され，8 件は軽度と評価された．

結論：

E2 0.10mg 空腹時単回経口投与及び E2 0.19mg 空腹時又は食後単回経口投与したときの忍容性は良好であった．

E2 及びその代謝物である E1 及び E1 の硫酸抱合体の Cmax や AUC(0-tlast)といった薬物動態学的パラメータは，E2 0.10mg～0.19mg の用量範囲で用量比例的であった．空腹時投与したときと食後投与したときを比較すると，E2 の濃度－時間曲線にはわずかな違いが認められたものの，主要評価項目である AUC(0-tlast)及び Cmax に関して空腹時投与と食後投与の間で統計学的な差はないことが示された．

2.7.6.2 内因性要因を検討した PK 試験報告書

試験 No.305044/報告書 No.A06581 （参考資料）

試験 No.305044/報告書 No.A06581

有効成分名：	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題：	閉経後の健康な日本人女性及び白人女性を対象に，SH T 594 B（E2 1.0mg + LNG 40μg）の単回経口投与並びに 28 日間の反復経口投与を行い，E2 及び LNG の薬物動態における人種間の類似性を検討することを目的とした多施設共同，多国籍，非対照，オープン試験	
治験責任医師：	[redacted]（日本），[redacted]（ドイツ）	
実施医療機関：	日本 1 施設，ドイツ 1 施設	
公表文献：	なし	
治験期間（年）	**最初の被験者の組み入れ日：** 20[redacted] 年 [redacted] 月 **最後の被験者の完了日：** 20[redacted] 年 [redacted] 月	**治験の相：** I
目的：	本治験の目的は，閉経後の健康な日本人女性及び白人女性を対象に，SH T 594 B（E2 1.0mg＋LNG 40μg）の単回経口投与及び 28 日間反復経口投与を行い，E2 及び LNG の薬物動態における人種間の類似性を検討することであった.	
方法：	本治験は，多施設共同，多国籍，非対照，オープン試験であった. 2 つの民族群（日本人と白人）に同一の治験薬を処方し，単回投与及び 28 日間反復投与するという方法で実施された. 薬物動態測定のため，採血が行われた. 解析：E2，E1 及び LNG（方法：ラジオイムノアッセイ［RIA］） 単回投与（第 1 期） 投与前及び単回経口投与後 48 時間後（E2，E1），144 時間後（LNG)まで採血が行われた. 反復投与法（第 2 期） 投与前，28 日目までの予め設定した時期（トラフ濃度）及び反復経口投与の最終投与（28 日目）の 48 時間後（E2，E1），144 時間後（LNG)まで採血が行われた.	
被験者数 （計画時，解析時）：	目標被験者数：64 例（32 例/民族群） 解析被験者数：安全性解析 64 例（32 例/民族群） 薬物動態解析 57 例（日本人群 28 例，白人群 29 例）	
診断及び主要な選択基準:	2 つの民族群（日本人及び白人），年齢 45 歳から 64 歳，FSH 濃度 40IU/L 以上，E2 濃度 10pg/mL 以下，閉経後の健康な女性，非喫煙者	
被験薬： 用量： 投与方法 バッチ番号：	SH T 594 B：E2 1.0mg 及び LNG 40μg を含有する錠剤 単回投与（第 1 期）：SH T 594 B を 1 錠 反復投与（第 2 期）：SH T 594 B を毎日 1 錠 経口 I*	
投与期間	単回投与（第 1 期）：1 回投与 反復投与（第 2 期）：28 日間	
対照薬：	該当なし	
評価基準 有効性： 安全性： 薬物動態（適切な場合）： 薬力学（適切な場合）：	 該当なし 有害事象，臨床検査，身体及び婦人科検査，バイタルサイン（血圧及び心拍数），心電図（ECG） 主要変数：E2 及び LNG の 28 日間反復投与後の最高濃度（C_{max}），投与 24 時間後までの濃度曲線下面積 AUC(0-24h)（定常状態での薬物動態プロフィール） 該当なし	
統計手法：	記述統計量，バイオアベイラビリティ民族間比較を主要変数の幾何平均の比率（日本人／白人）及びその 90%信頼区間を用いて評価した．追加解析として，共分散分析（ANCOVA）を行った.	

要約・結論

本治験の目的は，閉経後の健康な日本人女性及び白人女性を対象に SH T 594 B（E2 1.0mg/LNG 40μg 配合剤）を 28 日間反復経口投与し，E2 及び LNG 薬物動態の民族間類似性を評価することであった．

合計 64 例の非喫煙者，年齢 49 歳から 64 歳，血清中 FSH 濃度 40IU/L 以上，E2 濃度 10pg/mL 以下の女性が本治験に登録された．64 例（各民族群：32 例）の全被験者を安全性の解析対象（有害事象，臨床検査，身体及び婦人科検査，バイタルサイン，心電図），57 例（日本人 28 例，白人 29 例）を薬物動態解析対象とした．

薬物動態の成績：

次項の表に，日本人及び白人の閉経後女性に SH T 594 B を 28 日反復投与後の E2 及び LNG の主な薬物動態パラメーターを示す．

反復投与後，平均血清中 E2 濃度は約 5 日目に定常状態に達した．28 日目の E2 の C_{max} の幾何平均値は，日本人女性で 40.5pg/mL，白人女性で 27.5pg/mL であった．28 日目の AUC(0-24h)の幾何平均値は，日本人女性で 688pg･h/mL，白人女性で 413pg･h/mL であった．これらのパラメーターの変動係数（coefficient of variation：CV）は，日本人女性よりも白人女性で高かった．日本人女性の薬物動態パラメーターは，過去に実施された試験とほぼ同様であったのに対し，白人女性のパラメーターは，過去に実施した試験に比して明らかに低値を示した．総 E2 に関する主要変数の統計学的計算より幾何平均値を求め比較した．日本人女性に対する白人女性の比（日本人／白人）は，C_{max} では 1.473（90％信頼区間：1.216－1.784），AUC(0-24h)では 1.667（90％信頼区間：1.335－2.080）であった．

97%以上の血清中 E2 は，血清蛋白である性ホルモン結合グロブリン（SHBG）及びアルブミンと結合していた．28 日目における非結合型 E2 は，日本人女性で 2.26%，白人女性で 2.74%で，$C_{max,fu}$ の幾何平均値は日本人女性で 0.89 pg/mL 及び白人女性で 0.73 pg/mL であった．また，$AUC(0\text{-}24h)_{fu}$ の幾何平均値は，日本人女性で 15.2 pg･h/mL 及び白人女性で 10.9 pg･h/mL であった．非結合型 E2 では，日本人女性と白人女性の差がわずかであったことから，幾何平均値の比（日本人／白人）が，$C_{max,fu}$ では 1.226（90%信頼区間：0.979－1.534），$AUC(0\text{-}24h)_{fu}$ では 1.388（90%信頼区間：1.084－1.777）にまで縮小した．しかし，これらの 90%信頼区間は，類似性を示す指標として目標設定していた範囲内（0.7－1.43）を超えていた．

蛋白結合や SHBG 濃度のような薬物動態的特性とともに，体重などの人口統計学的データを考慮した場合でも，日本人と白人の差の要因を完全に解明できなかった．E2 の代謝に関与する酵素で，日本人女性で血清濃度がより高かったことを説明できるような民族的な遺伝子多型を示すものは知られていない．E2 の $t_{1/2}$ 及び R_1 値に，日本人女性と白人女性の差は示されなかったことから，両民族群間に代謝及び排泄に差があるとは考え難い．白人女性の E2 の AUC(0-24h)が明らかに低値を示しており，本試験中における白人女性の平均値が，他のプロゲスチンとの組み合わせで過去に実施された試験結果を下回っていることは，特筆すべき点である．一方，本治験における日本人女性の E2 の AUC(0-24h)は，過去に実施した日本人対象の試験や，さらに白人女性を対象とした試験とほぼ同様の結果であった．さらに，白人女性の血清中 E2 濃度のばらつきは日本人女性よりも大きく，類似範囲内に収まる信頼区間を得ることはできなかった要因と考えられる．以上の結果から，日本人女性と白人女性との間に E2 の薬物動態に何らかの差があるとは考え難い．

表 2.7.6-2：日本人女性及び白人女性への SH T 594 B の単回投与後（1 日目）及び 28 日間反復投与後（28 日目）の E2，LNG の薬物動態パラメーター

	パラメーター	単位	日本人女性 (N＝28)	白人女性 (N＝29)
E2	**Day 1**			
	C_{max}	pg/mL	23.2 (40.2%)	16.4 (42.1%)
	t_{max}	h	6 (1 - 12)	6 (2 - 12)
	$t_{1/2}$	h	13.6 (18.8%) *	13.9 (27.0%) †
	AUC(0-24h)	pg･h/mL	386 (38.9%)	232 (45.2%)
	AUC	pg･h/mL	638 (36.9%) *	381 (34.9%) ‡
	$C_{max,\ fu}$	pg/mL	0.51 (38.3)	0.48 (45.9)
	$AUC(0-24h)_{fu}$	pg･h/mL	8.52 (36.0)	6.78 (52.6)
	Day 28			
	C_{max}	pg/mL	40.5 (37.1%)	27.5 (52.6%)
	t_{max}	h	4 (1.5 - 12)	3 (1 - 8)
	$t_{1/2}$	h	13.8 (19.6%) *	13.3 (33.5%) §
	AUC(0-24h)	pg･h/mL	688 (39.5%)	413 (64.9%)
	$C_{max,\ fu}$	pg/mL	0.89 (44.0%)	0.73 (62.8%)
	$AUC(0-24h)_{fu}$	pg･h/mL	15.2 (44.9%)	10.9 (73.7%)
	R_1		1.8 (20.5%)	1.8 (36.5%)
	Lin_{AUC}		1.1 (21.3%) *	1.1 (30.8%) ‡
LNG	**Day 1**			
	C_{max}	pg/mL	1233 (37.2%)	1057 (38.5%)
	t_{max}	h	1 (0.5 - 3)	1 (0.5 - 1.5)
	$t_{1/2}$	h	20.7 (38.2%) ‖	18.6 (77.5%) ¶
	AUC(0-24h)	pg･h/mL	7165 (40.4%)	5835 (52.9%)
	AUC	pg･h/mL	12437 (55.4%) ‖	12663 (89.0%) ¶
	$C_{max,\ fu}$	pg/mL	9.4 (38.6%)	10.6 (34.0%)
	$AUC(0-24h)_{fu}$	pg･h/mL	54.5 (34.8%)	58.7 (38.4%)
	Day 28			
	C_{max}	pg/mL	1492 (27.3%)	1421 (35.7%)
	t_{max}	h	1 (0.5 - 3)	1 (0.5 - 2)
	$t_{1/2}$	h	30.6 (16.0%) #	30.9 (24.0%) **
	AUC(0-24h)	pg･h/mL	13625 (29.7%)	12346 (44.2%)
	$C_{max,\ fu}$	pg/mL	13.8 (34.9%)	15.3 (21.7%)
	$AUC(0-24h)_{fu}$	pg･h/mL	126 (31.4%)	133 (30.1%)
	R_1		1.9 (28.7%)	2.1 (35.1%)
	Lin_{AUC}		1.1 (32.3%) ‖	1.1 (47.6%) ¶

*：n＝23，†：n＝15，‡：n＝13，§：n＝20，‖：n＝12，¶：n＝9，#：n＝25，**：n＝22，
N＝被験者総数（PP 解析集団），n＝計算に組み込まれた被験者数

C_{max}: 投与後の血清中最高濃度
t_{max}: 投与後の最高濃度到達時間
$t_{1/2}$: 最終消失相の最終半減期
AUC(0-24h): 投与 24 時間後までの濃度曲線下面積
AUC: 投与後から無限時間まで外挿された濃度－時間曲線下面積
$C_{max,\ fu}$: 非結合薬物の血清中最高濃度
$AUC(0-24h)_{fu}$: 投与から 24 時間後までの非結合薬物の濃度曲線下面積
R_1: 28 日目対 1 日目の濃度曲線下面積の累積係数（総 E2 と LNG について算出）
Lin_{AUC}: 28 日目 の AUC(0-24h)対単回投与後の AUC の線形指数

薬物動態パラメーターは，幾何平均及び括弧内の幾何変動係数で表す．t_{max} に関しては，中央値及び括弧内にデータ範囲を表示する．

反復投与後，血清中 LNG 濃度は約 7 日後に定常状態に達した．投与 28 日目において，血清中 LNG 濃度は投与後約 1 時間に C_{max} に達し，幾何平均値は日本人女性では 1492pg/mL，白人女性では 1421pg/mL であった．28 日目の AUC(0-24h)の幾何平均値は，日本人女性では 13625 pg·h/mL，白人女性では 12346pg·h/mL であり，両民族群間において LNG の薬物動態は類似していた．この結果から，C_{max} 及び AUC(0-24h)の統計学的に算出された幾何平均の比率（日本人／白人）は，C_{max} が 1.050（90%信頼区間：0.915－1.205），AUC(0-24h)が 1.104（90%信頼区間：0.939－1.297）であった．

LNG は E2 よりも強く SHBG に結合し，両民族群において LNG の血清中蛋白結合率は約 99%であった．28 日目の非結合 LNG 画分の算術平均は，日本人女性で 0.95%，白人女性で 1.10%であった．非結合型 LNG の C_{max} 及び AUC(0-24h)の幾何平均値は，日本人で 13.8pg/mL 及び 126pg·h/mL，白人で 15.3pg/mL 及び 133pg·h/mL であった．これらのパラメーターの幾何平均の比率（日本人／白人）は，C_{max} で 0.901（90%信頼区間：0.795－1.022），AUC(0-24h)で 0.948（90%信頼区間：0.829－1.082）であり，これらの結果は生物学的同等性の範囲内（0.8－1.25），類似と判断する目標範囲内（0.7－1.43）にあることが示された．総 LNG 並びに非結合型 LNG の結果より，日本人女性と白人女性の LNG の薬物動態に差は認められなかった．

安全性の成績：

全治験期間中，合計 124 件（日本人 77 件，白人 47 件）の有害事象が発現し，全被験者の発現率は 81.3%（52/64 例），日本人群で 93.8%（30/32 例），白人群で 68.8%（22/32 例)であった．日本人群に発現した主な有害事象は，腟出血 53.1%（17/32 例），次いで乳房腫脹 40.6%（13/32 例），白帯下 31.3%（10/32 例），乳頭痛 28.1%（9/32 例），乳房痛 9.4%（3/32 例），腹部膨満感 9.4%（3/32 例)であった．一方，白人群に発現した主な有害事象は，頭痛 34.4%（11/32 例），点状出血 15.6%（5/32 例），体重増加 15.6%（5/32 例），感冒（MedDRA 用語「感冒症候群」例)12.5%（4/32 例），乳房腫大感（MedDRA 用語「乳房腫大」）9.4%（3/32 例)であった．

両民族群間に，有害事象の発現率及び症状に差異が認められ，白人群（68.8%，22/32 例)よりも日本人群（93.8%，30/32 例)の方が，有害事象の報告が多かった．また，日本人群と白人群を比較した場合，日本人群には腟及び乳房の症状がより多く認められ，白人群には頭痛や体重増加がより多く認められた．

全治験期間中，重篤な有害事象あるいは入院の報告はなかった．発現した有害事象は，全て E2 及び LNG を含有するホルモン製剤に一般的な症状，あるいは軽微な症状であった．

有害事象と治験薬との関連性は，「関連なし(none)」，「関連ないらしい(unlikely)」，「多分関連あり(possible)」，「おそらく関連あり(probable)」，「明らかに関連あり(definite)」，に分類された．全治験期間中に 52 例の被験者に何らかの有害事象が発現し，このうち，87%（45/52 例）が治験薬との関連性が「多分関連あり」又は「おそらく関連あり」と判定された．同様に，何らかの有害事象が発現し，治験薬との関連性が「多分関連あり」又は「おそらく関連あり」と判定された割合は，日本人では 97%（29/30 例），白人では 73%（16/22 例）であった．なお，「明らかに関連あり」に分類された有害事象は点状出血のみであった（2 例，いずれも白人被験者）．

全治験期間中，重症度が高度の有害事象が計 2 例の白人被験者に認められた（1 例は感冒及び副鼻腔炎，もう 1 例は頭痛，悪心及び嘔吐）．その他の有害事象は，全て軽度あるいは中等度であった．

「回復中」又は「回復せず」に分類された有害事象は，体重増加（5 例），腋窩の圧痛（MedDRA 用語：「圧痛」1 例），白血球数減少（1 例）であった．これらの有害事象に対して，何ら処置は行われなかった．その他の有害事象は，全て治験期間中に回復した．

追跡調査では，治験責任医師の評価により 4 例の日本人被験者に報告された所見，白血球数低値（白血球数低下，1 例），トリグリセライド増加（2 例）及びトリグリセライド減少（1 例）を除き，いずれの臨床検査項目にスクリーニング値からの臨床上問題となる変動は認められなかった．これらの所見は，有害事象として報告された．

身体検査，婦人科検査及び心電図検査では，追跡調査での婦人科検査の所見において 4 所見（子宮頸部ポリープ 2 例，腋窩の圧痛 1 例，及び白帯下 1 例）が 3 例の日本人被験者に認められた以外は，臨床的に問題となるような所見はなかった．これらの所見は有害事象として報告された．両民族群に，バイタルサインに特記すべき所見は報告されなかった．

日本人及び白人の閉経後女性を対象に実施した試験において，重大ではない有害事象が報告されたのみで，SH T 594 B は良好な忍容性を示した．

結論：

SH T 594 B（1 錠中に E2 1.0mg 及び LNG 40μg を含有する錠剤）の 28 日間反復経口投与後の E2 濃度は，日本人女性と白人女性の民族間において，見かけ上の差が認められた．本治験における日本人のデータは，過去に実施された日本人の試験データ，白人女性の試験データともほぼ同様であったが，本治験の白人女性のデータのみが，過去の試験データと明らかに異なる結果であった．そのため，潜在的な民族間の差異を示す決定的な証拠とはならないと考えられる．したがって，2 つの集団に認められた E2 の見かけ上の差は，日本人女性と白人女性における E2 の薬物動態の差に起因するものとは考えにくく，民族間の類似性があるとの仮説を証明できなかったともいえない．これら結果は，本治験における特別な試験下での治験製剤（SH T 594 B）のみに適応されるものである．

本治験において，LNG の薬物動態は，日本人女性と白人女性の民族間で類似していることが示された．

本治験期間中，重篤な有害事象又は入院の報告はなかった．有害事象は，全て E2 及び LNG を含有するホルモン製剤に一般的に知られた重大ではない事象であった．

本治験の両民族群とも，重大ではない有害事象が報告されたのみで，SH T 594 B の良好な忍容性が認められた

2.7.6.3 有効性及び安全性試験報告書

2.7.6.3.1 申請する適応症に関する比較対照試験報告書

プラセボ対照試験

試験 No.300107/報告書 No.BC69

試験 No.300103/報告書 No.A23185

用量反応対照試験

試験 No.010646/報告書 No.B123

Nihon Schering K.K.

試験 No.300107/報告書 No.BC69

有効成分の名称：	エストラジオール（E2）	
治験の標題：	自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症状を有する患者を対象に連続 2 周期（8 週間）投与し，SH T 546（E2 のみを有効成分として含有する製剤）の至適用量を検討することを目的とした多施設共同，無作為化，二重盲検，プラセボ対照比較試験	
治験責任医師：	24 名（日本）	
実施医療機関：	24 施設（日本）	
公表文献：	なし	
治験期間（年）：	**開始日（最初の被験者が登録された日）：** 20■ 年 ■ 月 ■ 日 **終了日（最後の被験者が完了した日）：** 20■ 年 ■ 月 ■ 日	**治験の相：** II
目的：	自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落に伴うホットフラッシュの回数の減少に対する SH T 546 の至適用量を設定した.	
方法：	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験	
被験者数 （計画時，解析時）：	計画被験者数：195 例（各群 65 例），20■ 年 ■ 月 ■ 日付の治験実施計画書改訂時に 240 例（各群 80 例）より変更 解析被験者数：登録被験者数 211 例 （E2 0.5mg 群:72 例，E2 1.0mg 群:71 例，プラセボ群:68 例） 安全性解析集団：211 例 （E2 0.5mg 群:72 例，E2 1.0mg 群:71 例，プラセボ群:68 例） FAS 解析集団：211 例 （E2 0.5mg 群:72 例，E2 1.0mg 群:71 例，プラセボ群:68 例） Valid case 集団：206 例 （E2 0.5mg 群:69 例，E2 1.0mg 群:71 例，プラセボ群:66 例）	
診断及び主要な選択基準:	更年期障害及び卵巣欠落症状と診断された患者で，下記の条件をすべて満たすものを対象とする．なお，入院・外来の別は問わない．なお，患者は本治験に複数回組み入れられてはならない. 1）40 歳以上 65 歳未満の患者 2）以下のいずれかを満たす患者 ・最終月経後 1 年以上経過している患者 ・最終月経後 6 ヵ月以上 1 年未満の患者で，来院 1 に測定した血清中 E2 濃度が 20pg/mL（RIA 法）以下かつ FSH 濃度が 30mIU/mL（RIA 法）以上の患者 ・両側卵巣摘出後 1 ヶ月以上経過している患者 ・閉経前の子宮摘出により最終月経日不明の場合は来院 1 の血清中 E2 濃度が 20pg/mL（RIA 法）以下かつ FSH 濃度が 30mIU/mL（RIA 法）以上の患者 3）投与開始前 7 日間（欠測日を除く 7 日間）でホットフラッシュを 1 日平均 3 回以上有し，症状の程度が中等度以上の患者 4）同意書に署名（患者本人）している患者	
被験薬： **用量：** **投与方法：** **バッチ番号：**	SH T 546 TD：1 錠中に E2 0.5mg を含有する錠剤 SH T 546 KC：1 錠中に E2 1.0mg を含有する錠剤 E2 0.5mg 又は 1.0mg 含有する錠剤，1 日 1 回 1 錠 経口 SH T 546 TD： J* ，SH T 546 KC： F*	
投与期間：	8 週間（2 周期，各周期 28 日間）	
対照薬： **用量** **投与方法：** **バッチ番号：**	SH T 594 PC：プラセボ 有効成分を含有しない錠剤，1 日 1 回 1 錠 経口 **H***	
投与期間：	8 週間（2 周期，各周期 28 日間）	

評価基準：	
有効性：	主要変数：ホットフラッシュ回数の減少率 副次変数：ホットフラッシュの程度，発汗及び不眠の程度，腟乾燥感の有無
安全性：	有害事象，バイタルサイン，一般臨床検査，乳房検診，及び子宮内膜細胞診
薬物動態（適切な場合）：	該当なし
薬力学（適切な場合）：	該当なし
統計手法：	記述統計量，主要変数について有意水準5%でのt-検定（両側）による仮説検定，Holmの下降手順を用いた評価を行った．副次変数について有意水準5%でのWilcoxon検定及びFisherの正確検定及びのHolmの下降手順を用いた評価を行った．

要約・結論

有効性の成績：

本治験は，自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落に伴う症状であるホットフラッシュ回数の減少率により，8週間投与によるSH T 546（有効成分としてE2のみを含有）の至適用量を検討することを目的として実施された．

FAS解析集団での最終時におけるホットフラッシュ回数の平均減少率は，E2 0.5mg群で－79.58%，E2 1.0mg群で－82.49%であったのに対し，プラセボ群では－57.89%であった．両実薬群は，いずれもプラセボ群より統計学的に有意な有効性を示した（p＜0.001:各実薬群 vs プラセボ群）．最終時において，E2 0.5mg群とE2 1.0mg群との間に，ホットフラッシュ回数の平均減少率に統計学的に有意な差は認められなかった．全般的に，FAS解析集団に関する結果報告とvalid case（VC）解析集団に関する結果報告に差異はなかった．

また，本治験薬の更年期症状に対する効果を副次変数として評価を行った．実薬群は共に，ホットフラッシュの程度，発汗の程度及び腟乾燥感の有無の改善に，プラセボ群よりも統計学的に有意な有効性を示した．不眠症に関しては，プラセボ群と比較して，両実薬群に統計学的に有意な改善は認められなかった．いくつかの有効性変数に比較的高いプラセボ効果が認められたものの，全般的に，両実薬群の更年期症状に対する効果は，プラセボよりも明らかに高かった．副次変数の解析結果より，E2 1.0mg群のホットフラッシュ程度及び発汗の程度の改善効果がE2 0.5mg群よりも早い時期（治療開始後4週間）に現れ，改善効果がより優れていたことが示された．ホットフラッシュ及び発汗の程度を再分類化（「中等度未満」，「中等度以上」）し検討するため，追加解析が実施された．臨床的に問題となる「中等度以上」に着目すると，E2 1.0mg群がプラセボ群と比較してホットフラッシュの程度（p＜0.001）及び発汗の程度（p＜0.001）に統計学的に有意な有効性を示したのに対し，E2 0.5mg群はプラセボ群との間に有意な差は認められなかった．FAS解析集団に関する結果報告とVC解析集団に関する結果報告に全般的に差異はなかった．

E2 0.5mg及び1.0mgは，血管運動神経症状及び腟乾燥感に対して有効であると考えられる．ホットフラッシュの回数の減少率にE2 0.5mg投与とE2 1.0mg群との間に統計学的に有意な差は認められなかったが，血管運動神経症状の程度に対する効果がより早く，より優れた改善効果が認められたことにより，自然閉経後の更年期症状及び両側卵巣摘出後の卵巣欠落症状を有する閉経後女性患者への至適用量はE2 1.0mgであると結論した．

安全性の成績：

投与期間中に合計 108 例（全投与例の 51.2%）に 1 件以上の何らかの有害事象が認められた．その内訳は，プラセボ群 34 例（50.0%），E2 0.5mg 群 34 例（47.2%）及び E2 1.0mg 群 40 例（56.3%）であった．いずれの用量群間にも，統計学的に有意な差は認められなかった．投与期間中に合計 59 例（全投与例の 28.0%）に 1 件以上の副作用（治験薬との関連性が否定できない有害事象）が認められた．その内訳は，プラセボ群 15 例（22.1%），E2 0.5mg 群 18 例（25.0%）及び E2 1.0mg 群 26 例（36.6%）であった．いずれの用量群間にも，統計学的に有意な差は認められなかった．

本治験で報告された有害事象は，閉経後の被験者集団に発現することが予期されていたものであった．治験薬との関連性が否定できない有害事象の症状と頻度は，ホルモン補充療法（Hormone Replacement Therapy：HRT）製剤に予期されていたものであった．ほとんどの有害事象の重症度は軽度及び中等度と判定され，高度と判定された本治験薬との関連性が否定できない有害事象はなかった．治験薬との関連性が否定できない有害事象のうち，最も多く発現した事象は，腟分泌物であり，エストロゲン製剤によくみられる副作用である．有害事象によって治験薬の投与を中止した被験者はなかった．2 例の被験者（E2 0.5mg 群：1 例，E2 1.0mg 群：1 例）に重篤な有害事象が発現した．1 例は明らかに投与前に発症していたと思われる子宮内膜腺癌（第Ⅳb 期）及び頸部リンパ節（左）への転移であり，もう 1 例は胸椎黄色靭帯骨化症（下肢痛）であった．治験責任医師及び治験依頼者が治験薬との関連性が否定できないと判断した重篤な有害事象はなかった．

一般臨床検査項目（E2 と FSH を除く）に，投与開始前及び終了時で治験薬の影響を示唆するような結果は認められなかった．臨床検査異常所見の発現，特に脂質パラメーター（トリグリセライドを除く）は，閉経後被験者集団に予期されていた結果であった．トリグリセライドの平均値の減少は予想しない結果であったが，これは臨床的に好ましい変動であった．参考基準値からの個々の逸脱は，ほとんどが軽微であり，治験責任医師は臨床的に問題となる変動とは判断されなかった．治験責任医師及び治験依頼者が臨床的に問題となると判断した臨床検査異常変動には，治験薬の安全性に問題を示すものはなかった．臨床検査値に及ぼす本治験薬の影響は認められなかった．

バイタルサインの結果に，投与開始前及び終了後で本治験薬の影響を示唆する変動は認められなかった．乳房検査及び子宮内膜細胞診は，投与前後でほぼ同様の所見であった．全般的に，乳房検査及び子宮内膜細胞診の調査項目に，本治験薬の安全性に問題となる所見は認められなかった．

以上より，本治験薬の安全性に問題はなく，忍容性が良好であることを確認した．

薬物動態／薬力学の成績

該当なし

結論：

自然閉経後の更年期障害及び両側卵巣摘出後の卵巣欠落症状を有する閉経後女性を対象に 8 週間投与を行い，E2 単剤（SH T 546）の至適用量は 1.0mg と結論した．

試験 No.300103/報告書 No.A23185

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）
治験の標題:	多施設共同試験による自然閉経後又は両側卵巣摘出に伴う骨粗鬆症に対して無作為割付二重盲検法でプラセボを対照とし SH T 594（E2/LNG）又は SH T 546（E2）を 104 週間投与した場合の E2 の骨量増加に対する至適用量の検討
治験総括医師	-
治験責任医師:	治験責任医師及び治験分担医師 84 名，治験調整医師 7 名（日本）
実施医療機関:	24 施設（日本）
公表文献:	該当なし
治験期間（年）	**開始日（最初の被験者が登録された日）：** 20[redacted]年[redacted]月[redacted]日 **治験の相:**
	終了日（最後の被験者が完了した日）： 20[redacted]年[redacted]月[redacted]日 Ⅱ
目的:	自然閉経後又は両側卵巣摘出に伴う骨粗鬆症を対象とし，104 週間投与により無作為割付二重盲検法においてプラセボを対照とした 3 群間比較試験により，E2 の骨量増加に対する至適用量を検討した．ただし，プラセボの投与期間は最初の 52 週間とした．
方法:	投与 52 週後に DXA 法により測定された骨密度及び投与前値からの骨密度変化率をプラセボ投与群と比較した．投与群への割付は，子宮の有無によって別々に実施し，子宮を有する被験者には E2/LNG 配合錠を E2 用量別に割付け，子宮摘出歴のある被験者については E2 錠を E2 用量別に割付けた．
被験者数（計画時，解析時）：	計画被験者数：計 308 例 解析被験者数：計 309 例 安全性解析対象 309 例，最大解析対象（FAS）299 例，治験実施計画書適合対象（PPS）261 例
診断及び主要な選択基準:	自然閉経後又は両側卵巣摘出に伴う骨粗鬆症患者 下記の条件をすべて満たす骨粗鬆症患者を対象とする．入院・外来の別は問わない．なお，同一患者は本治験に複数回組み入れられてはならない． 1）45 歳以上 75 歳以下の患者 2）自然閉経後又は両側卵巣摘出後，1 年以上経過している患者 3）WHO ガイドライン（1998 年）の骨粗鬆症診断基準で腰椎骨塩量が若年成人平均値の-2.5SD 以下の患者 骨粗鬆症と診断される腰椎（L_{2-4}）骨塩量の基準値 DXA 機種 / QDR / DPX BMD（g/cm^2）/ 0.71 / 0.83 4）子宮を有する患者のうち，子宮内膜組織診において正常と診断された患者｛ただし，子宮内膜組織診断ができなかった場合（子宮内膜組織がないか組織が不十分なため診断ができない場合），又は子宮口狭窄により子宮内膜組織診が実施できない場合は，経腟超音波検査にて子宮内膜厚が 4mm 以下の患者｝ 5）同意書に署名している患者
被験薬:	SH T 594 D ：1 錠中に E2 0.5mg 及び LNG 40μg を含有する錠剤 SH T 546 TD：1 錠中に E2 0.5mg を含有する錠剤 SH T 594 B ：1 錠中に E2 1.0mg 及び LNG 40μg を含有する錠剤 SH T 546 KC：1 錠中に E2 1.0mg を含有する錠剤
用量:	[子宮を有する患者] E2 0.5mg/LNG 40μg 配合剤又は E2 1.0mg/LNG 40μg 配合剤，1 日 1 回 1 錠 [子宮摘出患者] E2 0.5mg 単剤又は E2 1.0mg 単剤，1 日 1 回 1 錠 基礎治療薬として，[redacted]®（カルシウム：500 mg、ビタミン D3：200IU 含有）を 1 日 1 回 1 錠，経口投与
投与方法:	経口
バッチ番号:	SH T 594 D ：[redacted]，[redacted] SH T 546 TD： F* ，[redacted] SH T 594 B ： I* ，[redacted] SH T 546 KC： H* ，[redacted]

投与期間:	104 週間
対照薬:	SH T 594 PB：E2/LNG 配合剤のプラセボ錠 SH T 594 PC：E2 単剤のプラセボ錠
用量:	[子宮を有する患者] E2/LNG 配合剤のプラセボ錠を 1 日 1 回 1 錠 52 週間投与後，E2 1.0mg/LNG 40μg 配合剤を 1 日 1 回 1 錠 52 週間投与 [子宮摘出患者] E2 単剤のプラセボ錠を 1 日 1 回 1 錠 52 週間投与後，E2 1.0mg 単剤を 1 日 1 回 1 錠 52 週間投与 基礎治療薬として，[redacted]®（カルシウム：500 mg、ビタミン D3：200IU 含有）を 1 日 1 回 1 錠，経口投与
投与方法:	経口
バッチ番号:	[redacted]， J*
投与期間:	104 週間
評価基準:	
有効性:	主要変数：52 週後の腰椎（L_{2-4}）骨密度の変化率，104 週間の腰椎（L_{2-4}）骨密度の変化率 副次変数：骨代謝マーカー（intact-OC，骨型 ALP，intact-PTH）変化率の推移，無出血（性器出血）率の推移，52 週後及び 104 週後における子宮内膜過形成発現率 その他の有効性の変数：52 週後及び 104 週後における骨折の有無
安全性:	有害事象，理学検査，婦人科検査，バイタルサイン，一般臨床検査（血液学的検査，血液生化学的検査，尿検査）
薬物動態（適切な場合）:	年齢の影響を検討するため，E2，E1，E1-硫酸抱合体，SHBG 及び LNG 濃度の測定を 60 週後及び 104 週後に行う
薬力学（適切な場合）:	該当なし
統計手法:	52 週後における腰椎（L_{2-4}）骨密度の変化率を主要変数とし，多重性を考慮した下降手順の方法を用い，LNG 配合の有無を層とした並び替え検定により，プラセボと E2 用量群の比較を行った．また，被験薬投与群の 104 週間の腰椎骨密度変化率の推移について経時的解析を行った．骨代謝マーカー変化率の推移及び無出血（性器出血なし）率の推移及び子宮内膜過形成発現率を副次変数とし，各評価に適した解析法により投与群間の比較を行った．

要約・結論

自然閉経後又は両側卵巣摘出に伴う骨粗鬆症患者 309 例を無作為に E2 用量別の 3 群，すなわち E2 0.5mg/LNG 40μg 群（73 例），E2 1.0mg/LNG 40μg 群（157 例），プラセボ群（79 例）に割り付けた．子宮摘出歴のある被験者には E2 単剤を投与した．なお，すべての被験者に基礎治療として[redacted]（カルシウム 500mg/日及びビタミン D_3 200IU/日）を投与した．

309 例の被験者（平均年齢 61 歳，46～75 歳）に治験薬を投与し，うち 241 例が治験を完了した．少なくとも 1 回以上治験薬を投与した 309 例を安全性評価対象とした

被験者の大部分（91.0%，272/299 例）は，自然閉経後の骨粗鬆症患者であった．299 例中 72 例（24.1%）が子宮摘出歴，57 例（19.1%）が卵巣摘出歴を有していた．閉経時期の回答が得られた 235 例の平均閉経年齢は 49 歳（36～59 歳）であり，平均閉経後年数は 12 年（1～31 年）であった．

1 年間あたりの平均治験薬投与日数は 1 年目で 332 日，2 年目で 343 日であった．すべての投与群において 95%以上の被験者が 95%以上の投与を遵守した．

有効性の結果:

主要評価変数は 52 週目の腰椎（L_{2-4}）骨密度変化率であった．BMD の測定は，特定の解析手順及び特定の測定機器を用い，DXA 法で行った．

主要な有効性解析の結果（FAS），腰椎（L_{2-4}）骨密度変化率は，プラセボ投与群に比べ E2 用量 1.0mg 群及び E2 用量 0.5mg 群で有意に高かった．（いずれも p＝0.000，並び替え検定）．E2 用量 1.0mg 群の平均腰椎骨密度の変化率は，E2 用量 0.5mg 群に比べ高かった．プラセボ投与群の腰椎骨密度に変化は認められなかった．

腰椎骨密度の平均変化率は，104 週間継続して増加し，104 週目に E2 用量 0.5mg 群で 8%，E2 用量 1.0mg 群で 10%となった．E2 用量 0.5mg 群及び E2 用量 1.0mg 群間の腰椎骨密度変化率の差は有意であった（p＝0.008，並び替え検定）．腰椎骨密度の平均変化率は 2 年後（104 週後）に比べ 1 年後（52 週後）で高かった．投与期間中，LNG 配合の有無にかかわらず，E2 用量 0.5mg 群に比べ E2 用量 1.0mg 群で高い腰椎骨密度変化率を示した．しかしながら，腰椎骨密度の経時推移を解析した結果，E2 用量による有意な差は認められなかった（p＝0.058）．LNG 併用の有無による有意差は認められなかった（p＝0.192）．PPS 解析対象集団の解析結果は FAS 解析対象集団での解析結果を裏付ける結果であり，LNG 併用の影響は認められなかった．閉経後 10 年未満又は 10 年以上の被験者でも同様に骨密度増加効果を示した．腰椎骨密度が YAM -2.5SD 以上に回復した被験者は，E2 用量 1.0mg 群では 28 週後で 44%，52 週後で 50%，104 週後で 60%，E2 用量 0.5mg 群では 28 週後で 35%，52 週後で 44%，104 週後で 50%であった．

骨代謝マーカーのうち，intact-OC，骨型 ALP 及びデオキシピリジノリン（deoxypyridinoline：DPD）は E2 投与後に減少し，その変化は骨密度の変化と一致していた．これらの骨代謝マーカーは骨粗鬆症の鑑別診断及び治療効果のモニタリングに有用であると考えられる．

E2 により誘発される子宮内膜増殖は，LNG の併用により効果的に抑制された．E2 1.0mg/LNG 40μg を 52 週間投与した 118 例の子宮内膜過形成発現率の点推定値は 0%（95%信頼区間 0.0－3.1）であった．

治験期間を通して，E2 の用量（0.5mg 又は 1.0mg）にかかわらず，LNG 40μg は E2 による子宮内膜過形成を効果的に抑制した．52 週後及び 104 週後に子宮内膜過形成及び子宮内膜癌は認められなかった．E2 用量（0.5mg 又は 1.0mg）及びプラセボの群間に，子宮内膜萎縮/不活性の発現率に明らかな差は認められなかった．子宮内膜厚は E2/LNG 配合剤投与後，わずかに増加した．出血パターンの解析の結果，E2 用量 1.0mg 群に比べ E2 用量 0.5mg 群は，より良好な出血プロファイルを示した．しかしながら，服薬遵守について E2 用量群間に差は認められなかった．104 週間で合計 6 例の被験者が新規骨折を経験した（プラセボ投与群 4 例，E2 用量 0.5mg 群 1 例，E2 用量 1.0mg 群 1 例）．

投与 52 週後の有効性の結果を表に示した．

表 2.7.6.3.1-1 投与 52 週後の有効性の結果

パラメーター（単位）		プラセボ	E2 用量 0.5 mg	E2 用量 1.0 mg
骨密度変化率（%）		0.11±4.52[69]	6.57 ±3.94[62]***	7.95±4.82[129]***
治癒率#		7/69 ； 10.1%	27/62 ； 43.5%	64/129 ； 49.6%
新規骨折		1/69; 1.4% (0.0-7.8)	0/62; 0% (0.0-5.8)	0/127; 0% (0.0-2.9)
骨代謝マーカー変化率	Intact-OC (ng/mL)	6.37 ± 35.54 [69]	-30.98 ± 22.52 [62]***	-39.53 ± 21.88 [129]***
	骨型 ALP (U/L)	-2.57 ± 28.33 [69]	-37.37 ± 19.62 [62]***	-42.07 ± 19.51 [129]***
	Intact-PTH (pg/mL)	6.22 ± 37.14 [68]	11.21 ± 42.58 [62] NS	13.28 ± 46.06 [129] NS
	NTx (nmol BCE/mmol CRE)	11.35 ± 59.44 [69]	-38.72 ± 39.99 [62] NS	-36.29 ± 50.70 [125]***
	DPD (pmol/μmol CRE)	11.63 ± 38.16 [69]	-12.96 ± 33.34 [62]***	-10.65 ± 45.68 [129]***
	尿中カルシウム (g/L)	18.77 ± 120.93 [68]	12.72 ± 105.85 [62] NS	0.68 ± 101.66 [129] NS
	尿中リン (g/L)	58.55 ± 168.51 [69]	44.73 ± 108.87 [62] NS	63.51 ± 198.68 [129] NS
無出血率 子宮内膜過形成又は癌 子宮内膜萎縮又は不活性		92.6(82.1-97.9) [54] 0/37; 0 (0.0-9.5) 34/37; 91.9 (78.1-98.3)	84.0(70.9-92.8) [50] 0/39; 0 (0.0-9.0) 34/39; 87.2 (72.6-95.7)	69.8(59.6-78.7) [96] 0/80; 0 (0.0-4.5) 81/75; 92.6 (84.6-97.2)

数値は平均±SD[被験者数]又は発現率%（95%信頼区間）[被験者数]を示す

***：P＝0.000，P 検定によるプラセボ投与群との比較

NS：P 検定によるプラセボ投与群との比較で有意差なし

#:骨密度が若年成人平均－2.5SD 以上に改善した被験者の割合

安全性の結果：

52 週後に 309 例中 249 例（80.6%）に計 796 件，104 週後に 309 例中 276 例（89.3%）に計 1332 件の有害事象が認められた．そのうち，309 例中 203 例（65.7%）に副作用が認められた．

1 年目の投与群別有害事象発現率は，E2 1.0mg/LNG 40μg 群 87.2%（102/117 例），E2 0.5mg 群 81.3%（13/16 例），プラセボ（E2）群 80.0%（16/20 例），プラセボ（E2/LNG）群 79.7%（47/59 例），E2 0.5mg/LNG 40μg 群 73.7%（42/57 例）及び E2 1.0mg 群 72.5%（29/40 例）であった．1 年目の投与群別副作用発現率は，E2 1.0mg/LNG 40μg 群 66.7%（78/119 例），E2 1.0mg 群 55.0%（22/40 例），E2 0.5mg/LNG 40μg 群 47.4%（22/57 例），E2 0.5mg 群 50.0%（8/16 例），プラセボ（E2/LNG）群 39.0%（23/59 例）及びプラセボ（E2）群 30.0%（6/20 例）であった．E2 単剤又は E2/LNG 配合剤の投与を受けた被験者に報告された有害事象及び副作用の大部分は 1 年目に発現した．有害事象発現頻度が最も高かった器官分類は「生殖系および乳房障害」（42.4%，131/309 例）であり，続いて「感染症および寄生虫症」（27.2%，84/309 例），「胃腸障害」（21.7%，67/309 例）であった．1 年目の主な有害事象は乳房不快感（16.5%，51/309 例）であり，続いて鼻咽頭炎（15.9%，49/309 例）であった．乳房不快感の発現率は，プラセボ群及び E2 用量 0.5mg 群に比べ E2 用量 1.0mg 群で高かったものの，鼻咽頭炎の発現率に用量依存性は認められなかった．性器出血及び乳房痛の発現率が E2 1.0mg 群に比べ E2 1.0mg/LNG 40μg 群で高かった点を除き，E2 単剤及び E2/LNG 配合剤の有害事象プロファイルは類似していた．合計で 25/309 例（8.1%）の被験者に重症度が「高度」と判定された有害事象が，77/309 例（24.9%）の被験者に治験薬との関連性が「明らかに関連あり」と判定された有害事象が報告された．

死亡例の報告はなかった．治験期間中，19 例の被験者に 22 件の重篤な有害事象が発現し，うち 14 例の被験者は治験を完了，5 例は治験薬の投与を中止した．重篤な有害事象を発現したすべての被験者は，入院し，治療された．19 例 22 件の重篤な有害事象のうち 13 例 16 件は E2 用量 1.0mg 群で発現した．治験薬との因果関係が否定されなかった重篤な有害事象が 4 例の被験者に認められた．治験期間中，乳癌，子宮頸部癌又は血栓は認められなかった．

全ての被験者のうち 39 例が有害事象により治験を中止した．治験中止に至った有害事象のうち頻度の高かったものは性器出血（15 例），胃に関連する症状（4 例）であった．性器出血により治験を中止した被験者の頻度は，プラセボ群及び E2 0.5mg/LNG 40μg 群に比べ E2 1.0mg/LNG 40μg 群に高かった．

治験期間を通して，臨床検査値の平均値に臨床的に問題となる変動は認められなかった．E2 用量間に顕著な差は認められなかった．脂質代謝パラメーターには，総コレステロール，LDL コレステロール，リポ蛋白(a)の減少等好ましい変化が認められた．動脈硬化指数は E2 単剤投与群で改善し，E2/LNG 配合剤群では変動しなかった．臨床検査値の異常変動を伴う有害事象により，2 例が治験を中止した．

治験期間中，E2/LNG 配合剤の投与を受けた被験者に子宮内膜癌又は子宮内膜過形成は報告されなかった．子宮内膜厚について臨床的に意義のある変動は認められなかった．

バイタルサイン，身体的所見又は婦人科検査に，臨床的に問題となる変動は認められなかった．

薬物動態測定の結果：

薬物動態のモニタリングを 90 例で計画し，E2 0.5mg/LNG 40μg 群 18 例，E2 0.5mg 群 4 例，E2 1.0mg/LNG 40μg 群 45 例，E2 1.0mg 群 15 例の計 82 例の被験者の解析結果を得た．

血清中 E2 濃度（トラフ濃度）の平均値は，E2 0.5mg/LNG 40μg 群で 14.0pg/mL（CV 値：57%，以下同様），E2 0.5mg 群 22.8pg/mL（44%），E2 1.0mg/LNG 40μg 群で 33.4pg/mL（61%），E2 1.0mg 群 33.5pg/mL（45%）であった．E2 用量 0.5mg 群では，血清中 E2 濃度は E2/LNG 配合剤の投与群に比べ E2 単剤投与群で高かった．一方，E2 用量 1.0mg 群では，血清中 E2 濃度は E2/LNG 配合剤の投与例と E2 単剤の投与例で近似した値であった．血清中 E2 濃度は E2 投与量に依存して増加した．血清中 SHBG 濃度は，E2 単剤の投与例と比べて E2/LNG 配合剤の投与例で約 2 倍の高値であった．血清中 LNG 濃度は E2 0.5mg/LNG 40μg と E2 1.0mg/LNG 40μg で近似した値であった．

年齢分布を考慮すると，E2 0.5mg/LNG 40μg 群での血清中 E2 平均濃度は年齢 65 歳未満層で 12.6pg/mL（CV：69%，n＝9），年齢 65 歳以上層で 15.5pg/mL（CV：44%，n＝9）であった．E2 1.0mg/LNG 40μg 群での血清中 E2 平均濃度は年齢 65 歳未満層で 34.7pg/mL（CV：56%，n＝32），年齢 65 歳以上層で 30.4pg/mL（CV：75%，n＝13）であった．E2 1.0mg 群での血清中平均 E2 濃度は年齢 65 歳未満層で 28.7pg/mL（CV：45%，n＝7），年齢 65 歳以上層で 38.3pg/mL（CV：42%，n＝8）であった．同様の傾向が血清中 E1 及び E1 硫酸抱合体でも観察されたことより，血清中 E2，E1 及び E1 硫酸抱合体濃度に加齢に関連する明らかな傾向はないことが示唆された．それぞれの投与群での血清中 E2，E1，E1 硫酸抱合体及び LNG 濃度への年齢による影響を ANCOVA を用いて統計解析した結果，年齢依存性は示唆されなかった．

血清中 SHBG 濃度については明らかな結果は得られなかった．血清中 SHBG 濃度に対する E2 及び LNG の影響は年齢による影響より強いと考えられる．したがって，得られた結果から血清中 SHBG 濃度に対する年齢依存性の影響について結論を導くことはできない．

結論：

本試験により，E2 単剤及び E2/LNG 配合剤が骨粗鬆症を有する女性の骨密度増加に極めて有効であることが示された．有効性は E2 用量 0.5mg に比べ E2 用量 1.0mg で高かった．投与 6 ヶ月後に顕

著な骨密度増加効果が認められ，その効果は 2 年間持続した．骨に対する E2 の効果に LNG の併用の影響は認められなかった．

E2 単剤及び E2/LNG 配合剤は 0.5mg 及び 1.0mg の E2 用量で同様に良好な忍容性を示した．2 年間の E2 による治療を妨げるような安全性の問題点は，E2 の用量にかかわらず認められなかった．両 E2 用量において，LNG の併用は子宮内膜過形成の抑制に有効であった．

E2 用量 0.5mg 群に比べ E2 用量 1.0mg 群で投与 2 年後の骨密度増加効果が有意に高く，治癒率（腰椎骨密度が YAM -2.5SD 以上に回復した被験者の割合）も高かったこと，E2 用量 1.0mg 群において 2 年間投与した際に良好な安全性及び忍容性が確認されたことから，日本人骨粗鬆症患者に対する E2 の至適用量は 1.0mg であると結論した．

Nihon Schering K.K.

試験 No.010646/報告書 No.B123

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題:	前期第Ⅱ相試験（step１） ［更年期障害，卵巣欠落症状］	
治験総括医師	[redacted]	
治験責任医師:	[redacted]，他 計 33 名（日本）	
実施医療機関:	[redacted]，他 計 33 施設（日本）	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：** 19[redacted] 年 [redacted] 月 [redacted] 日	**治験の相:** Ⅱ
目的:	自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症状に対する SH T 546 の有効性並びに安全性について，E2 用量を探索的に検討した．	
方法:	3 用量群の群間比較試験（封筒法無作為割付，多施設共同研究） 被験薬を毎日一定時刻に定められた順に従い，28 日間を 1 周期として連続 8 週間（2 周期）服薬した．自覚症状，理学検査，血中ホルモン濃度，一般臨床検査，婦人科検査，出血状況，随伴症状・副作用等を観察，調査し，総合評価を行った．	
被験者数 **（計画時，解析時）：**	計画被験者数：計 90 例（各群 30 例） 解析被験者数：計 78 例（登録被験者数：88 例） 全般改善度対象被験者数：72 例 有用度対象被験者数　　：72 例 概括安全度対象被験者数：77 例	
診断及び主要な選択基準:	自然閉経後の更年期障害及び両側卵巣摘出により卵巣欠落症状を示す患者． なお，入院・外来の別は問わなかった． 1）最終月経後 1 年以上または両側卵巣摘出後 3 ヶ月以上の患者 2）下記症状が少なくとも 1 つあり，症状の程度が中等度以上の患者 a）ホットフラッシュ，b）発汗，c）腟萎縮症状（性交障害，乾燥感，腟炎など） 3）20～65 歳未満の患者	
被験薬:	SH T 546 TA　　：1 錠中に E2 0.5mg を含有する錠剤 SH T 546 KB　　：1 錠中に E2 1.0mg を含有する錠剤 SH T 546 LA　　：1 錠中に E2 2.0mg を含有する錠剤 SH T 594 FA　　：1 錠中に LNG 40μg を含有する錠剤	
用量:	E2 0.5mg 群：E2 0.5mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠 E2 1.0mg 群：E2 1.0mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠 E2 2.0mg 群：E2 2.0mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠	
投与方法:	E2 錠を 1 日 1 回 1 錠，毎日一定時刻に定められた順に従い，28 日間を 1 周期として連続 2 周期（8 週間）服薬を続けた．子宮内膜の増殖を抑制するために，各周期の 17 日目から 28 日目までの 12 日間は，LNG 錠を 1 日 1 回 1 錠，同時に服用した（E2 錠及び LNG 錠を 1 錠ずつ計 2 錠を同時に服用する）．ただし，子宮摘出例には LNG 錠を併用しなかった．	
バッチ番号:	SH T 546 TA　　：V* SH T 546 KB　　：R* SH T 546 LA　　：[redacted] SH T 594 FA　　：P*	
投与期間:	8 週間（28 日間を 1 周期として 2 周期）	
対照薬:	該当なし	

＊新薬承認情報提供時に置き換え

評価基準:	
有効性:	・全般改善度 ホットフラッシュ，発汗，腟萎縮症状に対する効果を主に，その他の症状に対する効果も考慮し，投与第 8 週（あるいは投与中止時）に 6 段階で判定した.
安全性:	・概括安全度 副作用の有無，症状，程度，処置，薬剤との関連性及び臨床検査成績を総合し，投与第 8 週（あるいは投与中止時）に 5 段階で判定した.
その他:	・有用度 全般改善度及び概括安全度を総合し，投与 8 週（あるいは投与中止時）に 6 段階で判定した.
薬物動態（適切な場合）:	該当なし
薬力学（適切な場合）:	該当なし
統計手法:	本試験は，前期第Ⅱ相試験であるためデータの解析は探索的に実施した. （検定の有意水準：背景因子の検定-両側 15%，Jonckheere 検定及び Dunnett 検定-片側 5%，その他の検定-両側 5%） 1）背景因子 Fisher 検定，Kruskal- Wallis 検定 2）有効性 ・全般改善度 Jonckheere 検定，Steel 検定，層別解析，薬剤（E2）・E1 濃度を共変量とした共分散分析 ・ホットフラッシュ回数 一元配置分散分析，Dunnett 検定，経時型分散分析 ・自覚症状 Kruskal-Wallis 検定，Steel-Dwass 検定，一元配置分散分析，Tukey 検定 ・血中ホルモン濃度，腟内細胞塗沫検査 t 検定，Tukey 検定 3）安全性 ・概括安全度，随伴症状，出血状況 Kruskal-Wallis 検定，Steel-Dwass 検定 ・概括安全度 薬剤（E2）・E1 濃度を共変量とした共分散分析 ・一般臨床検査，理学検査 t 検定，Tukey 検定 ・子宮細胞診 Kruskal-Wallis 検定，Tukey 検定 4）有用性 Kruskal-Wallis 検定，Steel-Dwass 検定，薬剤（E2）・E1 濃度を共変量とした共分散分析

要約・結論

主要評価項目の全般改善度では，有効（「中等度改善」以上）率が E2 用量 0.5mg 群 82.6%（19/23 例），E2 用量 1.0mg 群 91.7%（22/24 例），E2 用量 2.0mg 群 96.0%（24/25 例）であった. 副作用発現率は E2 用量 0.5mg 群 12.0%（3/25 例），E2 用量 1.0mg 群 8.0%（2/25 例），E2 用量 2.0mg 群 33.3%（9/27 例）であった. 副作用症状は乳房痛，乳房緊満感，下腹部膨満感，胃部不快感，湿疹などであり，臨床検査値異常は GOT，GPT，γ-GTP，ALP，フィブリノーゲン，血小板数，白血球数，白血球分画などに認められたが，重篤なものはなかった. 特に E2 用量 2.0mg 群でエストロゲン製剤に報告されている副作用が多く認められる傾向があった. 有用性では，有用（「有用」以上）率が E2 用量 0.5mg 群 82.6%（19/23 例），E2 用量 1.0mg 群 91.7%（22/24 例），E2 用量 2.0mg 群 88.0%（22/25 例）であった.

一方，E2 の血中濃度は用量依存的に増加し，投与 4 週及び 8 週後の血中濃度は E2 用量 0.5mg 群でそれぞれ 16.15±13.65pg/mL（平均±SD），26.86±23.66pg/mL，E2 用量 1.0mg 群で 41.85±25.87pg/mL，58.64±12.26pg/mL，E2 用量 2.0mg 群では 90.00±57.51pg/mL，87.16±49.00pg/mL まで増加した．E2 用量 1.0mg 群と E2 用量 2.0mg 群では更年期障害治療における E2 の有効血中濃度とされている閉経前女性の卵胞期初期濃度に達していた．E2 用量 0.5mg 群び E2 用量 1.0mg 群において有効性，安全性が確認され，また血中濃度の結果から本剤の E2 至適投与量は 0.5mg から 1.0mg と推定された．

LNG 40μg を併用し 28 日間以上服薬した被験者のうち，E2 用量 0.5mg 群 78.6%（11/14 例），E2 用量 1.0mg 群 86.7%（13/15 例）及び E2 用量 2.0mg 群 85.7%（12/14 例）の計 83.7%（36/43 例）に消退出血が認められた．投与後の子宮内膜，子宮頸部（腟部）細胞診で「問題あり」と判断された被験者は 3 例（E2 用量 1.0mg 群 2 例，E2 用量 2.0mg 群 1 例）であり，1 例（E2 用量 1.0mg 群）は投与前より疑陽性と判定され，他の 2 例は追跡調査で問題なしと判定された．以上のことから LNG 40μg の周期的投与は，周期的出血をもたらし子宮内膜の肥厚に対し有効であると推定された．

2.7.6.3.2 その他の臨床試験報告書

E2 投与中の LNG の子宮内膜保護効果［周期的投与法］

試験 No. 10730/報告書 No. A02614

試験 No. 10731/報告書 No. A02103

退行期骨粗鬆症患者及び卵巣機能欠落に伴う骨量減少例験に対する効果

試験 No. 010568/報告書 No. B006

【海外臨床試験】

自然閉経後の更年期障害・両側卵巣摘出による卵巣欠落症状に対する効果

試験 No. ■216/報告書 No. A00403

試験 No. ■216/報告書 No. A06276

試験 No. ■065/報告書 No. A00404

試験 No.010730/報告書 No.A02614

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題:	SH T 546 前期第Ⅱ相臨床試験（Step2）　［持続的投与方法］	
治験総括医師	[redacted]	
治験責任医師:	[redacted]，他 105 名（日本）	
治験実施施設:	[redacted]，他 105 施設（日本）	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：** 19[redacted] 年 [redacted] 月 [redacted] 日	**治験の相:** Ⅱ
目的:	自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症状を対象に，SH T 546 を持続的投与した場合の有効性，安全性並びに LNG の子宮内膜に対する至適用量を二重盲検群間比較試験により検討した.	
方法:	文書にて同意が得られかつ選択基準，除外基準を満たした被験者を，盲検下で 3 用量群（LNG 10μg 群：E2 1.0mg/LNG 10μg，LNG 20μg 群：E2 1.0mg/LNG 20μg，LNG 40μg 群：E2 1.0mg/LNG 40μg）に無作為に割り付けた．1 日 1 回各 1 錠（合計 2 錠）を，28 日間を 1 周期として連続 6 周期（24 週間）服薬させた．観察・評価項目として，子宮内膜組織診，出血状況，自覚症状，理学検査，血中ホルモン検査，一般臨床検査，婦人科検査，有害事象・副作用調査等を実施した.	
被験者数（計画時，解析時）：	計画被験者数：計 261 例（各群 87 例），240 例（各群 80 例）より変更 解析被験者数：計 254 例　（登録被験者数：268 例，除外被験者数：14 例） LNG 10μg 群：83 例 組織診解析対象被験者数　：49 例 出血解析対象被験者数　：78 例 改善度解析対象被験者数　：71 例 安全度解析対象被験者数　：83 例 有用度解析対象被験者数　：71 例 LNG 20μg 群：83 例 組織診解析対象被験者数　：48 例 出血解析対象被験者数　：82 例 改善度解析対象被験者数　：78 例 安全度解析対象被験者数　：83 例 有用度解析対象被験者数　：78 例 LNG 40μg 群：88 例 組織診解析対象被験者数　：51 例 出血解析対象被験者数　：81 例 改善度解析対象被験者数　：75 例 安全度解析対象被験者数　：88 例 有用度解析対象被験者数　：75 例	
診断及び主要な選択基準:	診断名：自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症状. 主要な選択基準：下記の条件を満たす患者．入院・外来の別は問わない. 1）子宮を有する患者 2）更年期障害の場合， 最終月経後 1 年以上経過している患者，又は 最終月経後 6 ヶ月以上経過し，血漿中 E2 濃度≦20pg/mL かつ血漿中 FSH 濃度≧30mIU/ml 以上の患者 両側卵巣摘出例の場合，卵巣摘出後 3 ヶ月以上の患者 3）少なくともホットフラッシュ，発汗，腟萎縮症状のうち 1 つ以上を有する患者 4）治験薬投与前 3 ヶ月以内に，子宮内膜及び子宮頸部（もしくは腟部）細胞診において，クラスⅠまたはクラスⅡと判定された患者 5）20 歳以上，65 歳未満の患者	

被験薬:	SH T 546 KB : 1 錠中に E2 1.0mg を含有する錠剤 SH T 594 H : 1 錠中に LNG10μg を含有する錠剤 SH T 594 I : 1 錠中に LNG20μg を含有する錠剤 SH T 594 FA : 1 錠中に LNG40μg を含有する錠剤
用量:	LNG10μg 群（10μg 群）：E2 1.0mg/LNG10μg LNG20μg 群（20μg 群）：E2 1.0mg/LNG20μg LNG40μg 群（40μg 群）：E2 1.0mg/LNG40μg
投与法:	1 日 1 回 E2 錠と LNG 錠（合計 2 錠）を，28 日間を 1 周期として連続 6 周期（24 週間）経口投与.
バッチ番号:	SH T 546 KB : S* SH T 594 H : [redacted] SH T 594 I : [redacted] SH T 594 FA : [redacted]
投与期間:	24 週間（6 周期）
対照薬:	該当なし
評価基準:	
有効性:	主要変数：最終観察日の子宮内膜組織診所見より算出された無効率（「増殖期」及び「過形成」の被験者を「無効」とし，無効例を各薬剤群の採用例で割った割合） 副次変数：性器出血状況，脂質系臨床検査値，症状別改善度（ホットフラッシュ回数・程度，発汗，腟萎縮症状），経腟超音波検査
安全性:	有害事象，副作用，一般臨床検査，理学検査，婦人科検査（子宮細胞診，乳房検査）
薬物動態（適切な場合）:	該当なし
薬力学（適切な場合）:	該当なし
統計手法:	主要変数及び副次変数は薬剤群毎に頻度分布を示し，95%信頼区間を Fisher の直接確率法で算出した．Steel 検定（LNG10μg 群を基準とした片側検定，有意水準は両側 5%）あるいは Dunnett 検定（LNG10μg 群を基準とした片側検定，有意水準は両側 5%）を用いて薬剤群間比較を行い優越性を検討した.

要約・結論

有効性の結果:

子宮内膜組織所見（主要変数解析被験者数 148 例）より算出された無効率は，LNG 10μg 群で 46.9%，LNG 20μg 群で 37.5%，LNG 40μg 群で 35.3%であり，有意な差は認められなかったが，用量の増加に伴い減少した．プロゲストゲンの持続的投与法の特徴は，子宮内膜を萎縮させることにより，エストロゲン投与による子宮内膜の増殖を抑制し，子宮内膜癌のリスクを下げることである．そのため，LNG の持続投与法も，子宮内膜萎縮率の差が抑制効果の判定基準として重要であると判断した．そこで萎縮率（萎縮内膜と評価された被験者を各薬剤群の採用例で割った割合）を検討した結果，LNG 10μg 群で 34.7%，LNG 20μg 群で 47.9%，LNG 40μg 群で 54.9%であった．LNG 40μg 群の萎縮率は LNG 10μg 群に対して有意な増加が認められた（p＝0.040）．無効率及び萎縮率から LNG 40μg は子宮内膜増殖作用を最も抑制することが明らかになった.

性器出血解析対象被験者 241 例において，各周期の性器出血発現率，性器出血発現パターンを点状出血及び破綻出血に区別し検討した．第 6 周期における性器出血発現率は LNG 10μg 群で 46.9%，LNG 20μg 群で 55.9%，LNG 40μg 群で 33.3%であり，最もコンプライアンスに影響する破綻出血発現率は，第 6 周期において LNG 10μg 群で 17.2%，LNG 20μg 群で 27.1%，LNG 40μg 群で 10.5%であったことから，性器出血において LNG40μg が最も好ましいと考えられた.

＊新薬承認情報提供時に置き換え

脂質代謝に及ぼす影響を検討したところ，総コレステロール及び LDL コレステロールは各群において有意な低下が認められた．トリグリセライドにおいては LNG 20μg 及び LNG 40μg 群で有意な低下が認められた．一方，HDL コレステロールでは，投与 24 週後において LNG 10μg 群で 5.2%の上昇，LNG 20μg 群で 2.6%の低下，LNG 40μg 群では 7.5%の有意な低下が認められ，LNG 10μg 群との群間比較においては LNG 20μg 及び LNG 40μg 群で有意な差が認められた．一方，総コレステロール／HDL コレステロール比は各群で低下が認められた．LDL コレステロール／HDL コレステロール比は LNG 10，20μg 群では有意な低下が認められたが，LNG 40μg 群ではわずかな低下であった．

更年期症状別改善度（ホットフラッシュ，発汗，膣萎縮症状），全般改善度及び有用度では，薬剤群間に有意差は認められなかった．

安全性の結果:

治験薬との関連性が否定できなかった主な有害事象（副作用）（5%以上の発現率）は，乳房不快感，性器分泌物，腹部膨満，乳房痛が認められた．これらは性ステロイドホルモンの投与の際に一般的にみられる症状であり，いずれも高度なものではなく，薬剤等による処置を行うことなく自然に消失した．

死亡例として，自殺企図が 1 例（LNG 10μg 群），死亡以外の重篤な有害事象として，十二指腸潰瘍のため入院した被験者が 1 例（LNG 20μg 群）認められた．

3 用量間で有害事象，副作用の発現率及び概括安全度に有意な差は認められなかった．

結論:

LNG 40μg は安全性にも問題なく，子宮内膜増殖作用及び性器出血を最も抑制し，E2 1.0mg の更年期症状に対する有効性に影響を及ぼさないことが明らかになった．脂質代謝への影響を考慮すると，E2 1.0mg とプロゲストゲン持続的投与法に用いる配合製剤の LNG の至適配合量は 40μg と結論した．

Nihon Schering K.K.

試験 No.010731/報告書 No.A02103

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）
治験の標題:	前期第Ⅱ相試験 （step2） ［周期的投与方法］
治験総括医師	[redacted]
治験責任医師:	[redacted]，他 計 74 名（日本）
実施医療機関:	[redacted]，他 計 74 施設（日本）
公表文献:	該当なし
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **治験の相:** Ⅱ
目的:	自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症を対象に周期的投与した場合の有効性，安全性並びに LNG の子宮内膜に対する至適用量を二重盲検群間比較試験により検討した．
方法:	3 用量の二重盲検群間比較試験（多施設共同研究）
被験者数 （計画時，解析時）：	計画被験者数：計 150 例（各群 50 例） 解析被験者数：（登録被験者数 159 例） 主要変数解析対象被験者数 75 例 （LNG 20μg 群：23 例，LNG 40μg 群：25 例，LNG 80μg 群：27 例）
診断及び主要な選択基準:	自然閉経後の更年期障害及び両側卵巣摘出により卵巣欠落症状を示す患者． 1）子宮を有する患者 2）下記のいずれか条件を満たす患者 （1）最終月経後 1 年以上経過している （2）最終月経後 6 ヶ月以上経過し，血漿中 E2 濃度≦20pg/mL，血漿中 FSH 濃度≧30mIU/mL である （3）卵巣摘出後 3 ヶ月以上経過している患者 3）ホットフラッシュ，発汗，膣萎縮症状（性交障害，乾燥感，膣炎等）のいずれか 1 つ以上を有する患者 4）投与開始前 3 ヶ月以内（前治療薬にエストロゲン剤が投与されていた場合は wash out 中または wash out 後）の子宮内膜細胞診，子宮頸部（膣部）細胞診でクラスⅠまたはⅡと判定されている患者 5）20 歳以上 65 歳未満である患者
被験薬:	SH T 546 KB ：1 錠中に E2 1.0mg を含有する錠剤 SH T 594 I ：1 錠中に LNG 20μg を含有する錠剤 SH T 594 FA ：1 錠中に LNG 40μg を含有する錠剤 SH T 594 GA ：1 錠中に LNG 80μg を含有する錠剤
用量:	LNG 20μg 群：E2 1.0mg 錠＋LNG 20μg 錠(各周期 17-28 日)，1 日 1 回各 1 錠 LNG 40μg 群：E2 1.0mg 錠＋LNG 40μg 錠(各周期 17-28 日)，1 日 1 回各 1 錠 LNG 80μg 群：E2 1.0mg 錠＋LNG 80μg 錠(各周期 17-28 日)，1 日 1 回各 1 錠
投与方法:	E2 錠を 1 日 1 回 1 錠，原則的に朝食後，定められた順に従い，28 日間を 1 周期として連続 4 周期（16 週間）服薬した．各周期の 17 日目から 28 日目までの 12 日間は，E2 錠 1 錠と同時に LNG 錠を 1 日 1 回 1 錠服薬した．
バッチ番号:	SH T 546 KB ：S* SH T 594 I ：[redacted] SH T 594 FA ：[redacted] SH T 594 GA ：[redacted]
投与期間:	16 週間（28 日間を 1 周期として 4 周期）
対照薬:	該当なし

＊新薬承認情報提供時に置き換え

評価基準:	
有効性:	主要変数：子宮内膜組織診所見より算出した無効率 副次変数：出血状況，脂質系検査値，症状別改善度
安全性:	有害事象，副作用，一般臨床検査（血液学的検査，血液生化学的検査，尿検査），理学検査（血圧，脈拍，体重），婦人科検査（子宮内膜細胞診，子宮頸部〔腟部〕細胞診）
その他	全般改善度，概括安全度，有用度
薬物動態（適切な場合）:	該当なし
薬力学（適切な場合）:	該当なし
統計手法:	主要変数及び副次変数は薬剤群毎に頻度分布を示し，95%信頼区間を Fisher の直接確率法で算出した．Steel 検定（LNG 20μg 群を基準とした片側検定，有意水準は 5%）あるいは Dunnett 検定（LNG 20μg 群を基準とした片側検定，有意水準は 5%）を用いて薬剤群間の比較を行い優越性を検討した．

要約・結論

有効性の結果:

子宮内膜組織診所見（主要変数解析被験者数 75 例）より算出した無効率（増殖期または過形成と判定され，LNG の配合効果が無効であった被験者を，各薬剤群の採用例で割った割合）は LNG 20μg 群 43.5%（10/23 例），LNG 40μg 群 16.0%（4/25 例），LNG 80μg 群 7.4%（2/27 例）と用量依存的に減少し，LNG 40μg 群及び LNG 80μg 群の無効率は LNG 20μg 群を有意に下回った（LNG 20μg 群 対 LNG 40μg 群 p＝0.035，LNG 20μg 群 対 LNG 80μg 群 p＝0.003）．消退出血，点状出血及び破綻出血に区別した各周期での出血発現パターンは，LNG 20μg 群より優れている傾向が LNG 40μg 群及び LNG 80μg 群に認められた．症状別改善度（ホットフラッシュ，発汗，腟萎縮症状），全般改善度，概括安全度，有用度及び副作用発現率では，薬剤群間の有意差は認められなかった．血中 E2 濃度に薬剤群間の有意差は認められず，投与終了時には閉経前女性の卵胞期初期濃度に達していた．脂質系臨床検査値の総コレステロール，LDL コレステロールが各薬剤群とも投与 16 週後に低下し，HDL コレステロールは LNG 20μg 群と比較して LNG 80μg 群に有意な低下が認められた（LNG 20μg 群 対 LNG 80μg 群 p＝0.001）．

安全性の結果:

有害事象，副作用及び理学検査値，臨床検査値の異常変動の発現率に薬剤群間の有意差は認められなかった．臨床検査値の異常変動と判定された項目も治験薬との因果関係は否定された．

結論:

E2 1.0mg の子宮内膜増殖作用に対して LNG は用量依存的な抑制作用を示し，必要な配合量は 40μg 以上と推定された．また，LNG 20μg から 80μg の併用投与は，E2 1.0mg の更年期症状に対する有効性に影響を与えないと判断された．しかし，LNG 80μg 群では LNG 20μg 群と比較し HDL コレステロールの有意な低下が認められた（LNG 20μg 群 対 LNG 80μg 群 p＝0.001）．一般的に HDL コレステロールは抗動脈硬化作用を有し，E2 により上昇することが知られている．LNG 80μg の脂質代謝に及ぼす影響を考慮し，E2 1.0mg に対する LNG の至適配合量は 40μg と示唆された．

試験 No.010568/報告書 No.B006

有効成分の名称:	エストラジオール（E2）/ レボノルゲストレル（LNG）	
治験の標題:	前期第Ⅱ相試験（step1） ［退行期骨粗鬆症，卵巣機能欠落に伴う骨量減少例］	
治験総括医師	[redacted]	
治験責任医師:	[redacted]，他 計 33 名（日本）	
実施医療機関:	[redacted]，他 計 33 施設（日本）	
公表文献:	該当なし	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：** 19[redacted] 年 [redacted] 月 [redacted] 日	**治験の相:** Ⅱ
目的:	女性の退行期骨粗鬆症患者及び卵巣機能欠落に伴う骨量減少例に対する有効性と安全性及び E2 の概略の至適用量を探索的に検討した．	
方法:	封筒法（非盲検）により，被験者を子宮の有無に関わらず E2 用量別（0.5mg，1.0mg，2.0mg 又はプラセボ）に割付けた．治験薬を処方する際，子宮を有する被験者には割付けた E2 錠と LNG 錠（又はプラセボ）を併用投与，子宮摘出歴のある被験者には割付けた E2 錠（又はプラセボ）のみを単独投与することとした． E2 0.5mg，1.0mg，2.0mg 又はプラセボ錠を 1 日 1 回 1 錠，毎朝一定の時刻に定められた順に従い，28 日間を 1 周期として連続 24 週間（6 周期）投薬した． 子宮内膜の肥厚を回避するために，各周期の 17 日目から 28 日目までの 12 日間は，LNG40μg 又はプラセボ錠を 1 日 1 回 1 錠，同時に服用した（E2 錠及び LNG 錠を 1 錠ずつ計 2 錠を同時に服用した．）．ただし，子宮摘出例には LNG 錠を服用しないこととした． 基礎治療薬として乳酸カルシウム 0.8g を 1 日 1 回 1 包，毎日夕食後に服薬した．腰背痛，骨所見，骨代謝に関する生化学的検査，血清ホルモン検査，一般臨床検査，婦人科検査，出血状況，副作用及び随伴症状等を観察，調査し，総合評価を行った．	
被験者数 （計画時，解析時）：	計画被験者数：計 100 例（各群 25 例） 解析被験者数：（登録被験者数：103 例） 骨密度採用被験者数：60 例 疼痛全般改善度採用被験者数：74 例 安全性採用被験者数：100 例	
診断及び主要な選択基準:	女性の退行期骨粗鬆症患者 1）退行期骨粗鬆症の診断基準（厚生省長寿科学研究骨粗鬆症班，1993 年）において，スコアが 4 点（ほぼ確実）以上の患者 2）年齢は 65 歳未満の患者 3）入院・外来の別は問わなかった 卵巣機能欠落に伴う骨量減少例 1）DXA 法による腰椎（L_{2-4}）の骨密度（bone mineral density：BMD）が，Peak Bone Mass より 20%以上減少している患者 2）自然閉経後 10 年未満あるいは卵巣摘出後 10 年未満の患者 3）入院・外来の別は問わなかった	

被験薬:	SH T 546 TA：1 錠中に E2 0.5mg を含有する錠剤 SH T 546 KB：1 錠中に E2 1.0mg を含有する錠剤 SH T 546 LA：1 錠中に E2 2.0mg を含有する錠剤 SH T 594 FA：1 錠中に LNG 40μg を含有する錠剤
用量:	[子宮を有する患者] E2 用量 0.5mg 群：E2 0.5mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠 E2 用量 1.0mg 群：E2 1.0mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠 E2 用量 2.0mg 群：E2 2.0mg 錠＋LNG 40μg 錠（各周期 17-28 日），1 日 1 回各 1 錠 [子宮摘出患者] E2 用量 0.5mg 群：E2 0.5 mg 錠，1 日 1 回 1 錠 E2 用量 1.0mg 群：E2 1.0 mg 錠，1 日 1 回 1 錠 E2 用量 2.0mg 群：E2 2.0 mg 錠，1 日 1 回 1 錠
投与方法:	E2 錠を 1 日 1 回 1 錠，毎朝一定の時刻に定められた順に従い，28 日間を 1 周期として連続 24 週間（6 周期）服用した． 子宮内膜の肥厚を回避するために，各周期の 17 日目から 28 日目までの 12 日間は，LNG 錠を 1 日 1 回 1 錠，同時に服用した（E2 錠及び LNG 錠を 1 錠ずつ計 2 錠を同時に服用した．）．ただし，子宮摘出例は LNG 錠を服用しなかった． 基礎治療薬剤として乳酸カルシウム 0.8g を 1 日 1 回 1 包，毎日夕食後に服用した．
バッチ番号:	SH T 546 TA: V* SH T 546 KB: R* SH T 546 LA: [redacted] SH T 594 FA: [redacted], P*
投与期間:	24 週間（28 日間を 1 周期として 6 周期）
対照薬:	SH T 546 PA：E2 プラセボ錠 SH T 594 PA：LNG プラセボ錠
用量:	[子宮を有する患者] プラセボ群：E2 プラセボ錠+LNG プラセボ錠（各周期 17-28 日），1 日 1 回各 1 錠 [子宮摘出患者] プラセボ群：E2 プラセボ錠，1 日 1 回 1 錠
投与方法:	E2 プラセボ錠を 1 日 1 回 1 錠，毎朝一定の時刻に定められた順に従い，28 日間を 1 周期として連続 24 週間（6 周期）服薬した． 子宮を有する患者は，各周期の 17 日目から 28 日目までの 12 日間は，LNG プラセボ錠を 1 日 1 回 1 錠，同時に服用した（E2 プラセボ錠及び LNG プラセボ錠を 1 錠ずつ計 2 錠を同時に服用した）． 基礎治療薬剤として乳酸カルシウム 0.8g を 1 日 1 回 1 包，毎日夕食後に服用した．
バッチ番号:	SH T 546 PA：[redacted] SH T 594 PA：[redacted]
投与期間:	24 週間（28 日間を 1 周期として 6 周期）
評価基準:	
有効性:	主要変数： ・腰椎骨密度増加率 （二重エネルギーX 線吸収測定法，dual energy X-ray absorptiometry：DXA 法）第 2～第 4 腰椎（L_{2-4}）の骨塩量（BMC），骨面積（AREA）及び骨密度（BMD）を DXA 法により測定した．BMD 測定値の，投与最終時期の増加率（骨密度増加率）を主要評価項目とした． 副次変数： 1）腰背痛重症度 腰背部の疼痛が認められる場合，安静時自発痛，圧痛，歩行時の疼痛による障害度の程度について 4 段階で調査した．

有効性（続き）：	2）骨所見 ・胸椎・腰椎X線所見及び骨折の有無 第8胸椎・第3腰椎のX線撮影（各々正面，側面の2方向）を行い，骨萎縮度分類に基づいて評価した．骨折（椎体変形)の有無及びその数を調査した． ・マイクロデンシトメトリー（Microdensitometry：MD）法 第2中手骨のX線撮影を行った． 3）骨代謝に関する生化学的検査 ・血清中パラメーター intact-オステオカルシン（Osteocalcin：OC），N端-OC，骨型アルカリフォスファターゼ（alkaline phosphatase：ALP），酒石酸抵抗性酸性フォスファターゼ（tartrate-resis-tant acid phosphatase：TRAP），Ⅰ型プロコラーゲンC末端プロペプチド（type Ⅰ procollagen C-terminal propeptide：PICP），intact-副甲状腺ホルモン（parathyroid hormone：PTH），1,25-$(OH)_2D$，カルシトニン ・尿中パラメーター 総ハイドロキシプロリン，ピリジノリン，デオキシピリジノリン，Ca，P，クレアチニン 4）血清ホルモン検査 E2，E1，FSH，LH，SHBG 5）疼痛（腰背痛）全般改善度 治験終了時（あるいは治験中止時）に腰背痛に対する効果を6段階で判定した．
安全性:	1）概括安全度 副作用の有無，症状，程度，処置，薬剤との関連性及び臨床検査成績を総合し，治験終了時(あるいは治験中止時）に5段階で判定した． 2）婦人科検査 乳房検診，子宮細胞診（内膜，腟部，頸部），子宮内膜組織診（可能な場合） 3）出血状況
薬物動態（適切な場合）：	該当なし
薬力学（適切な場合）：	該当なし
統計手法:	本試験は前期第Ⅱ相試験であるため，データ解析を探索的に実施した． 有意水準は，投与群間の比較可能性の検定では両側15%，用量（投与群）・反応の傾向性検定（最大対比法）並びにDunnett検定では片側5%，それ以外の検定は両側5%とした． 1）投与群間の比較可能性の検討 背景因子について分布又は基本統計量を投与群別に集計し，投与群間の検定をFisherの直接確率検定あるいはKruskal-Wallis検定により行った． 2）有効性 ・骨密度増加率 最大対比法，Dunnett検定によるプラセボ群との比較を行った． ・腰背痛重症度，骨萎縮度分類，骨折 Steel検定によるプラセボ群との比較を行った． ・MD法，生化学的検査，血清ホルモン検査 Dunnett検定によるプラセボ群との比較を行った． ・疼痛全般改善度 最大対比法，Steel検定によるプラセボ群との比較を行った． 3）安全性 ・概括安全度 最大対比法，Steel検定によるプラセボ群との比較を行った． ・有害事象及び副作用 Steel検定によるプラセボ群との比較を行った．

要約・結論

有効性の結果:

有効性指標の主要評価項目は DXA 法による腰椎 L_{2-4} の骨密度増加率とした．副次的評価項目として腰背痛重症度推移，MD 法による第 2 中手骨密度増加率，胸椎・腰椎 X 線所見及び新規骨折の有無，疼痛（腰背痛）改善度，骨代謝マーカー増加量，血清ホルモン増加量についても検討した．

主要評価項目である DXA 法による骨密度増加率は，最終週でプラセボ群 0.892±3.523%（平均値±標準偏差），E2 用量 0.5mg 群 1.091±5.760%，E2 用量 1.0mg 群 3.767±3.605%，2.0mg 群 2.810±4.522%であり，E2 用量 1.0mg 群及び 2.0mg 群では投与 12 週後より骨量の増加がみられた．骨量の増加は E2 用量 1.0mg 群及び 2.0mg 群とも同様であった．E2 用量 0.5mg 群はプラセボ群と同様のわずかな骨量の増加であった．最大対比法で用量反応パターンを推定した結果，投与 12 週後ではプラセボ群＜E2 用量 0.5mg 群＜E2 用量 1.0mg 群＝E2 用量 2.0mg 群のパターンにおいて有意差（p＝0.0437）が認められ，投与 24 週後ではプラセボ群＝E2 用量 0.5mg 群＜E2 用量 1.0mg 群＜E2 用量 2.0mg 群のパターン（p＝0.0599），最終週ではプラセボ群＜E2 用量 0.5mg 群＜E2 用量 1.0mg 群＝E2 用量 2.0mg 群のパターン（p＝0.0757）が認められた．血清中 E2 増加量と骨密度増加率に相関関係が認められた．また，E2 用量と血清中 E2 濃度に用量依存性が認められていることからも用量と骨密度増加率の相関が推察された．

MD 法による第 2 中手骨密度増加の指標として MCI，ΔGSmin，ΣGS/D の増加率を用いて評価した．しかし各投与群においてプラセボ群と比較して明確なデータは得られなかった．また，骨代謝に関する生化学的検査において，骨形成マーカーである intact-OC，N 端-OC，骨型 ALP の軽度の減少が各投与群でみられ，骨吸収マーカーであるピリジノリン，デオキシピリジノリンは各投与群で有意な減少が認められた．その他の骨代謝マーカーには特に影響が認められなかった．骨形成マーカーの低下は骨吸収を抑制した結果としてみられた変化と推察され，E2 の骨密度増加作用は骨吸収を抑制した結果であると考えられた．この骨吸収抑制作用は E2 用量 0.5mg 群から認められた．血清中 E2 濃度増加量は，E2 用量 0.5mg 群，E2 用量 1.0mg 群及び E2 用量 2.0mg 群で投与 24 週後にそれぞれ 33.67±12.06pg/ml，51.48±39.07pg/ml 及び 140.32±63.39pg/ml であった．一般的に骨粗鬆症に対する E2 の投与量は血中濃度を卵胞初期濃度である 30～60pg/ml に維持する投与量が至適とされている．腰背痛重症度推移，疼痛（腰背痛）改善度においては，E2 群において改善が認められているが，骨粗鬆症における痛みの発生機序は複雑で，E2 の効果の指標として適当でないと考えられている．胸椎・腰椎 X 線所見において，治験期間中の新たな骨折は認められなかった．

安全性の結果:

安全性に関して，重篤な有害事象の発現は認められなかった．有害事象発現率はプラセボ群で 18.2%，E2 用量 0.5mg 群で 48.0%，E2 用量 1.0mg 群で 18.5%，E2 用量 2.0mg 群で 34.6%であった．副作用発現率はプラセボ群で 4.5%，E2 用量 0.5mg 群で 36.0%，E2 用量 1.0mg 群で 14.8%，E2 用量 2.0mg 群で 34.6%であった．Steel 検定を用いてプラセボ群との比較を行ったところ，有害事象発現率は E2 用量 0.5mg 群で有意（p＝0.0421）に高く，副作用発現率は E2 用量 0.5mg 群（p＝0.0125）及び E2 用量 2.0mg 群 （p＝0.0153）で有意に高かった．E2 用量 1.0mg 群と比較し，E2 用量 0.5mg 群で逆に増加が認められた理由は不明であるが，偶発的な事象と考えられる．E2 用量 2.0mg 群では本剤の薬理作用に起因すると考えられる帯下，乳房緊満感などのエストロゲン製剤で報告されている副作用が多く認められた．E2 用量 1.0mg 群では異型を伴わない子宮内膜増殖症が 1 例に認められたが，投与終了後の追跡調査においては，問題となる子宮内膜病変は認められなかった．一般臨床検査においては，投与前と比較して有意な減少や増加を示す項目が散見されたが，すべて正常範囲内の変動又は臨床上好ましい変動で問題となる所見は認められなかった．概括安全度

（「ほぼ安全である」以上）はプラセボ群で 100%，E2 用量 0.5mg 群で 88%，E2 用量 1.0mg 群で 88.9%，E2 用量 2.0mg 群で 88.0%と比較的安全性は高いと考えられた．

結論:

E2 と LNG の併用投与は退行期骨粗鬆症患者及び骨量減少例に対し有効かつ安全な薬剤であると考えられた．また E2 の至適用量はおおむね 1.0mg と推定された．

Nihon Schering K.K.

試験 No.[redacted]216/報告書 No.A00403

有効成分の名称：	17ß-エストラジオール（E2）/レボノルゲストレル（LNG）	
治験の標題：	170 例の閉経後女性を対象に E2 1.0mg 及び LNG 40μg の持続的経口配合製剤を 13 周期（1 周期：28 日間）投与し，子宮内膜，出血パターン，更年期症状，骨代謝及び血液凝固機能に及ぼす影響を調査することを目的とした多施設共同，オープン試験	
治験責任医師：	[redacted]	
実施医療機関：	15 施設（ハンガリー）	
公表文献：	-	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted]年[redacted]月[redacted]日 **終了日（最後の被験者が完了した日）：** 20[redacted]年[redacted]月[redacted]日	**治験の相：** Ⅱ
目的：	主要目的：E2/LNG 配合剤（SH T 594 B）の 13 周期（1 周期を 28 日間として 52 週間）投与し，閉経後女性の子宮内膜過形成に対する保護効果に関する有効性を評価する． 副次目的：SH T 594 B の子宮内膜組織像，出血パターン，更年期症状，骨代謝，脂質代謝，血液凝固機能，臨床検査項目及び全般安全性の評価を行う．	
方法：	多施設共同，オープン試験	
被験者数（計画時，解析時）：	計画被験者数：200 例 解析被験者数：（スクリーニング被験者数：206 例，登録被験者数：167 例） ITT 解析集団：166 例 ITT 完了集団：119 例 FAS 解析集団：145 例 PP 解析集団： 105 例	
診断及び主要な選択基準:	次の条件を満たす閉経後女性； • 年齢 45 歳以上 • 子宮を有しており，子宮内膜組織診が陰性と診断された，又は診断に不十分な組織であった場合には超音波検査で子宮内膜厚が 5mm 未満であることが確認された者 • 登録時に自然閉経後 2 年以上経過している者 • 症状スコアに挙げられた更年期症状／症状群のうち，中等度以上の症状を 2 つ以上有する者 • 同意書に署名した者 • 過去に本治験に参加していない者	
被験薬： **用量：** **投与方法：** **バッチ番号：**	SH T 594 B 1 日 1 回 1 錠：E2 1.0mg 及び LNG 40μg 経口 K* （割り付け番号 126 以上への配給番号：L* ）	
投与期間：	52 週間，28 日間を 1 周期として 13 周期	
対照薬：	該当なし	
評価基準： **有効性:**	子宮内膜過形成の発現率，子宮内膜組織形態の変動，出血パターン，更年期症状，骨代謝マーカー 主要評価解析は PP 解析集団で行い，FAS 解析集団での追加解析を行った．選択基準を満たし，少なくとも一回投与を受け，また重大な治験実施計画書違反が無かった全被験者を FAS 解析集団とした．さらに，13 周期を完了し，投与前及び終了時において子宮内膜組織診の結果が得られている被験者を PP 解析集団とした．	
安全性：	代謝及び血液凝固・線溶系検査，有害事象，血液学的検査，血液生化学検査，尿検査	

統計手法：	結果データを全て記述統計量にて示した．評価項目について，治療前後の比較解析を行った．合計スコアの変動を t-検定，正常分布が得られない場合には Wilcoxon 検定を用いて解析を行った．カテゴリー変数の変動は Wilcoxon 検定によって，二項分布データは symmetry 検定によって解析を行った．95%信頼区間を算出した．臨床検査データは規定の正常基準値から範囲内又は範囲外への変動を示すシフトテーブルによって解析した．

要約・結論

有効性の成績：

本治験の主要評価項目は，子宮内膜過形成の発現率であった．子宮内膜組織診の所見は，施設毎及び中央病理組織判定医師の 2 名により判定され，双方の判定結果に不一致が認められた場合は，第 3 人目の病理判定医師が判定を行った．その結果，13 周期投与後又は途中中止例に子宮内膜過形成の発現は認められなかった．治験中，過形成の認められない子宮内膜ポリープが 2 例に認められた．過形成の非発現率の 95%信頼区間は，97－100%と算出された．

1 年間の投与終了後，PP 解析集団（105 例）における「子宮内膜不活性／萎縮」に区分された被験者の割合は 44%から 64%に増加した．同時に，「良性の子宮内膜表面上皮及び腺上皮の細片（strips of benign surface and glandular lining epithelium）」に区分された被験者の割合は 24%から 6%に減少した．投与期間中，「増殖期子宮内膜」あるいは「分泌期子宮内膜」に区分された被験者の割合に，問題となるような変動は認められなかった．「増殖期子宮内膜」は，投与前の 3%から治験終了時には 2%にまで減少し，「分泌期子宮内膜」は 2%から 4%に増加した．1 年間の投与終了後，「月経期子宮内膜」及び「子宮内膜不活性／萎縮及び子宮内膜ポリープ」と診断された被験者が，それぞれ 1 例ずつ認められた．治験終了時において，23%の被験者が「診断に不十分な組織」と判定されたが，超音波検査によって子宮内膜厚が 5mm 未満であることが確認されたため，これらの被験者を「子宮内膜不活性／萎縮」に区分し評価を行った．よって，治験終了時に「子宮内膜不活性／萎縮」と判定された被験者の割合は 87%であった．

ITT 完了集団（119 例）での結果にも，同じ傾向が認められた．「子宮内膜不活性／萎縮」に区分された被験者の割合は，43%から 65%に上昇した．同時に，「良性の子宮内膜表面上皮及び腺上皮の細片」に区分された被験者の割合は 24%から 6%に減少した．「増殖期子宮内膜」は，投与前の 3%から治験終了時には 2%まで減少し，「分泌期子宮内膜」は 2%から 3%に上昇した．「月経期子宮内膜」及び「子宮内膜不活性／萎縮及び子宮内膜ポリープ」と診断された被験者が，それぞれ 1 例ずつ認められた．治験終了時において，22%の被験者が「診断に不十分な組織」と判定されたが，経腟超音波検査によって子宮内膜厚が 5mm 未満であることが確認されたことから，これらの被験者を「子宮内膜不活性／萎縮」と区分し評価を行った．よって，治験終了時に「子宮内膜不活性／萎縮」と判定された被験者の割合は 87%であった．

治験中，PP 及び FAS の両解析集団において，性器出血の発現した被験者数は減少した．1 年間の投与終了後，この被験者の割合は，PP 解析集団において第 1 周期の 27.6%から 10.6%に，FAS 解析集団において 36.4%から 10.5%に減少した．最初の 3 周期において，出血日数の増加及び症状の悪化が見られたが，その後，点状出血又は出血の日数は着実に減少し，症状も軽減された．また，治験終了時，最も高頻度に記載された出血量の程度は点状出血であった．点状出血又は出血の平均期間は，投与開始 1 箇月目の 3.4 日から治験終了時には 1.1 日まで減少した．

投与前後を比較して，全ての更年期症状の頻度は顕著に低下し，症状の程度も軽減した．また，全ての更年期症状において，第 7 周期目まで一定して統計学的に有意な減少が認められた．第 8 周期目以降，更年期症状が認められた被験者は非常に少なかったことから，投与第 8 周期目を超えると症状の変化は少なくなり，第 10 周期を超えると新たな症状の変化は全く見られなくなった．PP 解析集団において，更年期症状評価尺度の平均スコアは，投与前の 12.2 ポイントから，投与終了時には 1.4 にまで減少した（FAS 解析集団においては，12.4 から 1.4 に減少）．統計学的試験結果は，投与前から第 10 周期終了時まで，有意な減少を示したが第 10 周期から第 13 周期までの変動は有意ではなかった．

骨代謝マーカーは有意な変動を示した．FAS 解析集団において，投与終了時に骨形成マーカーの OC が 38.4%（$p<0.05$），骨型 ALP が 4.5%（有意差なし）低下した．骨吸収マーカーも同様に，crosslaps が 33.3%（$p<0.05$），デソキシピリジノリンが 4.1%（有意差なし）低下した．

投与期間中，婦人科検査に問題となる異常所見は認められず，子宮内膜の超音波検査では，投与前後を比較して子宮内膜厚の変動はなかった．

有効性に関する総合評価は，治験責任医師及び被験者の両方で，「良い（good）」～「とても良い（very good）」と評価し，治験終了後，治験責任医師の 74%及び被験者の 73%が，本治験薬による治療を「とても良い（very good）」と評価した（FAS 解析集団）．

安全性の成績：

64 例（37%）の被験者に合計 105 件の有害事象が認められた．108 例（63%）の被験者には，有害事象が全く認められなかった． 13 例（8%）に重症度が「高度」，26 例（15%）に「中等度」，25 例（15%）に「軽度」の有害事象がそれぞれ 1 件以上認められた．

主な有害事象は，腟出血（32 件），高血圧（7 件），乳房痛（6 件），子宮筋腫の肥大（4 件）であった．

105 件中 61 件の有害事象は，治験薬との関連性について「多分関連あり(possible)」，「おそらく関連あり(probable)」又は「明らかに関連あり(definite)」と評価された．治験薬との関連性判定が「多分関連あり(possible)」以上の主な事象は，腟出血（32 件），次いで乳房痛（6 件），子宮筋腫の肥大（3 件）であった．

合計 29 例（安全性解析集団で 28 例，施設番号 6 で 1 例）が，有害事象により治験薬投与を中止した．最も高率の中止理由は腟出血であった．有害事象のため投与中止となったその他の事象は乳房痛，四肢痛，発疹，高血圧，腹痛及び末梢性浮腫であった．

入院による重篤な有害事象が 1 件認められた．被験者 1 例は，持続性の腟出血で投与開始から 2 箇月後，外科的処置（掻爬術）を受けた．治験薬との関連性は否定されなかった．この被験者は回復し，終了時組織診の結果は「子宮内膜不活性／萎縮及び子宮内膜ポリープ」であった．

投与開始時において，ホルモン検査値の評価により，被験者の閉経後状態の確認が行われた．治験終了時の FSH 濃度の平均値は，投与前値と比較して有意な減少が認められた（−38.4%）．また，E2 の平均値は有意に上昇した（＋66.7%）．

脂質代謝検査では，総コレステロール（−9.7%），LDL コレステロール（−4.9%），アポリポ蛋白 B（−8.3%）及びリポ蛋白(a)（−30.3%）に，それぞれ有意な減少が認められた．また，統

計学的な有意差はなかったもののトリグリセライドに顕著な減少が認められた（－6.3%）．好ましくない影響としては，HDL（－6.7%）及びアポリポ蛋白 AI（－12.5%）に有意な減少が認められた．しかしながら，動脈硬化指数である LDL／HDL に有意な変動はなかった（＋3.5%）．

血液凝固・線溶系検査では，投与前と比較して，終了時のプラスミノーゲンアクチベーターインヒビター（plasminogen activator inhibitor：PAI）（－27.8%）及びフィブリノーゲン（－5.7%）に有意な減少が認められた．第Ⅶ因子は増加した（5.1%，有意差なし）．凝血抑制系の指標であるアンチトロンビンⅢ（antithrombin Ⅲ：ATⅢ）は有意に減少した（－13.2%）．フィブリン分解生成物はわずかに減少した（－2.9%）．

投与前後を比較して，血液学的検査，血液生化学的検査，尿検査及びバイタルサインの結果に重大な変動はなかった．投与終了時，被験者 1 例においてスメア細胞診（腟部及び頸部）の結果に異常が認められ（パパニコロウ分類 クラスⅢ），マンモグラフィーにおいて 4 例に異常所見が認められた（嚢胞 3 例，乳房線維嚢胞 1 例）．

治験終了時，本治験薬投与による治療の忍容性について被験者の 72%が「とても良い（very good）」，被験者の 22%が「良い（good）」と評価した．

結論：

閉経後女性を対象に SH T 594 B の 1 年間持続的投与において，子宮内膜過形成あるいは子宮癌の発現は全く認められなかった．本治験薬投与により，子宮内膜萎縮／不活性に明らかな増加が認められた結果，無月経が増加し，出血及び点状出血の発現が減少した．また，更年期症状の発現回数及び症状の程度が速やかに軽減した．

これらの治験薬投与による効果に伴い，ホルモン検査値に変化が認められた．被験者の閉経状態を確認するために測定した投与前の FSH 及び E2 濃度と比べて，治験終了時の平均 FSH 濃度は有意に低下し（－38.4%），平均 E2 濃度は有意に上昇した（＋66.7%）．

さらに，SH T 594 B の骨に対する好ましい総合的効果として，投与 1 年後の骨吸収マーカー及び骨形成マーカー（crosslaps 及び OC)が有意に減少した．

脂質代謝にも良好な効果が認められた．本治験において，総コレステロール，LDL コレステロール，アポリポ蛋白 B 及びリポ蛋白(a)に有意な減少が認められた．また，有意差は認められなかったもののトリグリセライドが著しく減少した（－6.3%）．脂質代謝に対する好ましくない影響として，HDL 及びアポリポ蛋白 AI に有意な減少が認められた．しかしながら，動脈硬化指数である LDL／HDL 比に有意な変動は認められなかった．

本治験における血液凝固・線溶系検査項目の顕著な影響は，線維素溶解活性上昇の兆候の 1 つである PAI に有意な減少が見られたことであった．フィブリノーゲンは有意に減少し，第Ⅶ因子は有意ではないが増加し，凝固促進因子の亢進が示唆された．抗凝固作用の測定項目である ATⅢが，13.2%と有意に減少したことは，好ましくない影響の可能性を示す所見と考えられる．

持続性の腟出血により，数例の被験者が本治験薬投与を中止した．本治験薬との関連性ありと判断されたその他の有害事象は，乳房痛及び子宮筋腫の肥大であった．しかしながら，有害事象の発現は稀であり，ほとんどの症状は軽度又は中等度であった．投与中に，血圧，脈拍数及び体重に重大な変動は認められなかった．大多数の被験者が本治験薬投与による治療の有効性及び忍容性を，それぞれ「とても良い（very good）」と評価した．

試験 No.[redacted]216 の 1 年延長試験/報告書 No.A06276

有効成分の名称：	17ß-エストラジオール（E2）/レボノルゲストレル（LNG）
治験の標題：	170 例の閉経後女性を対象に E2 1.0mg 及び LNG 40μg の持続的経口配合製剤を 13 周期（1 周期：28 日間）投与し，子宮内膜，出血パターン，更年期症状，骨代謝及び血液凝固機能に及ぼす影響を調査することを目的とした多施設共同，オープン試験－延長試験－
治験責任医師：	**試験 [redacted]216** [redacted] **延長試験** [redacted]
実施医療期間：	**臨床試験 [redacted]216：** 15 施設（ハンガリー） **延長試験：**7 施設（ハンガリー）
公表文献：	-
治験期間（年）：	試験 [redacted]216： 開始日（最初の被験者が登録された日）：　19[redacted] 年 [redacted] 月 [redacted] 日 終了日（最後の被験者が完了した日）：　20[redacted] 年 [redacted] 月 [redacted] 日 **延長試験：** **開始日（最初の被験者が登録された日）：**　19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：**　20[redacted] 年 [redacted] 月 [redacted] 日
治験の相：	Ⅱ
目的：	**試験 [redacted]216** 主要目的：E2/LNG 配合剤（SH T 594 B）の 13 周期（1 周期を 28 日間として 52 週間）投与し，閉経後女性の子宮内膜過形成に対する保護効果に関する有効性を評価する． 副次目的：SH T 594 の子宮内膜組織像，出血パターン，更年期症状，骨代謝，脂質代謝，血液凝固機能，臨床検査項目及び全般安全性の評価を行う． **延長試験** 主要目的：閉経後女性を対象に 13 周期延長（1 周期を 28 日間として，計 26 周期）して E2/LNG 配合剤を持続的投与し，子宮内膜過形成に対する保護効果に関する有効性を評価する． 副次目的：13 周期延長（1 周期を 28 日間として，計 26 周期）持続的投与による，子宮内膜組織形態，出血パターン，更年期症状，骨代謝，代謝及び凝固・線溶系臨床検査項目及び全般安全性の評価を行う．
方法：	多施設共同，オープン試験
被験者数（計画時，解析時）：	**臨床試験 [redacted]216** 計画被験者数：200 例 解析被験者数：（スクリーニング被験者数：206 例，登録被験者数：167 例） ITT 解析集団：166 例　　ITT 完了集団：119 例 FAS 解析集団：145 例　　PP 解析集団： 105 例 **延長試験** 計画被験者数：50 例 解析被験者数：（Visit7 の来院日の登録例：51 例） 安全性解析集団：51 例　　ITT 解析集団：51 例 ITT 完了集団：39 例　　PP 解析集団： 31 例

診断及び主要な選択基準:	**臨床試験 ■216** 次の条件を満たす閉経後女性； • 年齢 45 歳以上 • 子宮を有しており，子宮内膜組織診が陰性と診断された，又は診断に不十分な組織であった場合には超音波検査で子宮内膜厚が 5mm 未満であることが確認された者 • 登録時に自然閉経後 2 年以上経過している者 • 症状スコアに挙げられた更年期症状／症状群のうち，中等度以上の症状を 2 つ以上有する者 • 同意書に署名した者 • 過去に本治験に参加していない者 **延長試験** 選択基準 • 計画書番号 ■216 の治験を重大な治験実施計画書逸脱なしで完了し，治験薬に対する忍容性が良好な被験者で，さらに 1 年投与の継続を希望する者 • Visit7（7 回目来院日）の超音波検査で，子宮内膜厚が 8mm 以下であった者 • 延長試験の同意書に署名した者 追加選択基準 （Visit7 の検査結果を確認すること） • 施設毎及び中央病理学者の評価で子宮内膜組織診の所見が陰性（子宮内膜過形成，子宮内膜ポリープ，子宮内膜癌等の所見がない）であった者 • マンモグラフィーの結果が正常であった者（Visit7）	
被験薬： **用量：** **投与方法：**	SH T 594 B 1 日 1 回 1 錠：E2 1.0mg 及び LNG 40μg 経口	
バッチ番号	**試験 ■216:** K* （割り付け番号 126 以上への配給番号：L* ）	**延長試験：** K* （n＝26），L* （n＝25） （試験 ■216 からの予備投与；Visit7-7* の投与 52～56 週：[redacted]）
投与期間：	**試験 ■216:** 52 週間（28 日間を 1 周期として 13 周期）	**延長試験：** 52 週間（28 日間を 1 周期として 13 周期）
比較療法：	該当せず	
評価基準：		
有効性：	**試験 ■216：**子宮内膜過形成の発現率（主要有効性変数），子宮内膜組織形態の変動，出血パターン，更年期症状，骨代謝マーカー 主要評価解析は PP 解析集団で行い， FAS 解析集団での追加解析を行った．選択基準を満たし，少なくとも一回投与を受け，また重大な治験実施計画書違反が無かった全被験者を FAS 解析集団とした．さらに，13 周期を完了し，投与前及び終了時において子宮内膜組織診の結果が得られている被験者を PP 解析集団とした． **延長試験：**子宮内膜過形成の発現率，子宮内膜組織形態の変動，出血パターン，更年期症状，骨代謝マーカー 主要評価解析は PP 解析集団で行い，ITT 完了集団での追加解析を行った．	
安全性：	**試験 ■216 及び延長試験：**代謝及び血液凝固・線溶系検査，有害事象，血液学的検査，血液生化学検査，尿検査	
統計手法：	**試験 ■216 及び延長試験:** 結果データを全て記述統計量にて示した．評価項目について，治療前後の比較解析を行った．合計スコアの変動を t-検定，正常分布が得られない場合には Wilcoxon 検定を用いて解析を行った．カテゴリー変数の変動は Wilcoxon 検定によって，二項分布データは symmetry 検定によって解析を行った．95%信頼区間を算出した．臨床検査データは規定の正常基準値から範囲内又は範囲外への変動を示すシフトテーブルによって解析した．	

要約・結論

［本試験報告書の「2. 概要」の項には試験 ■216 の投与 1 年目の結果も記載されていたが，報告書 No.A00403 の記載と重複するため省略し，ここでは延長試験成績に関する成績のみ記載する．］

有効性の成績：

試験 ■216：報告書 No.A00403 の頁参照

延長試験：

表 2.7.6.3.2-1 延長試験の有効性一覧（第 7 来院日から第 11 来院日への変化 ）

集団	PP 解析集団:n＝31，ITT 完了集団:n＝39，ITT 解析集団:n＝51	
パラメーター	第 7 来院日 （延長投与開始前）	第 11 来院日 （延長試験終了時）
主要評価項目		
子宮内膜過形成 発現例数	PP 解析集団＋ITT 完了集団 0 例	PP 解析集団＋ITT 完了集団 0 例
95%信頼区間　PP 解析集団： ITT 完了集団：	0.0% － 11.22% 0.0% － 9.03%	
副次有効性評価項目		
子宮内膜形態 被験者数： 子宮内膜不活性／萎縮(組織病理結果に基く)	PP 解析集団（ITT 完了集団） 68%（62%）	PP 解析集団（ITT 完了集団） 68%（64%）
子宮内膜不活性／萎縮（判定規定に基く*） 診断に不十分な組織（判定規定に基く*） *「診断に不十分な組織」で，子宮内膜厚 5㎜ 未満の被験者を「子宮内膜不活性／萎縮」に区分された.	100%（100%） 0%（0%）	100%（92%） 3%（8%）
点状出血又は出血 被験者数 発現件数 平均出血日数（日）	PP 解析集団：14 周期目 2 人（7%） 2 例 0.7	PP 解析集団: 26 周期目 0 人（0%） 0 例 0
更年期症状（軽度／中等度） 関節及び筋障害 神経過敏，易刺激性 全身の活力低下／記憶障害 尿路障害 うつ症状 睡眠障害 心部不定愁訴 性欲障害 腟乾燥 ホットフラッシュ／発汗	PP 解析集団 19% 19% 16% 13% 7% 7% 7% 7% 3% 0%	PP 解析集団 13% 10% 16% 13% 10% 13% 7% 7% 3% 0%
更年期症状評価尺度 スコアポイント ［平均］	PP 解析集団 1.1	PP 解析集団 1.2

延長試験の有効性一覧（第 7 来院日から第 11 来院日への変化 ）（つづき）

パラメーター	第 7 来院日（延長投与開始前）				第 11 来院日（延長試験終了時）				P 値（t-検定）
副次有効性評価項目									
骨代謝 ［平均値］	PP 解析集団				PP 解析集団				
骨型アルカリホスファターゼ	54 U/L				43 U/L				0.1692
オステオカルシン	14 ng/ml				11 ng/ml				0.2221
Deoxypyridinoline	7 nmol/mmol				20 nmol/mmol				0.0209
Crosslaps	2448 pmol/L				2673 pmol/L				0.4925
有効性に関する総合評価	PP 集団				PP 集団				
	とても良い	良い	まあまあ良い	不十分	とても良い	良い	まあまあ良い	不十分	
治験責任医師判定の分布［ % ］	90	10	0	0	87	13	0	0	
被験者判定の分布［ % ］	84	16	0	0	84	16	0	0	

子宮内膜過形成

本治験の主要評価項目は，子宮内膜過形成の発現率であった．子宮内膜組織診の所見は，施設毎及び中央病理組織判定医師の 2 名により判定され，双方の判定結果に不一致が認められた場合，第 3 人目の病理組織判定医師が判定を行った．その結果，13 周期の延長試験終了後（1 周期を 28 日間として，計 26 周期）又は中止例（投与中止・脱落者）に子宮内膜過形成の発現は認められなかった．よって，過形成発現率の 95%信頼区間は，PP 解析集団で 0.0－11.22%，ITT 完了集団で 0.0－9.03%であった．

子宮内膜組織形態

延長試験期間を通して，PP 解析集団の被験者 31 例及び ITT 完了集団の被験者 39 例に認められた病理組織の判定は，「子宮内膜不活性／萎縮」もしくは「診断に不十分な組織」の 2 種類だけであった．これら 2 種類の判定結果の PP 解析集団での割合は，延長投与開始前（第 7 来院日）及び 13 周期延長試験終了時（第 11 来院日）で全く同率であった（「子宮内膜不活性／萎縮」68%，「診断に不十分な組織」32%）．延長投与開始前及び延長試験終了時において，超音波検査によって子宮内膜厚が 5mm 未満であることが確認されたことから，「診断に不十分な組織」に区分されていた全被験者を「子宮内膜不活性／萎縮」に区分し評価を行った．

ITT 完了集団において，64%の被験者が「子宮内膜不活性／萎縮」であり，36%が「診断に不十分な組織」であった．超音波検査によって子宮内膜厚が 5mm 未満であることが確認されたことから，さらに 11 例の被験者を「子宮内膜不活性／萎縮」の区分し評価を行った．よって，延長試験終了時，92%（39 例）の被験者が「子宮内膜不活性／萎縮」に区分され，その他，8%の被験者は超音波検査で子宮内膜厚が 5mm 以上（5mm～7mm）であることが確認されたため，「診断に不十分な組織」に区分された．

出血パターン（点状出血又は出血）

点状出血又は出血が発現した被験者の割合は，延長試験開始前（第 7 来院日）の 7%から，延長試験終了時（第 11 来院日）には 0%にまで減少した．また，出血が発現した被験者数も 2 例から 0 例に減少し，出血の平均減少日数は 0.7 日から 0 日となった(PP 解析集団)．

更年期症状

PP 解析集団では，被験者が更年期症状を有する頻度は，延長投与開始前及び延長試験終了時のいずれにおいても，全般的に低かった（第 7 来院日で 0～19%，第 11 来院日で 0～16%）．延長試験期間中，症状の発現した被験者数に，最も改善が見られた更年期症状は，神経過敏／易刺激性（9%減少），関節及び筋障害（6%減少）であった．睡眠障害（6%上昇）及びうつ状態（3%上昇）には悪化が見られた．

骨代謝

13 周期の延長投与終了後，骨形成マーカーである OC 及び，骨型 ALP に，有意な減少は見られなかった．骨吸収マーカーであるデソキシピリジノリンは有意な増加を示した（p＝0.0209）．一方で crosslaps も有意ではなかったが増加が認められた．

有効性に関する総合評価

PP 解析集団において，治験責任医師及び被験者の有効性評価に，重要な経時変動は認められなかった．治験終了時，本治験薬の有効性を，87%の治験責任医師及び 84%の被験者が「とても良い」，残りの治験責任医師及び被験者は「良い」と評価した．ITT 解析集団においては，投与期間を通して「とても良い」の判定に明らかな増加がみられ，終了時の判定は 86%（治験責任医師）及び 83%（被験者）であった．

安全性の成績：

試験 ■216：報告書 No.A00403 の頁参照

延長試験：

延長試験期間中，10 例（20%）の被験者に，合計 14 件の有害事象（1 件の重篤な有害事象を含む）が認められた．41 例（80%）の被験者には，有害事象は全く認められなかった．重症度が「高度」の有害事象 1 件が 1 例（2%）（重篤な有害事象例）に，中等度の有害事象 6 件が 5 例（10%）に，軽度の有害事象 7 件が 5 例（10%）に，それぞれ発現した．

最も高頻度に報告された有害事象は，腰椎坐骨神経痛（3 件／3 例），次いで小筋腫（2 件／2 例），腟出血（2 件／1 例），急性気管支炎（2 件／2 例）であった．

14 件中 6 件の有害事象は，治験薬との関連性が「多分関連あり(possible)」と評価された．最も高頻度に治験薬との関連性を「多分関連あり(possible)」と評価された有害事象は，小筋腫（2 件／2 例）及び腟出血（2 件／1 例：軽度の腟出血及び点状出血），次いで片不全麻痺を伴う急性高血圧（1 件／1 例），消化性潰瘍（1 件／1 例）であった．

合計 3 例の被験者が，有害事象により治験薬の投与を中止した．血糖値の上昇，片不全麻痺を伴う急性高血圧，消化性潰瘍（各 1 件）が，それぞれの中止理由であった．

入院による重篤な有害事象 1 件が発現した．被験者 1 例に，延長試験の第 117 日目に片不全麻痺を伴う急性高血圧が認められ，治験責任医師は治験薬 SH T 594 B との関連性を「関連ないらしい（unlikely）」と評価した．

SH T 594 B の 13 周期の延長投与中，有意ではないがわずかな FSH の上昇が認められた．FSH 値はほぼ安定し，エストロゲン作用上昇の臨床的兆候を示さなかった状況で，E2 が 0.13 nmol/L から 0.35 nmol/L へ有意に増加した要因は明らかではないが，おそらく施設効果（center effect）の 1 つではないかと考えられる．

脂質代謝検査について，好ましい影響の一つであるトリグリセライドの約 27%の減少は，有意でかつ顕著であった．HDL 及び LDL コレステロールの増加により，総コレステロールが増加した．LDL コレステロール，総コレステロール，アポリポ蛋白 AI 及びアポリポ蛋白 B の増加は有意であった．総コレステロール／HDL コレステロールの比率に変動はなかったが，LDL コレステロール／HDL コレステロールの比率は有意に上昇した．リポ蛋白(a)には変動はなかった．投与 1 年後での測定値を考慮した場合（試験 ■216 の総被験者），投与 2 年後においてコレステロール値（総コレステロール，HDL コレステロール，LDL コレステロール）が，ほぼ投与開始前に回復したことは特筆すべき点である．一方，トリグリセライドは 2 年目の投与期間でさらに減少し，リポ蛋白(a)は 1 年目の値が継続した．

血液凝固・線溶系検査では，最も顕著であった好ましい影響は ATⅢ（抗凝血因子）の有意な増加，第Ⅶ因子（凝固促進因子）及び PAI（抗線維素溶解因子）の減少であった．フィブリノーゲン及びフィブリン分解生成物に有意な変動はなかった．

延長試験の投与前後を比較して，血液学的検査，血液生化学検査，尿検査，バイタルサイン，婦人科検査及びスメア細胞診（膣部及び頸部）の結果に重大な変動は認められなかった．

延長試験終了時，本治験薬投与による治療の忍容性を，被験者の 81.0%が「とても良い」，16.7%が「良い」，2.4%が「不十分」と評価した．また，治験責任医師の 83.3%が「とても良い」，14.3%が「良い」，2.4%が「不十分」（有害事象「消化性潰瘍」が発現したため）と評価した．

結論：

試験 ■216：報告書 No.A00403 の頁参照

延長試験：

閉経後女性を対象に 1 年間延長した SH T 594 B の持続的投与中，子宮内膜過形成及び子宮癌の発現はなかった．ITT 完了集団の被験者 39 例のうち 92%が，最終診断で「子宮内膜不活性／萎縮」に区分され，残りの被験者は「診断に不十分な組織」に区分された．これらの結果は，13 周期の投与期間を通して出血の発現率が低かったことと整合している．また，治験終了時には全ての被験者が無出血に至った．

延長試験開始時において，更年期症状の発現率は既に非常に低く，13 周期の延期投与期間を通して重大な変化はなかった．更年期症状の神経過敏／易刺激性，関節及び筋障害に最も改善が認められた．睡眠障害及びうつ症状は，わずかに悪化した．

骨吸収亢進の可能性を示唆するデソキシピリジノリンの増加を除き，骨代謝マーカーに有意な変化は認められなかった．

脂質代謝検査ではトリグリセライドの有意でかつ顕著な減少が認められ，好ましい影響の一つであると考えられた．変動が認められなかったリポ蛋白(a)以外，他の脂質パラメーターは増加し，投与前値に回復した（試験 ■216 の投与前）．

血液凝固・線溶系検査における ATⅢの有意な増加，第Ⅶ因子及び PAI の有意な減少は，血液凝固系に全般的な亢進がみられたことを示唆している．

20%の被験者に有害事象が発現した．1 件の重篤な有害事象（左側片不全麻痺）以外，その症状は軽度又は中等度の事象であった．主な有害事象は，腰椎坐骨神経痛であり，次いで小筋腫，腟出血，急性気管支炎であった．投与中，血圧，心拍，及び体重に重大な変動はなかった．大半の被験者が，本治験薬投与による治療の有効性及び忍容性を，それぞれ「とても良い（very good）」と評価した．

Nihon Schering K.K.

試験 No.[redacted]065/報告書 No.A00404

有効成分の名称：	17ß-エストラジオール（E2）/レボノルゲストレル（LNG）	
治験の標題：	390 例の閉経後女性を対象に E2 1.0mg 及び LNG 40μg，又は結合型エストロゲン（CEE）0.625mg 及び酢酸メドロキシプロゲステロン（MPA）2.5mg の持続的経口配合製剤を 13 周期（1 周期：28 日間）投与し，子宮内膜，更年期症状，出血パターンの影響を調査することを目的とした多施設共同，非盲験，無作為化，並行群間比較試験	
治験責任医師：	更年期専門クリニック及び開業医の医師（ハンガリー，チェコ共和国）	
実施医療機関：	ハンガリー16 施設，チェコ共和国 8 施設	
公表文献：	-	
治験期間（年）	**開始日（最初の被験者が登録された日）：** 19[redacted] 年 [redacted] 月 [redacted] 日 **終了日（最後の被験者が完了した日）：** 20[redacted] 年 [redacted] 月 [redacted] 日	**治験の相：** Ⅲ
目的：	主要目的：更年期症状評価尺度の総スコアの変動に対する SH T 594 B 及び[redacted]（CEE 0.625mg/MPA 2.5mg）の同等性を検証した． 副次目的：13 周期（1 周期 28 日）の治験薬投与による，子宮内膜組織形態，子宮内膜過形成の発現，出血パターン，更年期症状，全般安全性及び忍容性を評価した．	
方法：	非盲験，無作為化，並行群間，多施設共同，多国籍試験	
被験者数（計画時，解析時）：	計画被験者数：390 例 解析被験者数：（登録被験者数：359 例） ITT 安全性解析集団：359 例（SH T 594 B 群：237 例，CEE/MPA* 群：122 例） ITT 完了集団：296 例（SH T 594 B 群：199 例，CEE/MPA* 群：97 例） PP 解析集団：252 例（SH T 594 B 群：169 例，CEE/MPA* 群：83 例）	
診断及び主要な選択基準:	次の条件を満たす閉経後女性； • 年齢 45 歳以上 • 子宮を有しており，子宮内膜組織診が陰性と診断された，又は診断に不十分な組織であった場合には超音波検査で子宮内膜厚が 5mm 未満であることが確認された者 • 登録時に自然閉経後 1 年以上経過している者 • 症状スコアに挙げられた更年期症状／症状群のうち，中等度以上の症状を 2 つ以上有する者．その 2 つの症状のうち 1 つは，ホットフラッシュ／発汗であること．総スコアが 10 ポイント以上であること • 同意書に署名した者	
被験薬： **用量：** **投与方法：** **バッチ番号：**	SH T 594 B （E2 1.0mg 及び LNG 40μg を含有する製剤） 1 日 1 回 1 錠 経口 ハンガリー：M*　　，チェコ共和国：N*	
投与期間：	52 週間，13 周期	
対照薬： **用量：** **投与経路：** **バッチ番号：**	CEE/MPA*（CEE 0.625mg 及び MPA 2.5mg を含有する製剤） 1 日 1 回 1 錠 経口 ハンガリー：M*　　，チェコ共和国：N*	
投与期間：	52 週間，13 周期	
評価基準： **有効性：** **安全性：**	 更年期症状評価尺度（主要評価項目），更年期症状，子宮内膜組織診，超音波検査，出血パターン（副次評価項目） 有害事象，血液学的検査，血液生化学検査，尿検査	
統計手法：	主要評価項目：投与前から終了時までの更年期症状評価尺度の変動を両群間で比較した．SH T 594 B のCEE/MPA* に対する非劣性（同等性）及び優位性の有無は，Wilcoxon sign rank 検定による検証検定を行った． 副次評価項目：群内での投与開始前後の比較，及び変動の群間比較を行った．連続分散変数は t 検定を用いて，また正常分布が得られない場合には，Wilcoxon 検定を用いて検定を行った．95%信頼区間を算出した． カテゴリー分類変数の変動は Wilcoxon 検定を用いて，名義尺度変数は symmetry 検定を用いて解析を行った．	

要約・結論

有効性の成績：

合計 359 例の閉経後女性（平均年齢：53.5 歳）が SH T 594 B（237 例）あるいは CEE/MPA*（122 例）の投与群に無作為に組み入れられ，これを ITT 集団とした．このうち，13 周期の投与期間を完了し，重大な治験実施計画書違反のなかった 252 例（SH T 594 B 群：169 例 及び CEE/MPA* 群：83 例）を PP 解析集団とした．また 13 周期を完了し，投与前と治験終了時の子宮内膜組織診の結果が得られた 296 例（SH T 594 B 群：199 例 及び CEE/MPA* 群：97 例）の ITT 完了集団について，追加解析が実施された．

投与前の人口統計学的特性，医学的，外科的及び婦人科的な既往歴，薬物治療歴あるいは更年期症状，子宮内膜組織形態に両投与群の差異はなかった．

主要な評価項目：更年期症状評価尺度

PP 解析集団において，SH T 594 B 群での更年期症状評価尺度の平均スコアは，投与前の 14.5 ポイントから 13.1 ポイント（95%信頼区間：12.47－13.62）減少し，投与終了時は 1.4 ポイントであった．CEE/MPA* 群でも，平均スコアは投与前の 14.3 ポイントから 13.1 ポイント（95%信頼区間：12.27－13.91）減少し，投与終了時は 1.2 ポイントであった．結果として，投与群間の差は 0.01 ポイントとなり，有意差は認められなかった（p＝0.93）．

ITT 集団でも同じような結果が得られた．SH T 594 B 群において，平均スコアは投与前の 14.5 ポイントから 12.0 ポイント（95%信頼区間：11.38－12.53）減少し，投与終了時には 2.5 ポイントであった．一方，CEE/MPA* 群では，平均値は 11.8 ポイント（95%信頼区間：11.02－12.61）減少し，14.5 ポイントから 2.6 ポイントになった．結果として，投与群間の差は 0.2 ポイントと，有意差は認められなかった（p＝0.78）．

反応率

反応率とは，投与前と第 7 来院日を比較して，更年期症状評価尺度の総スコアに 50%以上の改善が認められた被験者の割合と定義した．投与群間に反応率の有意な差はなかった．PP 解析集団の SH T 594 B 群の 96.4%の被験者に 50%以上の改善が認められた．同様に，CEE/MPA* 群の 97.6%の被験者に 50%以上の改善改善が認められた．ITT 集団において，投与前の総スコアと比較して，両投与群共に 91%の被験者に 50%以上の改善が認められた．

更年期症状

PP 解析集団と ITT 解析集団で，両投与群のいずれにおいても，本治験中に全ての更年期症状の発現が減少し，その症状の程度に軽減が認められた．

投与前，PP 解析集団の全被験者（両投与群の 100%）がホットフラッシュ，発汗を有していたが，治験終了時には，SH T 594 B 群で 5%，CEE/MPA* 群で 7%の被験者にこれらの症状が認められるのみであった．同様に睡眠障害も，投与前の発現率は SH T 594 B 群で 95%，CEE/MPA* 群で 93%であったが，治験終了時には SH T 594 B 群で 10%及び 12%に減少した．神経過敏／易刺激性は SH T 594 B 群で 91%から 21%，CEE/MPA* 群で 95%から 14%に，膣乾燥感は SH T 594 B 群で 75%から 4%，CEE/MPA* 群で 78%から 2%に，うつ状態は SH T 594 B 群で 75%から 7%，CEE/MPA* 群で 82%から 4%に減少した．

全ての更年期症状の程度に，顕著な改善が認められた．治験終了時，SH T 594 B 群では 100%，CEE/MPA* 群でも 99%の被験者にホットフラッシュ，発汗の症状の程度に改善が見られた．また，SH T 594 B 群の 93%，及び CEE/MPA* 群の 89%に睡眠障害の改善が認められ，これよりも低い改善率ながら心部不定愁訴では SH T 594 B 群 61%及び CEE/MPA* 群 71%，尿路障害では SH T 594 B 群 60%及び CEE/MPA* 群 53%に改善が認められた．

治験期間中，更年期症状の変化に関して投与群間に有意差はなかった．

子宮内膜組織形態

子宮内膜組織形態は，PP 解析集団（SH T 594 B 群：169 例，CEE/MPA* 群：83 例）及び ITT 完了集団（SH T 594 B 群：199 例，CEE/MPA* 群：97 例）で解析を実施した．両解析集団において，いずれの投与群でも，全般的に治験薬投与中に「子宮内膜不活性／萎縮」へと変化する明らかな傾向が認められた．

PP 解析集団において，SH T 594 B 投与中，「子宮内膜不活性／萎縮」に区分された被験者の割合は 36%から 53%に増加した．一方，「良性の子宮内膜表面上皮及び腺上皮の細片」に区分された被験者の割合は 14%から 1%に減少した．CEE/MPA* 投与中，「子宮内膜不活性／萎縮」に区分された被験者の割合は，33%から 47%に増加した．一方，「良性の子宮内膜表面上皮及び腺上皮の細片」に区分された被験者の割合は 28%から 5%に減少した．投与期間中，「増殖期子宮内膜」あるいは「分泌期子宮内膜」に区分された被験者の割合に，有意な変動はなかった．SH T 594 B 群では，「増殖期子宮内膜」に区分された被験者の割合は，投与前及び治験終了時共に 4%であった（「分泌期の子宮内膜」に区分された被験者の割合は 1%）．一方，CEE/MPA* 群では，「増殖期子宮内膜」に区分された被験者の割合は，投与前 6%から治験終了時には 3.6%に減少し，「分泌期子宮内膜」に区分された被験者の割合は，0%から 1.2%に増加した．治験終了時，CEE/MPA* 群の 1 例（1.2%）に「月経期子宮内膜」が認められた．また，SH T 594 B 群に「子宮内膜ポリープを伴う子宮内膜不活性／萎縮」の判定が 2 例，「子宮体下部のみ（lower uterine segment only）」が 1 例に認められた．第 7 来院日において，SH T 594 B 群の 38%，CEE/MPA* 群の 35%の被験者が「診断に不十分な組織」と判定されたが，超音波検査によって子宮内膜厚は 5mm 未満であることが確認されたため，これらの被験者を「子宮内膜不活性／萎縮」に区分し評価を行った．よって，治験終了時に「子宮内膜不活性／萎縮」と判定された被験者の総割合は SH T 594 B 群で 91%，CEE/MPA* 群で 82%であった．

ITT 完了集団において，SH T 594 B 投与中，「子宮内膜不活性／萎縮」に区分された被験者の割合は 33%から 55%に増加した．一方，「良性の子宮内膜表面上皮及び腺上皮の細片」に区分された被験者の割合は，15%から 2%に減少した．CEE/MPA* 投与中，「子宮内膜不活性／萎縮」に区分された被験者の割合は，33%から 50%に増加した．一方，「良性の子宮内膜表面上皮及び腺上皮の細片」に区分された被験者の割合は，29%から 4%に減少した．治験終了時，SH T 594 B 群で「増殖期子宮内膜」に区分された被験者の割合は，5%から 3.5%に，CEE/MPA* 群で 6.2%から 3.1%に減少した．「分泌期子宮内膜」に区分された被験者の割合は，ほぼ変化がなかった（SH T 594 B 群で 1%から 1.5%，CEE/MPA* 群で 0%から 1%）．治験終了時，CEE/MPA* 群の 2 例（2.1%）に「月経期子宮内膜」が認められた．また，SH T 594 B 群に「子宮内膜ポリープを伴う子宮内膜不活性／萎縮」の判定が 2 例，「子宮体下部のみ（lower uterine segment only）」が 1 例に認められた．第 7 来院日において，SH T 594 B 群の 36%，CEE/MPA* 群の 34%の被験者が「診断に不十分な組織」と判定されたが，超音波検査によって子宮内膜厚が 5mm 未満であることが確認されたため，これらの被験者を「子宮内膜不活性／萎縮」に区分し評価を行った．よって，治験終了時に「子宮内膜不活性／萎縮」と判定された被験者の総割合は SH T 594 B 群で 91%，CEE/MPA* 群で 84%であった．

治験期間中，「複合型過形成」の判定が SH T 594 B 群の 1 例に認められた．よって，SH T 594 B 投与による過形成発現率の 95%信頼区間は，0.01－2.77%と算出された．CEE/MPA* 投与による過形成発現率の 95%信頼区間は，0.0－3.73%と算出された．

性器出血

全般的に，投与第 3 周期目以降，有意な出血発現数の減少，期間の短縮及び出血量（程度）の軽減が認められた．このことは，PP 解析集団及び ITT 解析集団の両投与群に認められ，投与群間に差異はなかった．

PP 解析集団において，SH T 594 B 群の 43%及びCEE/MPA* 群の 34%の被験者に，全治験期間中を通して点状出血又は出血は全く発現しなかった．SH T 594 B 群では，出血が認められた被験者の割合が，第 1 周期目の 33%から第 13 周期目には 10%まで減少した．CEE/MPA* 群では，第 1 周期目の 39%から第 13 周期目には 11%まで減少した．

SH T 594 B 群では，第 1 周期目に被験者に記録された出血日数は合計 323 日間であった．最も高頻度にみられた出血量の程度は，「点状出血」又は「軽度」であった．点状出血又は出血の発現日数は，第 2 周期目には 477 日に増加したが，第 3 周期目以降，一定した減少が認められた．第 13 周期目では，151 日の点状出血又は出血の発現日数が報告されたのみであった．「中等度」あるいは「高度」の出血が発現した被験者の割合は，第 2 周期目には 1%から 1.4%に上昇したが，第 13 周期目には 0.2%にまで減少した．

CEE/MPA* 群では，第 1 周期目に記録された出血日数は合計 201 日であった．最も高頻度に見られた出血量の程度は，「点状出血」又は「軽度」の出血であった．第 2 周期目以降治験終了時まで，点状出血又は出血の発現日数に一定の減少が見られた．「中等度」又は「高度」の出血が発現した被験者の割合は，第 1 周期目の 1.3%から第 13 周期目には 0%まで減少した．

SH T 594 B 群の被験者に，第 1 周期目は平均 0.6 件の出血が発現したが，第 13 周期目には 0.2 件にまで減少した．CEE/MPA* 群の被験者の出血は，第 1 周期目の 0.8 件から第 13 周期目の 0.2 件まで減少した．

SH T 594 B 群での点状出血又は出血の平均期間（1 件当たり）は，第 1 周期目の 5.2 日間から第 13 周期目には 0.8 日間まで減少した．CEE/MPA* 群での点状出血又は出血の平均期間は，第 1 周期目の 3.7 日間から第 13 週期目には 0.6 日間まで減少した．

婦人科検査／超音波検査

PP 解析集団の SH T 594 B 群において，スクリーニング時に認められた 2 例の被験者の異常所見（骨盤内及び腟）は，治験終了時には正常所見に回復していた．CEE/MPA* 群では，スクリーニング時から治験終了までに，婦人科検査所見に変動は認められなかった．

SH T 594 B 群の 99%の被験者で，スクリーニング時及び治験終了時の経腟超音波検査による子宮内膜厚を測定し，各観察日の平均子宮内膜厚は 2.8mm～3.1mm の範囲であった．CEE/MPA* 群では，スクリーニング時（第 1 来院日）で 99%，治験終了時（第 7 来院日）で 98%の被験者の子宮内膜厚を測定し，各観察日の平均子宮内膜厚は 2.9mm～3.0mm の範囲であった．

総合評価

治験責任医師及び被験者が治験薬投与による治療の有効性を評価した．

SH T 594 B 群では，第 1 周期目完了後，治験薬投与による治療を治験責任医師の 31%が「とても良い（very good）」，60%が「良い（good）」，10%が「まあまあ良い（moderate）」，0%が「不十分（poor）」と評価した．治験終了時では，治験責任医師の 82%が「とても良い」，18%が「良い」，0%が「まあまあ良い」，0%が「不十分」と評価した．CEE/MPA* 群にも同様の結果が示され，第 1 周期目完了後，治験責任医師の 36%が「とても良い」，51%が「良い」，12%が「まあまあ良い」，1%が「不十分」と評価した．その後の投与周期で「不十分」と評価した治験責任医師はいなかった．治験終了時，治験責任医師の 81%が「とても良い」，17%が「良い」，2%が「まあまあ良い」，0%が「不十分」と評価した（PP 解析集団）．

SH T 594 B 群では，第 1 周期目完了後，治験薬の有効性を被験者の 31%が「とても良い」，56%が「良い」，12%が「まあまあ良い」と評価し，「不十分」と評価した被験者はなかった．治験終了時，被験者の 81%が「とても良い」，19%が「良い」，1%が「まあまあ良い」と評価し，「不十分」と評価した被験者は 0%であった．CEE/MPA* 群にも同様の結果が示され，第 1 周期目完了後，被験者の 35%が「とても良い」，48%が「良い」，16%が「まあまあ良い」，1%が「不十分」と評価した．その後の評価で「不十分」と評価した被験者はなかった．治験終了時，被験者の 82%が「とても良い」，16%が「良い」，2%が「まあまあ良い」，0%が「不十分」と評価した（PP 解析集団）．

安全性の成績：

投与期間中，合計 215 件の有害事象が報告された．SH T 594 B 群の被験者 97 例（41%）に，151 件の有害事象が認められた．また，CEE/MPA* 群の被験者 48 例（39%）に，64 件の有害事象が認められた．両投与群の，それぞれ約 60%の被験者には，有害事象が全く認められなかった．SH T 594 B 群において有害事象の重症度は 16%の被験者が軽度，14%が中等度，11%が高度であった．CEE/MPA* 群において有害事象の重症度は，18%の被験者が軽度，13%が中等度，8%が高度であった．

主な有害事象は（SH T 594 B 群及び CEE/MPA* 群の順に），腟出血（全件数の 27%及び 16%）であり，次いで高血圧（6%及び 6%），尿路感染（6%及び 2%），感染（3%及び 5%），気管支炎（4%及び 3%），WBC 異常（4%及び 3%），子宮筋腫の肥大（3%及び 5%），腟炎（3%及び 5%）であった．

SH T 594 B 群では，合計 23 件の有害事象により 22 例の被験者が治験薬の投与を中止した．CEE/MPA* 群では，10 件の有害事象により 10 例の被験者が治験薬の投与を中止した．治験薬の投与の中止に至った有害事象のうち，最も高頻度に報告されたのは腟出血であった（SH T 594 B 群：9 例，CEE/MPA* 群：5 例）．

SH T 594 B 群に発現した全有害事象の 55%及び CEE/MPA* 群に発現した全有害事象の 56%が，治験薬との関連性は「関連なし（not）」あるいは「関連性ないらしい（unlikely）」と判断された．また，SH T 594 B 群の 41%及び CEE/MPA* 群の 44%が「多分関連あり(possible)」あるいは「おそらく関連あり(probable)」と判断され，SH T 594 B 群の 4%が「明らかに関連あり(definite)」と判断された．CEE/MPA* 群で「明らかに関連あり」と判断された有害事象はなかった．「多分関連あり」あるいは「おそらく関連あり」と判断された主な有害事象は，腟出血（SH T 594 B 群 37 例，及び CEE/MPA* 群 10 例），次いで子宮筋腫の肥大（3 例及び 2 例），γ-GTP 増加（3 例及び 0 例），高血圧（1 例及び 2 例）であった．SH T 594 B 群の 6 例の「明らかに関連あり」と判断された有害事象の内訳は，腟出血（4 例），腹痛（1 例）及び不眠症（1 例）であった．

全治験期間中，合計 16 件の重篤な有害事象が報告された．2 件（子宮内膜癌及び乳癌）は投与群への組み入れ（無作為化）以前のスクリーニング期間中に発現した．投与期間中，13 件の重篤な有害事象が報告された（8 件が SH T 594 B 群，5 件が CEE/MPA* 群）．SH T 594 B 群の 8 件の内訳は，死亡 1 例（自殺），腟出血による入院及び掻爬術 2 例，子宮頸管ポリープによる入院及び掻爬術 1 例，直腸癌の手術 1 例，甲状腺結節の切除術 1 例，子宮及び付属器の全摘出 1 例，子宮頸部低グレード病変 1 例であった．CEE/MPA* 群の 5 件の内訳は，腟出血による入院及び掻爬術 3 例，胆嚢切除術 2 例であった．SH T 594 B 群の被験者 1 例に関しては，重篤な有害事象 1 例が投与終了より 2 箇月後に報告された（複雑型過形成による入院及び掻爬術）．重篤な有害事象の報告頻度は，両投与群で同様であった．「多分関連あり」あるいは「おそらく関連あり」と評価された腟出血による掻爬術（5 例）及び複雑型過形成（1 例）を除き，その他の全ての重篤な有害事象は治験薬との関連性について「関連なし(not)」又は「関連ないらしい(unlikely)」と判定された．

治験期間中，評価された臨床検査値，バイタルサインに重要な変動は認められず，投与群間に差はなかった．

治験責任医師及び被験者の忍容性評価は，第 1 周期目完了後から投与終了時へ，両投与群で「良い」から「とても良い」に回答傾向がみられた．治験終了時，治験薬の忍容性を，SH T 594 B 群の治験責任医師は，80%が「とても良い」，18%が「良い」，1%が「まあまあ良い」，1%が「不十分」と評価した．CEE/MPA* 群にも同様の結果が示され，77%が「とても良い」，20%が「良い」，3%が「まあまあ良い」，0%が「不十分」と評価した．治験終了時における総合的な治験薬の忍容性評価を，SH T 594 B 群の被験者は，81%が「とても良い」，17%が「良い」，1%が「まあまあ良い」，1%が「不十分」と評価した．CEE/MPA* 群の被験者は，総合的な治験薬の忍容性評価を，79%が「とても良い」，18%が「良い」，3%が「まあまあ良い」，0%が「不十分」と評価した．

結論：

本治験の主要目的は，SH T 594 B と CEE/MPA* の更年期症状に対する有効性の同等性を，更年期症状評価尺度の総スコアの変動によって示すことであった．1 年間の投与終了後，両投与群において，更年期症状評価尺度の平均総スコアが 13.1 ポイント減少した．投与中，SH T 594 B 群の 97%の被験者，CEE/MPA* 群の 98%の被験者において，症状スコアに 50%以上の改善が認められた．

更に，両投与群において，全ての更年期症状の発現数が減少し，その症状は軽減された．特に，投与開始前には両投与群ともに 90%を超える被験者に認められた「ホットフラッシュ／発汗」，「睡眠障害」，「神経過敏／易刺激性」及び「うつ症状」の複合症状群が顕著に減少し，1 年間の投与終了後には 10%未満にまで減少した．また，治験期間中，全ての更年期症状の程度が大幅に軽減した．

子宮内膜組織形態は，1 年間の投与終了後，両投与群において「良性の子宮内膜表面上皮及び腺上皮の細片」から「子宮内膜不活性／萎縮」への変化が明らかに認められた．「増殖期内膜」又は「分泌期内膜」と判定された被験者の割合に有意な変動はなかった．「複雑型過形成」の発現は，SH T 594 B 群で認められた 1 例のみであった．

治験期間中，出血の発現数の減少，期間の短縮及び出血量（程度）の軽減が認められた．いずれの投与群でも第 2 周期目以降にこの軽減効果が認められた．

しかしながら，治験薬の投与を中止する被験者もみられた．腟出血は最も頻度の高い有害事象であり，両投与群に同程度に認められた.その他の有害事象の発現率は低く，全般的に軽度であった．バイタルサインあるいは臨床検査値に変動はなかった．

大多数の被験者は，両治験薬の有効性及び忍容性を「とても良い」と評価した.

SH T 594 B によるホルモン補充療法を１年間投与後，更年期症状の改善，子宮内膜組織形態の変化，点状出血及び出血の軽減，全般的安全性及び忍容性は，CEE/MPA* と同等であると結論した.

Nihon Schering K.K.

2.7.6.4　　付録

Nihon Schering K.K.

2.7.6.4.1　概要補遺

申請する適応症に関する有効性を評価した試験（試験 010646，300107）

試験番号　：010646（報告書 No.B123）

治験の標題：前期第Ⅱ相試験（step１）［更年期障害，卵巣欠落症状］

1.　試験方法の概略

自然閉経後の更年期障害又は両側卵巣摘出による卵巣欠落症状を有する患者 88 例を対象に，多施設共同，無作為化（封筒法），非盲検，並行群間比較試験を行い，E2 の至適用量を探索的に検討した．E2 錠（0.5mg 錠，1.0mg 錠又は 2.0mg 錠）を 1 日 1 回 1 錠，連続 8 週間（2 周期）投与した．子宮を有する被験者には，LNG 40μg 錠 1 日 1 錠を各周期 17～28 日目（12 日間）に周期的投与法にて併用した（図 1 参照）．

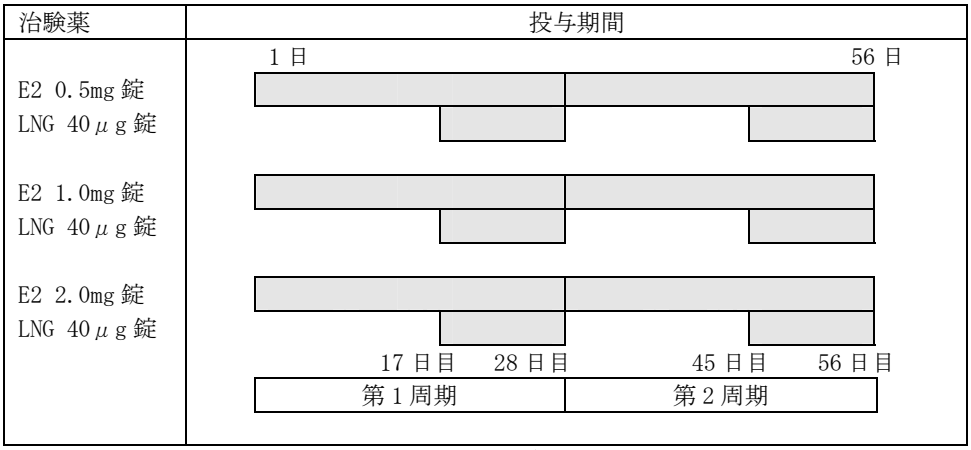

図 1 投与スケジュール

2.　試験対象集団

(1)　主要な組入れ・除外基準

1)　組入れ基準

下記の条件を満たす自然閉経後の更年期障害患者及び両側卵巣摘出により卵巣欠落症状を示す患者．なお，入院と外来の別は問わない．

1.　最終月経後 1 年以上又は両側卵巣摘出後 3 箇月以上の患者

2.　下記症状が少なくとも 1 つあり，症状の程度が中等度以上の患者

　　a）ホットフラッシュ　b）発汗　c）腟萎縮症状（性交障害，乾燥感，腟炎など）

3.　20 歳以上 65 歳未満

2)　除外基準

1. 心理テスト（自己評価抑うつ尺度（self-rating depression scale：SDS））により，心因性の不定愁訴（うつ病）と判断された患者

2. 乳癌，乳腺症，良性乳房腫瘍，子宮内膜癌又は子宮内膜増殖症を有するもの，あるいはその疑いのある患者

3. 血栓塞栓症患者又はその既往を有する患者

4. 高度の高血圧症を有する患者

5. 重度の糖尿病を有する患者

6. 重篤な肝障害，腎障害又は心疾患を有する患者

7. ポルフィリン血症を有する患者

8. 原因不明の不正出血を有する患者

9. その他，治験責任医師が不適当と判断した患者

(2)　解析対象集団

自然閉経後の更年期障害 68 例，両側卵巣摘出による卵巣欠落症状 20 例，合計 88 例を封筒法無作為割付により 3 群（E2 用量 0.5mg 群，E2 用量 1.0mg 群及び E2 用量 2.0mg 群）に割り付けた．被験者の内訳を図 2に示す．

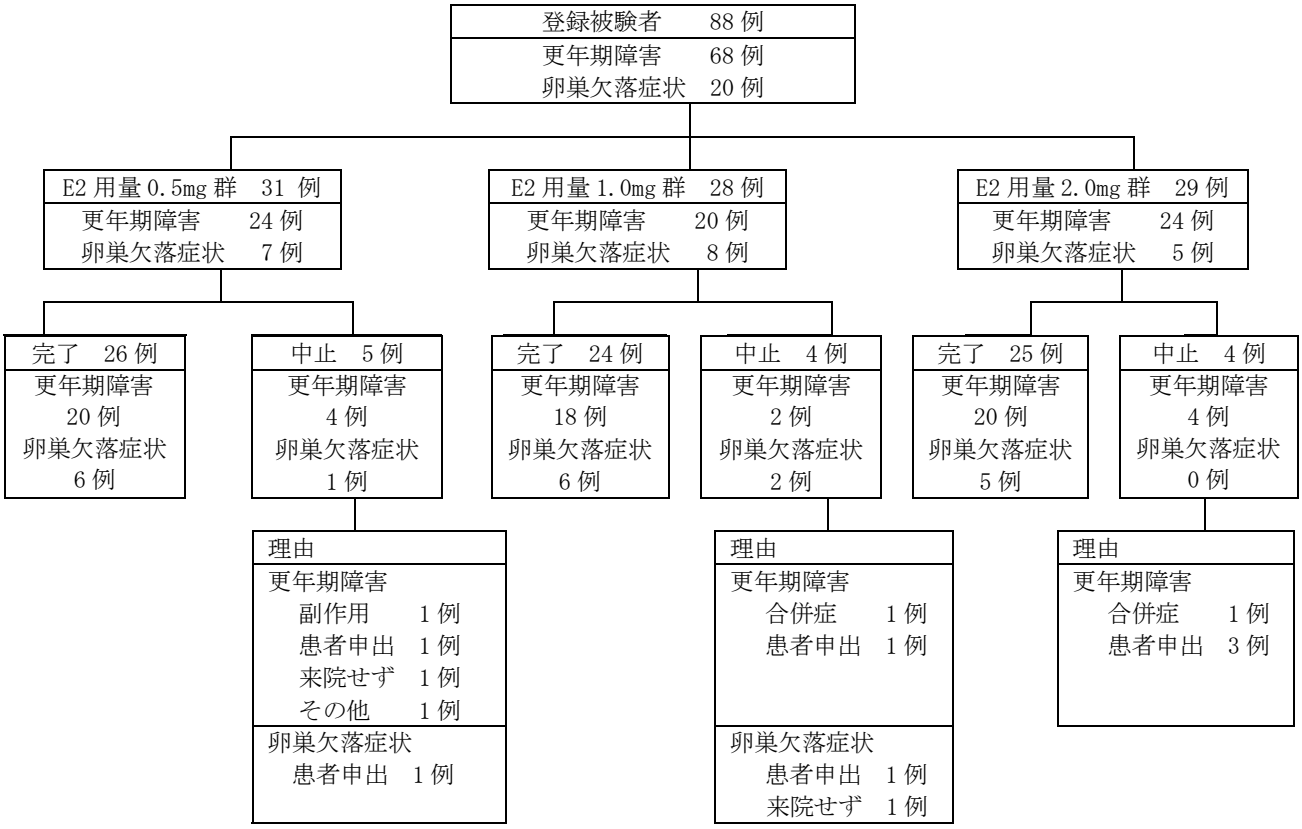

図 2 被験者の内訳

総括報告書 No. B123，図 10-1-1

治験薬を投与した被験者のうち投与完了被験者は 75 例（E2 用量 0.5mg 群：26 例，E2 用量 1.0mg 群：24 例，E2 用量 2.0mg 群：25 例）であった．また，投与開始後何らかの理由で中止脱落した被験者は 13 例であった．中止脱落の理由としては，患者の申し出が 7 例と最も多く，次いで副作用又は合併症が 3 例であった．中止例数と中止理由に明らかな投与群間の違いは認められなかった．

有効性，安全性の解析に関する被験者の取扱いを症例検討会で決定した．解析対象集団の内訳を図 3に示す．選択基準又は除外基準に違反した被験者，治療方法の不遵守があった被験者，服薬が 1 周期に満たない早期中止例は改善度の解析から除外した．組入れ被験者 88 例のうち解析対象例は 78 例，そのうち全般改善度の評価対象例は 72 例，安全性評価対象例は 77 例であった．

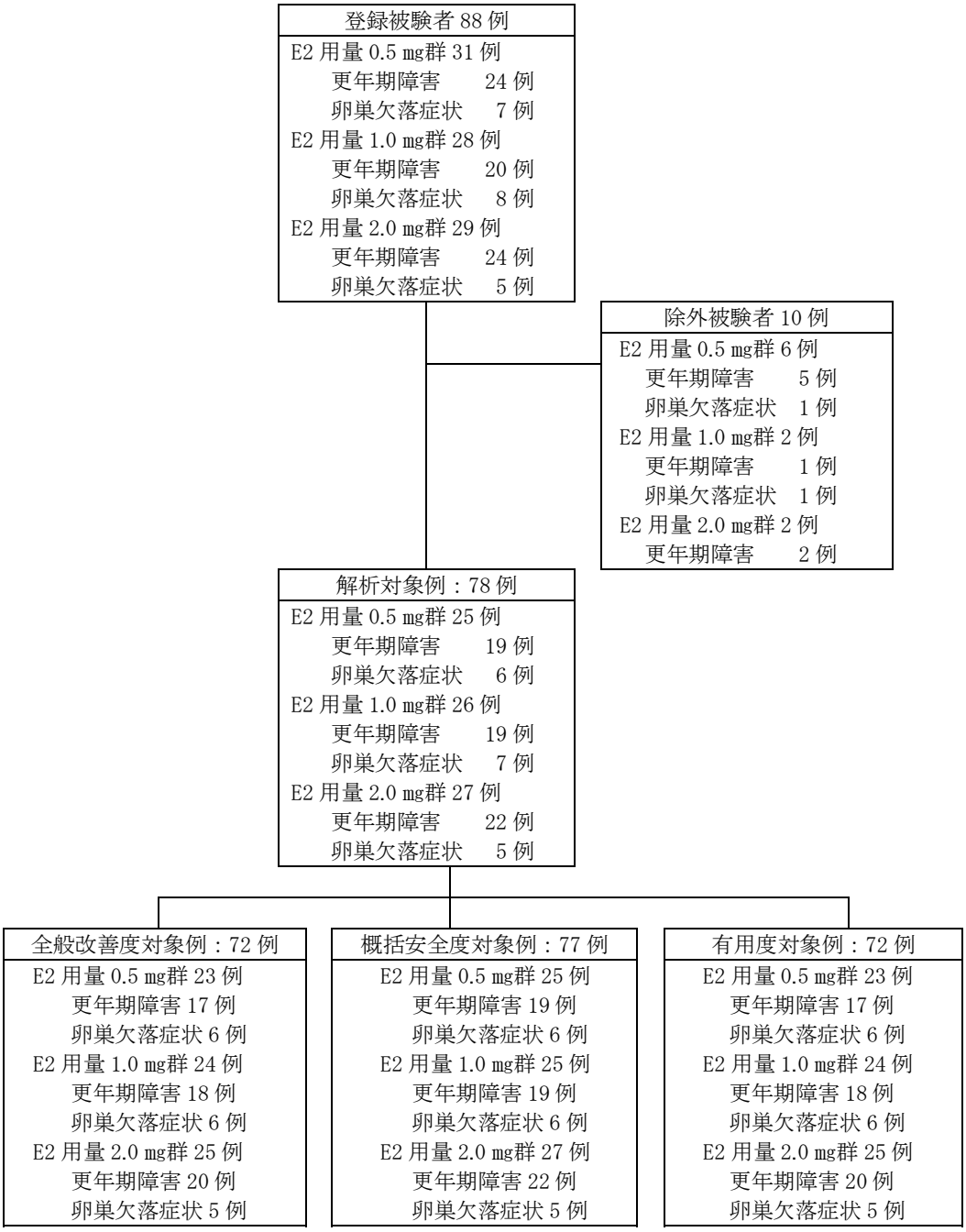

図 3 解析対象集団の内訳

総括報告書 No. B123, 図 11-1-1

(3)　人口統計学的及び他の基準値の特性

解析対象とした 78 例の被験者の人口統計学的特性及び他の基準値の特性を表 1に示す．年齢，診断名，閉経後期間及びホットフラッシュの回数と程度に関する投与群間の偏りは認められなかった．

表 1 人口統計学的特性及び他の基準値の特性（解析対象例）

項目		E2 用量 0.5mg 群 N=25	E2 用量 1.0mg 群 N=26	E2 用量 2.0mg 群 N=27	検定
		被験者数(%)			
年齢	40 歳未満	1 (4.0)	1 (3.8)	0 (0.0)	Kruskal-Wallis p=0.409
	40～49 歳	9 (36.0)	7 (26.9)	6 (22.2)	
	50～59 歳	14 (56.0)	17 (65.4)	17 (63.0)	
	60 歳以上	1 (4.0)	1 (3.8)	4 (14.8)	
	平均±SD	50.7±5.5	51.6±5.9	52.8±4.9	
	最小	38	39	44	
	最大	60	65	63	
診断名	更年期障害	19 (76.0)	19 (73.1)	22 (81.5)	Fisher P=0.795
	卵巣欠落症状	6 (24.0)	7 (26.9)	5 (18.5)	
閉経後の期間	不明	3 (12.0)	2 (7.7)	7 (25.9)	Kruskal-Wallis p=0.518
	両側卵巣摘出	6 (24.0)	7 (26.9)	5 (18.5)	
	1 年未満	1 (4.0)	1 (3.8)	1 (3.7)	
	1 年～3 年未満	7 (28.0)	7 (26.9)	5 (18.5)	
	3 年～5 年未満	3 (12.0)	4 (15.4)	2 (7.4)	
	5 年以上	5 (20.0)	5 (19.2)	7 (25.9)	
	平均±SD	3.6±3.4	3.0±1.9	4.6±3.7	
	最小	0	0	0	
	最大	12	7	11	
ホットフラッシュの回数（/日）	0 回	1 (4.0)	2 (7.7)	1 (3.7)	Kruskal-Wallis p=0.760
	1～3 回未満	3 (12.0)	5 (19.2)	4 (14.8)	
	3～6 回未満	13 (52.0)	8 (30.8)	15 (55.6)	
	6 回以上	8 (32.0)	11 (42.3)	7 (25.9)	
	平均±SD	5.4±3.5	6.0±5.3	4.8±3.7	
	最小	0	0	0	
	最大	16	20	20	
ホットフラッシュの程度	無	1 (4.0)	2 (7.7)	1 (3.7)	Kruskal-Wallis p=0.867
	軽度	2 (8.0)	4 (15.4)	4 (14.8)	
	中等度	18 (72.0)	15 (57.7)	18 (66.7)	
	高度	4 (16.0)	5 (19.2)	4 (14.8)	
血中 E2 濃度	未実施	1 (4.0)	0 (0.0)	1 (3.7)	Kruskal-Wallis p=0.231
	20pg/mL 以下	23 (92.0)	23 (88.5)	23 (85.2)	
	20pg/mL 超	1 (4.0)	3 (11.5)	3 (11.1)	
	平均±SD	11.6±42.6	16.8±47.6	9.2±19.2	
	最小	1	1	1	
	最大	211	191	72	

総括報告書 No.B123，表 11-2-1

3.　有効性の結果

(1)　ホットフラッシュの回数

ホットフラッシュの回数の推移を表 2に，ホットフラッシュの回数減少率の推移を表 3及び図 4に示す．本剤を投与した E2 用量 0.5mg 群では，投与前と比較した最終評価時（8 週後又は中止時）におけるホットフラッシュの回数の平均減少率が 86.01%であった．経時的解析の結果，いずれの投与群においても投与前から顕著な減少が認められた（p＝0.0001）．

表 2 ホットフラッシュの回数の推移

時期	E2 用量群	被験者数	ホットフラッシュの回数				一元配置分散分析	Dunnett 検定
			平均	SD	最小値	最大値		
投与前	合計	70	5.80	4.21	1.0	20.0	0.491	E2 0.5mg 対 E2 1.0mg：p= 0.907 E2 0.5mg 対 E2 2.0mg：p=0.522
	E2 0.5mg	23	5.61	3.49	1.5	16.0		
	E2 1.0mg	23	6.63	5.29	1.0	20.0		
	E2 2.0mg	24	5.19	3.70	1.0	20.0		
2 週後	合計	60	3.03	2.40	0.0	10.4	0.340	E2 0.5mg 対 E2 1.0mg：p= 0.726 E2 0.5mg 対 E2 2.0mg：p= 0.188
	E2 0.5mg	21	3.29	2.32	0.0	10.0		
	E2 1.0mg	20	3.40	2.82	0.0	10.4		
	E2 2.0mg	19	2.36	1.95	0.0	8.0		
4 週後	合計	68	1.83	2.27	0.0	10.0	0.649	E2 0.5mg 対 E2 1.0mg：p= 0.825 E2 0.5mg 対 E2 2.0mg：p= 0.472
	E2 0.5mg	22	1.84	2.04	0.0	7.0		
	E2 1.0mg	22	2.16	2.72	0.0	10.0		
	E2 2.0mg	24	1.53	2.07	0.0	8.0		
8 週後	合計	65	0.59	1.18	0.0	6.0	0.638	E2 0.5mg 対 E2 1.0mg：p= 0.879 E2 0.5mg 対 E2 2.0mg：p= 0.563
	E2 0.5mg	22	0.55	1.06	0.0	4.0		
	E2 1.0mg	21	0.79	1.43	0.0	6.0		
	E2 2.0mg	22	0.45	1.07	0.0	4.0		
最終	合計	68	0.60	1.16	0.0	6.0	0.741	E2 0.5mg 対 E2 1.0mg：p= 0.858 E2 0.5mg 対 E2 2.0mg：p=0.611
	E2 0.5mg	22	0.55	1.06	0.0	4.0		
	E2 1.0mg	22	0.75	1.41	0.0	6.0		
	E2 2.0mg	24	0.50	1.03	0.0	4.0		

総括報告書 No.B123，表 11-4-2

表 3 ホットフラッシュの回数の減少率の推移

時期	E2 用量群	被験者数	ホットフラッシュの回数減少率(%) 平均	SD	最小値	最大値	一元配置分散分析	Dunnett 検定
2 週後	合計	60	-38.47	37.47	-100.0	33.3	0.401	E2 0.5mg 対 E2 1.0mg : p=0.348 E2 0.5mg 対 E2 2.0mg : p=0.153
	E2 0.5mg	21	-30.38	35.65	-100.0	33.3		
	E2 1.0mg	20	-39.32	37.17	-100.0	0.0		
	E2 2.0mg	19	-46.51	39.84	-100.0	33.3		
4 週後	合計	68	-68.30	33.97	-100.0	66.7	0.681	E2 0.5mg 対 E2 1.0mg : p=0.608 E2 0.5mg 対 E2 2.0mg : p=0.323
	E2 0.5mg	22	-64.93	41.97	-100.0	66.7		
	E2 1.0mg	22	-66.36	33.49	-100.0	0.0		
	E2 2.0mg	24	-73.19	26.26	-100.0	0.0		
8 週後	合計	65	-88.96	24.89	-100.0	33.3	0.588	E2 0.5mg 対 E2 1.0mg : p=0.592 E2 0.5mg 対 E2 2.0mg : p=0.266
	E2 0.5mg	22	-86.01	32.00	-100.0	33.3		
	E2 1.0mg	21	-87.41	24.82	-100.0	0.0		
	E2 2.0mg	22	-93.39	15.66	-100.0	-33.3		
最終	合計	68	-88.71	24.48	-100.0	33.3	0.717	E2 0.5mg 対 E2 1.0mg : p=0.554 E2 0.5mg 対 E2 2.0mg : p=0.329
	E2 0.5mg	22	-86.01	32.00	-100.0	33.3		
	E2 1.0mg	22	-87.99	24.37	-100.0	0.0		
	E2 2.0mg	24	-91.86	15.84	-100.0	-33.3		

総括報告書 No.B123, 表 11-4-3

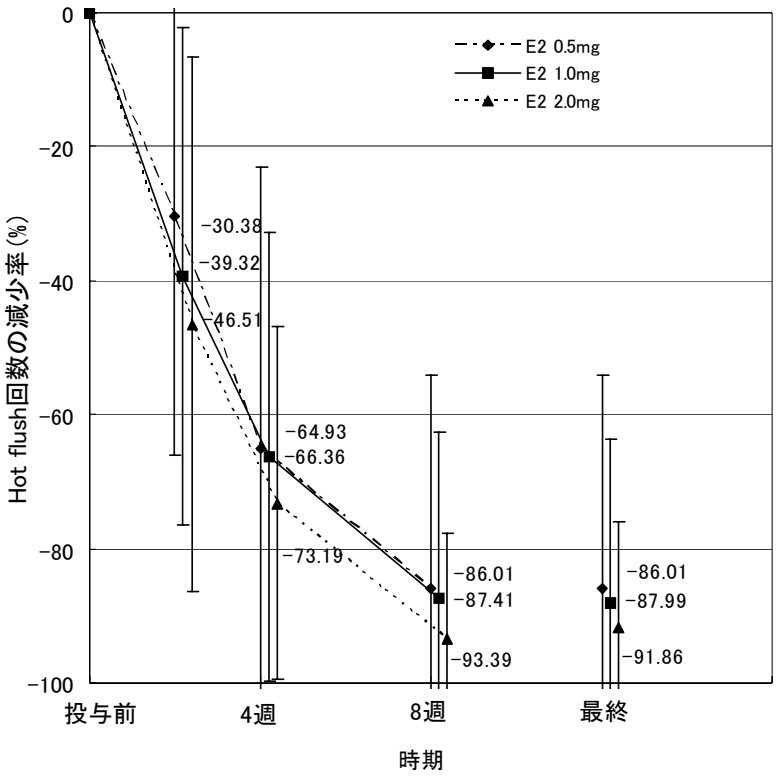

図 4 ホットフラッシュの回数減少率の推移（%）

平均と SD で示す．総括報告書 No.B123, 表 11-4-3 から作図

4 週後，8 週後，最終評価時（8 週後又は中止時）におけるホットフラッシュの回数減少率に，投与群間に有意差は認められなかった（一元配置分散分析及び Dunnett 検定，表 3及び表 4 参照）．

表 4 ホットフラッシュの回数減少率の比較

E2 用量群	被験者数	平均(%)±SD	最小値	最大値	一元配置分散分析	Dunnett 検定
合計	68	-88.71±24.48	-100.0	33.3	0.717	E2 0.5mg 対 E2 1.0mg : p=0.554 E2 0.5mg 対 E2 2.0mg : p=0.329
E2 0.5mg	22	-86.01±32.00	-100.0	33.3		
E2 1.0mg	22	-87.99±24.37	-100.0	0.0		
E2 2.0mg	24	-91.86±15.84	-100.0	-33.3		

8 週後又は中止時の結果．総括報告書 No.B123，14-2-3

(2) ホットフラッシュの程度

表 5に示すとおり，ホットフラッシュの程度は各投与群とも顕著に改善した．本剤を投与した E2 用量 0.5mg 群では投与前のホットフラッシュの程度の平均スコアが 2.04 であった．ホットフラッシュの程度の改善は 2 週後から認められ，最終評価時（8 週後又は中止時）には平均値が 0.36 まで減少した．4 週後，8 週後，最終評価時（8 週後又は中止時）とも投与群間に有意差は認められなかった（一元配置分散分析及び Tukey 検定）．最終評価時（8 週後又は中止時）の有効率（中等度改善以上を示した被験者の割合）は，E2 用量 0.5mg 群で 86.4%（19/22 例）であった．改善度の判定結果に投与群間の有意差は認められなかった（Kruskal-Wallis 検定及び Tukey 検定，表 6 参照）．

表 5 ホットフラッシュの程度の推移

時期	E2 用量群	被験者数	平均	SD	最小値	最大値	一元配置分散分析	Tukey 検定
投与前	合計	70	2.04	0.55	1	3	1.000	E2 0.5mg 対 E2 1.0mg : p=1.000 E2 0.5mg 対 E2 2.0mg : p=1.000 E2 1.0mg 対 E2 2.0mg : p=1.000
	E2 0.5mg	23	2.04	0.47	1	3		
	E2 1.0mg	23	2.04	0.64	1	3		
	E2 2.0mg	24	2.04	0.55	1	3		
2 週後	合計	60	1.27	0.66	0	3	0.442	E2 0.5mg 対 E2 1.0mg : p=0.996 E2 0.5mg 対 E2 2.0mg : p=0.526 E2 1.0mg 対 E2 2.0mg : p=0.486
	E2 0.5mg	21	1.33	0.73	0	3		
	E2 1.0mg	20	1.35	0.59	0	2		
	E2 2.0mg	19	1.11	0.66	0	2		
4 週後	合計	68	0.85	0.68	0	3	0.841	E2 0.5mg 対 E2 1.0mg : p=0.974 E2 0.5mg 対 E2 2.0mg : p=0.932 E2 1.0mg 対 E2 2.0mg : p=0.830
	E2 0.5mg	22	0.86	0.77	0	3		
	E2 1.0mg	22	0.91	0.61	0	2		
	E2 2.0mg	24	0.79	0.66	0	2		
8 週後	合計	65	0.37	0.63	0	3	0.849	E2 0.5mg 対 E2 1.0mg : p=0.940 E2 0.5mg 対 E2 2.0mg : p=0.969 E2 1.0mg 対 E2 2.0mg : p=0.837
	E2 0.5mg	22	0.36	0.73	0	3		
	E2 1.0mg	21	0.43	0.60	0	2		
	E2 2.0mg	22	0.32	0.57	0	2		
最終	合計	68	0.38	0.62	0	3	0.970	E2 0.5mg 対 E2 1.0mg : p=0.969 E2 0.5mg 対 E2 2.0mg : p=0.998 E2 1.0mg 対 E2 2.0mg : p=0.982
	E2 0.5mg	22	0.36	0.73	0	3		
	E2 1.0mg	22	0.41	0.59	0	2		
	E2 2.0mg	24	0.38	0.58	0	2		

総括報告書 No.B123，表 11-4-6

表 6 ホットフラッシュの程度の改善度（最終）

E2 用量群	ホットフラッシュの程度の改善 被験者数(%)					評価対象外	解析対象	中等度改善以上 (%)	Kruskal-Wallis 検定	Tukey 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	12 (54.5)	7 (31.8)	2 (9.1)	1 (4.5)	0 (0.0)	1	22	19 (86.4)	p=0.754	0.5 対 1.0 p=0.804	65.1～97.1
E2 1.0mg	14 (63.6)	6 (27.3)	1 (4.5)	1 (4.5)	0 (0.0)	2	22	20 (90.9)		0.5 対 2.0 p=0.789	70.8～98.9
E2 2.0mg	16 (66.7)	4 (16.7)	4 (16.7)	0 (0.0)	0 (0.0)	1	24	20 (83.3)		1.0 対 2.0 p=0.999	62.6～95.3

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(3) 発汗

発汗の程度は各投与群とも顕著に改善した．本剤を投与した E2 用量 0.5mg 群では投与前の発汗の程度の平均スコアが 1.95 であった．発汗の程度の改善は 2 週後から認められ，最終評価時（8 週後又は中止時）には平均スコアが 0.62 まで減少した．一元配置分散分析では投与群間に有意差は認められなかった．8 週後及び最終評価時（8 週後又は中止時）には，投与群間に有意差は認められなかった（Tukey 検定，表 7 参照）．また，最終評価時（8 週後又は中止時）の有効率（中等度改善以上を示した被験者の割合）は，E2 用量 0.5mg 群で 71.4%（15/21 例）であった．改善度の判定結果に投与群間の有意差は認められなかった（Kruskal-Wallis 検定及び Tukey 検定，表 8 参照）．

表 7 発汗の程度の推移

時期	E2 用量群	被験者数	平均	SD	最小値	最大値	一元配置分散分析	Tukey 検定
投与前	合計	64	2.09	0.61	1	3	0.401	E2 0.5mg 対 E2 1.0mg：p=0.400 E2 0.5mg 対 E2 2.0mg：p=0.587 E2 1.0mg 対 E2 2.0mg：p=0.939
	E2 0.5mg	22	1.95	0.58	1	3		
	E2 1.0mg	20	2.20	0.62	1	3		
	E2 2.0mg	22	2.14	0.64	1	3		
2 週後	合計	55	1.18	0.72	0	3	0.471	E2 0.5mg 対 E2 1.0mg：p=0.675 E2 0.5mg 対 E2 2.0mg：p=0.915 E2 1.0mg 対 E2 2.0mg：p=0.452
	E2 0.5mg	20	1.15	0.81	0	3		
	E2 1.0mg	17	1.35	0.49	1	2		
	E2 2.0mg	18	1.06	0.80	0	3		
4 週後	合計	62	0.84	0.75	0	3	0.870	E2 0.5mg 対 E2 1.0mg：p=0.987 E2 0.5mg 対 E2 2.0mg：p=0.930 E2 1.0mg 対 E2 2.0mg：p=0.866
	E2 0.5mg	21	0.86	0.85	0	3		
	E2 1.0mg	19	0.89	0.66	0	2		
	E2 2.0mg	22	0.77	0.75	0	2		
8 週後	合計	59	0.47	0.73	0	3	0.473	E2 0.5mg 対 E2 1.0mg：p=0.448 E2 0.5mg 対 E2 2.0mg：p=0.741 E2 1.0mg 対 E2 2.0mg：p=0.876
	E2 0.5mg	21	0.62	0.86	0	3		
	E2 1.0mg	18	0.33	0.59	0	2		
	E2 2.0mg	20	0.45	0.69	0	2		
最終	合計	62	0.50	0.74	0	3	0.573	E2 0.5mg 対 E2 1.0mg：p=0.542 E2 0.5mg 対 E2 2.0mg：p=0.861 E2 1.0mg 対 E2 2.0mg：p=0.840
	E2 0.5mg	21	0.62	0.86	0	3		
	E2 1.0mg	19	0.37	0.60	0	2		
	E2 2.0mg	22	0.50	0.74	0	2		

総括報告書 No.B123，表 11-4-6

表 8 発汗の改善度（最終）

E2 用量群	発汗改善度　被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の95%信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	9 (42.9)	6 (28.6)	3 (14.3)	3 (14.3)	0 (0.0)	2	21	15 (71.4)	p=0.151	0.5 対 1.0 p=0.128	47.8～88.7
E2 1.0mg	13 (68.4)	5 (26.3)	1 (5.3)	0 (0.0)	0 (0.0)	5	19	18 (94.7)		0.5 対 2.0 p=0.559	74.0～99.9
E2 2.0mg	13 (59.1)	4 (18.2)	4 (18.2)	1 (4.5)	0 (0.0)	3	22	17 (77.3)		1.0 対 2.0 p=0.620	54.6～92.2

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(4) 腟乾燥感

腟乾燥感は各投与群とも顕著に改善した．本剤を投与した E2 用量 0.5mg 群では投与前の腟乾燥感の程度の平均スコアが 1.23 であった．腟乾燥感の改善は 2 週後から認められ，最終評価時（8 週後又は中止時）には，平均スコアが 0.67 まで減少した．最終評価時（8 週後又は中止時）の平均スコアには，投与群間に有意差は認められなかった（一元配置分散分析及び Tukey 検定，表 9 参照）．最終評価時（8 週後又は中止時）の有効率（中等度改善以上を示した被験者の割合）も，E2 用量 0.5mg 群の 41.7%（5/12 例）と比較して E2 用量 1.0mg 群，E2 用量 2.0mg 群において高い傾向にあった．改善度の判定結果に投与群間の有意差は認められなかった（Kruskal-Wallis 検定及び Tukey 検定，表 10 参照）．

表 9 腟乾燥感の程度の推移

時期	E2 用量群	被験者数	平均	SD	最小値	最大値	一元配置分散分析	Tukey 検定
投与前	合計	41	1.51	0.75	0	3	0.211	E2 0.5mg 対 E2 1.0mg：p=0.195 E2 0.5mg 対 E2 2.0mg：p=0.455 E2 1.0mg 対 E2 2.0mg：p=0.783
	E2 0.5mg	13	1.23	0.44	1	2		
	E2 1.0mg	12	1.75	0.75	1	3		
	E2 2.0mg	16	1.56	0.89	0	3		
2 週後	合計	34	0.82	0.72	0	2	0.248	E2 0.5mg 対 E2 1.0mg：p=0.656 E2 0.5mg 対 E2 2.0mg：p=0.665 E2 1.0mg 対 E2 2.0mg：p=0.219
	E2 0.5mg	12	0.83	0.83	0	2		
	E2 1.0mg	10	1.10	0.57	0	2		
	E2 2.0mg	12	0.58	0.67	0	2		
4 週後	合計	39	0.64	0.58	0	2	0.216	E2 0.5mg 対 E2 1.0mg：p=0.193 E2 0.5mg 対 E2 2.0mg：p=0.737 E2 1.0mg 対 E2 2.0mg：p=0.507
	E2 0.5mg	12	0.83	0.72	0	2		
	E2 1.0mg	12	0.42	0.51	0	1		
	E2 2.0mg	15	0.67	0.49	0	1		
8 週後	合計	36	0.53	0.61	0	2	0.250	E2 0.5mg 対 E2 1.0mg：p=0.273 E2 0.5mg 対 E2 2.0mg：p=0.975 E2 1.0mg 対 E2 2.0mg：p=0.357
	E2 0.5mg	12	0.67	0.65	0	2		
	E2 1.0mg	11	0.27	0.47	0	1		
	E2 2.0mg	13	0.62	0.65	0	2		
最終	合計	39	0.51	0.60	0	2	0.403	E2 0.5mg 対 E2 1.0mg：p=0.375 E2 0.5mg 対 E2 2.0mg：p=0.836 E2 1.0mg 対 E2 2.0mg：p=0.670
	E2 0.5mg	12	0.67	0.65	0	2		
	E2 1.0mg	12	0.33	0.49	0	1		
	E2 2.0mg	15	0.53	0.64	0	2		

総括報告書 No.B123，表 11-4-6

表 10 腟乾燥感の改善度（最終）

E2 用量群	腟乾燥感改善度　被験者数（%）					評価対象外	解析対象	中等度改善以上（%）	Kruskal-Wallis 検定	Tukey 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	2 (16.7)	3 (25.0)	2 (16.7)	5 (41.7)	0 (0.0)	11	12	5 (41.7)	p=0.227	0.5 対 1.0 p=0.229	15.2～72.3
E2 1.0mg	7 (58.3)	1 (8.3)	1 (8.3)	3 (25.0)	0 (0.0)	12	12	8 (66.7)		0.5 対 2.0 p=0.538	34.9～90.1
E2 2.0mg	5 (33.3)	5 (33.3)	1 (6.7)	3 (20.0)	1 (6.7)	10	15	10 (66.7)		1.0 対 2.0 p=0.654	38.4～88.2

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(5) 不眠

不眠は各投与群とも顕著に改善した．4 週後，8 週後，最終評価時（8 週後又は中止時）には，本剤を投与した E2 用量 0.5mg 群と比較して，E2 用量 1.0mg 群及び E2 用量 2.0mg 群の症状改善効果はより優れる傾向が認められ，一元配置分散分析では投与群間の有意差は認められなかった．Tukey 検定では，4 週後の症状程度のスコアは E2 用量 0.5mg 群と比較して E2 用量 2.0mg 群で有意に低かった（p＝0.046，表 11 参照）．最終評価時（8 週後又は中止時）の改善度の判定結果（表 12 参照）には，E2 用量群間で有意差（Kruskal-Wallis 検定，p＝0.024）が認められ，E2 用量 0.5mg 群と比較して E2 用量 2.0mg 群で有意に高かった（Tukey 検定，p＝0.029）．

表 11 不眠の程度の推移

時期	E2 用量群	被験者数	平均	SD	最小値	最大値	一元配置分散分析	Tukey 検定
投与前	合計	34	1.79	0.81	0	3	0.170	E2 0.5mg 対 E2 1.0mg：p=0.295 E2 0.5mg 対 E2 2.0mg：p=0.206 E2 1.0mg 対 E2 2.0mg：p=1.000
	E2 0.5mg	13	1.46	0.78	0	2		
	E2 1.0mg	8	2.00	0.76	1	3		
	E2 2.0mg	13	2.00	0.82	1	3		
2 週後	合計	30	1.13	0.97	0	3	0.680	E2 0.5mg 対 E2 1.0mg：p=0.786 E2 0.5mg 対 E2 2.0mg：p=0.975 E2 1.0mg 対 E2 2.0mg：p=0.669
	E2 0.5mg	11	1.18	0.98	0	3		
	E2 1.0mg	8	0.88	0.99	0	2		
	E2 2.0mg	11	1.27	1.01	0	3		
4 週後	合計	31	0.87	0.88	0	3	0.053	E2 0.5mg 対 E2 1.0mg：p=0.262 E2 0.5mg 対 E2 2.0mg：p=0.046 E2 1.0mg 対 E2 2.0mg：p=0.786
	E2 0.5mg	11	1.36	0.92	0	3		
	E2 1.0mg	8	0.75	0.89	0	2		
	E2 2.0mg	12	0.50	0.67	0	2		
8 週後	合計	32	0.69	0.86	0	3	0.495	E2 0.5mg 対 E2 1.0mg：p=0.744 E2 0.5mg 対 E2 2.0mg：p=0.476 E2 1.0mg 対 E2 2.0mg：p=0.947
	E2 0.5mg	12	0.92	0.90	0	3		
	E2 1.0mg	8	0.63	0.92	0	2		
	E2 2.0mg	12	0.50	0.80	0	2		
最終	合計	33	0.70	0.85	0	3	0.532	E2 0.5mg 対 E2 1.0mg：p=0.738 E2 0.5mg 対 E2 2.0mg：p=0.520 E2 1.0mg 対 E2 2.0mg：p=0.973
	E2 0.5mg	12	0.92	0.90	0	3		
	E2 1.0mg	8	0.63	0.92	0	2		
	E2 2.0mg	13	0.54	0.78	0	2		

総括報告書 No.B123，表 11-4-6

表 12 不眠の改善度（最終）

E2 用量群	不眠改善度 被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の95%信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	1 (8.3)	4 (33.3)	4 (33.3)	0 (0.0)	3 (25.0)	11	12	5 (41.7)	p=0.024	0.5 対 1.0 p=0.127	15.2～72.3
E2 1.0mg	5 (62.5)	1 (12.5)	0 (0.0)	2 (25.0)	0 (0.0)	16	8	6 (75.0)		0.5 対 2.0 p=0.029	34.9～96.8
E2 2.0mg	8 (61.5)	2 (15.4)	2 (15.4)	1 (7.7)	0 (0.0)	12	13	10 (76.9)		1.0 対 2.0 p=0.985	46.2～95.0

最終評価時（8 週後又は中止時）の結果 総括報告書 No.B123，表 11-4-5

(6) 腟炎

腟炎は本剤を投与した E2 用量 0.5mg 群と E2 用量 1.0mg 群で顕著に改善したが，投与群間の有意差は認められなかった（表 13 参照）.

表 13 腟炎の改善度（最終）

E2 用量群	腟炎改善度 被験者数（%）					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の95%信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	1 (25.0)	1 (25.0)	0 (0.0)	1 (25.0)	1 (25.0)	19	4	2 (50.0)	p=0.843	0.5 対 1.0 p=0.952	6.8～93.2
E2 1.0mg	1 (25.0)	1 (25.0)	0 (0.0)	2 (50.0)	0 (0.0)	20	4	2 (50.0)		0.5 対 2.0 p=0.979	6.8～93.2
E2 2.0mg	1 (14.3)	1 (14.3)	1 (14.3)	3 (42.9)	1 (14.3)	18	7	2 (28.6)		1.0 対 2.0 p=0.821	3.7～71.0

最終評価時（8 週後又は中止時）の結果 総括報告書 No.B123，表 11-4-5

(7) 精神神経症状

精神神経症状（頭痛，めまいなど）の改善度に E2 用量群間の有意差（Kruskal-Wallis 検定，p＝0.026）が認められた．本剤を投与した E2 用量 0.5mg 群と比較して，E2 用量 2.0mg 群では有意に優れ（Tukey 検定，p＝0.043），E2 用量 1.0mg 群では有意差はなかったものの，優れる傾向が認められた（表 14 参照）.

表 14 精神神経症状の改善度（最終）

E2 用量群	精神神経症状改善度 被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の95%信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	2 (14.3)	1 (7.1)	5 (35.7)	4 (28.6)	2 (14.3)	9	14	3 (21.4)	p=0.026	0.5 対 1.0 p=0.058	4.7～50.8
E2 1.0mg	6 (40.0)	5 (33.3)	1 (6.7)	3 (20.0)	0 (0.0)	9	15	11 (73.3)		0.5 対 2.0 p=0.043	44.9～92.2
E2 2.0mg	7 (38.9)	5 (27.8)	4 (22.2)	1 (5.6)	1 (5.6)	7	18	12 (66.7)		1.0 対 2.0 p=0.993	41.0～86.7

最終評価時（8 週後又は中止時）の結果 総括報告書 No.B123，表 11-4-5

(8)　運動器系症状

運動器系症状（肩こり，腰痛など）は各投与群とも改善したが，投与群間の有意差は認められなかった（表 15 参照）．

表 15 運動器系症状の改善度（最終）

E2 用量群	運動器系症状改善度　被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	4 (25.0)	2 (12.5)	4 (25.0)	5 (31.3)	1 (6.3)	7	16	6 (37.5)	p=0.945	0.5 対 1.0 p=0.984	15.2～64.6
E2 1.0mg	3 (17.6)	6 (35.3)	1 (5.9)	7 (41.2)	0 (0.0)	7	17	9 (52.9)		0.5 対 2.0 p=0.932	27.8～77.0
E2 2.0mg	4 (21.1)	5 (26.3)	5 (26.3)	3 (15.8)	2 (10.5)	6	19	9 (47.4)		1.0 対 2.0 p=0.993	24.4～71.1

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(9)　知覚障害

知覚障害（手足のしびれなど）は各投与群で改善したが，投与群間の有意差は認められなかった（表 16 参照）．

表 16 知覚障害の改善度（最終）

E2 用量群	知覚障害改善度　被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	1 (10.0)	4 (40.0)	1 (10.0)	4 (40.0)	0 (0.0)	13	10	5 (50.0)	p=0.262	0.5 対 1.0 p=0.377	18.7～81.3
E2 1.0mg	1 (11.1)	1 (11.1)	0 (0.0)	7 (77.8)	0 (0.0)	15	9	2 (22.2)		0.5 対 2.0 p=0.818	2.8～60.0
E2 2.0mg	2 (25.0)	3 (37.5)	1 (12.5)	1 (12.5)	1 (12.5)	17	8	5 (62.5)		1.0 対 2.0 p=0.322	24.5～91.5

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(10) 排尿障害

排尿障害の改善度は各投与群とも低かった（表 17 参照）．

表 17 排尿障害の改善度（最終）

E2 用量群	排尿障害改善度 被験者数(%)					評価対象外	解析対象	中等度改善以上(%)	Kruskal-Wallis 検定	Tukey 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変	悪化						
E2 0.5mg	0 (0.0)	2 (25.0)	0 (0.0)	5 (62.5)	1 (12.5)	15	8	2 (25.0)	p=0.432	0.5 対 1.0 p=0.896	3.2～65.1
E2 1.0mg	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	20	4	0 (0.0)		0.5 対 2.0 p=0.725	—
E2 2.0mg	0 (0.0)	1 (25.0)	1 (25.0)	2 (50.0)	0 (0.0)	21	4	1 (25.0)		1.0 対 2.0 p=0.285	0.6～80.6

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123，表 11-4-5

(11) 全般改善度

中等度以上の改善が，本剤を投与した E2 用量 0.5mg 群，E2 用量 1.0mg 群及び E2 用量 2.0mg 群でそれぞれ 82.6%（19/23 例），91.7%（22/24 例）及び 96.0%（24/25 例）の被験者に認められ，E2 用量に依存して増加する傾向が認められた．全般改善度の判定結果に投与群間の有意差は認められなかった（表 18 参照）．年齢，診断名，罹病期間，閉経後期間，前治療薬の有無，併用薬の有無などの背景因子によって区分した被験者部分集団で比較した結果，全般改善度にこれらの要因による影響は認められなかった（(13)部分集団における結果の比較 参照）．

表 18 全般改善度（最終）

E2 用量群	全般改善度 被験者数(%)				合計	中等度改善以上(%)	Jonckheere 検定*	Dunnett 検定	有効率の 95% 信頼区間
	著明改善	中等度改善	軽度改善	不変					
E2 0.5mg	11 (47.8)	8 (34.8)	3 (13.0)	1 (4.3)	23	19 (82.6)	p=0.094	0.5 対 1.0 p=0.157	61.2～95.0
E2 1.0mg	16 (66.7)	6 (25.0)	1 (4.2)	1 (4.2)	24	22 (91.7)		0.5 対 2.0 p=0.143	73.0～99.0
E2 2.0mg	16 (64.0)	8 (32.0)	1 (4.0)	0 (0.0)	25	24 (96.0)			79.6～99.9

最終評価時（8 週後又は中止時）の結果　総括報告書 No.B123　表 11-4-1

*：対立仮説；E2 0.5mg ≦ E2 1.0mg ≦ E2 2.0mg

(12) 血中 E2 濃度

血中 E2 濃度の推移を表 19に，血中 FSH 濃度の推移を表 20に示す．8 週後の平均血中 E2 濃度は本剤を投与した E2 用量 0.5mg 群で 26.86pg/mL，E2 用量 1.0mg 群で 58.64pg/mL であり，いずれも閉経前女性の卵胞初期濃度（20～60pg/mL）に達していた．血中 E2 濃度は E2 投与量に依存して増加し，4 週後及び 8 週後における E2 用量 0.5mg 群と E2 用量 2.0mg 群の間に有意差が認められた．一方，血中 FSH 濃度は E2 投与量に依存して減少し，4 週後における E2 用量 0.5mg 群と E2 用量 2.0mg 群の間に有意差が認められた．

表 19 血中 E2 濃度（pg/mL）の推移

時期	E2 用量群	被験者数	平均 (pg/mL)	SD	最小値	最大値	投与前との比較 (t 検定)	Tukey 検定
投与前	合計	69	6.53	21.12	0.5	161.6	-	E2 0.5mg 対 E2 1.0mg：p=0.478 E2 0.5mg 対 E2 2.0mg：p=0.894 E2 1.0mg 対 E2 2.0mg：p=0.744
	E2 0.5mg	22	3.10	3.75	0.7	17.2	-	
	E2 1.0mg	23	10.47	33.51	0.5	161.6	-	
	E2 2.0mg	24	5.92	14.34	1.2	72.2	-	
4 週後	合計	68	49.82	48.09	1.8	220.1	-	E2 0.5mg 対 E2 1.0mg：p=0.063 E2 0.5mg 対 E2 2.0mg：p=0.000 E2 1.0mg 対 E2 2.0mg：p=0.000
	E2 0.5mg	22	16.15	13.65	3.1	53.8	0.000	
	E2 1.0mg	23	41.85	25.87	1.8	98.0	0.001	
	E2 2.0mg	23	90.00	57.51	2.2	220.1	0.000	
8 週後	合計	27	60.96	39.89	9.5	177.3	-	E2 0.5mg 対 E2 1.0mg：p=0.147 E2 0.5mg 対 E2 2.0mg：p=0.003 E2 1.0mg 対 E2 2.0mg：p=0.153
	E2 0.5mg	7	26.86	23.66	9.5	75.6	0.032	
	E2 1.0mg	10	58.64	12.26	45.7	86.7	0.000	
	E2 2.0mg	10	87.16	49.00	26.7	177.3	0.000	

総括報告書 No.B123，表 11-4-8

表 20 血中 FSH 濃度（mIU/mL）の推移

時期	E2 用量群	被験者数	平均 (mIU/mL)	SD	最小値	最大値	投与前との比較 (t 検定)	Tukey 検定
投与前	合計	69	83.97	32.04	28.0	223.5	-	E2 0.5mg 対 E2 1.0mg：p=0.519 E2 0.5mg 対 E2 2.0mg：p=0.751 E2 1.0mg 対 E2 2.0mg：p=0.161
	E2 0.5mg	22	85.07	32.69	36.6	175.9	-	
	E2 1.0mg	23	74.70	25.87	28.0	122.5	-	
	E2 2.0mg	24	91.84	35.60	38.9	223.5	-	
4 週後	合計	68	49.61	21.81	9.0	126.8	-	E2 0.5mg 対 E2 1.0mg：p=0.006 E2 0.5mg 対 E2 2.0mg：p=0.001 E2 1.0mg 対 E2 2.0mg：p=0.703
	E2 0.5mg	22	63.82	21.44	21.8	126.8	0.000	
	E2 1.0mg	23	45.13	17.06	9.0	69.4	0.000	
	E2 2.0mg	23	40.49	20.21	10.5	107.0	0.000	
8 週後	合計	29	42.46	16.06	10.9	71.1	-	E2 0.5mg 対 E2 1.0mg：p=0.310 E2 0.5mg 対 E2 2.0mg：p=0.056 E2 1.0mg 対 E2 2.0mg：p=0.546
	E2 0.5mg	7	53.29	10.75	35.8	71.1	0.033	
	E2 1.0mg	11	42.42	12.52	20.8	59.1	0.003	
	E2 2.0mg	11	35.61	19.04	10.9	67.1	0.000	

総括報告書 No.B123，表 11-4-8

(13) 部分集団における結果の比較

投与 8 週後（又は中止時）の全般改善度を，年齢（50 歳未満，50 歳以上），診断名（更年期障害，卵巣欠落症状），罹病期間（3 年未満，3 年以上），閉経後期間（3 年未満，3 年以上），前治療薬の有無，併用薬の有無によって区分した被験者部分集団で比較した結果，これらの要因による全般改善度への影響は認められなかった（表 21 ～表 28参照）．

表 21 全般改善度の層別解析（年齢による層別）

E2 用量群	年齢	全般改善度　被験者数				解析対象	中等度改善以上 被験者数(%)	95% 信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	50 歳未満	5	2	2	0	9	7 (77.8)	40.0～ 97.2
	50 歳以上	6	6	1	1	14	12 (85.7)	57.2～ 98.2
E2 1.0mg	50 歳未満	8	0	0	0	8	8 (100.0)	63.1～100.0
	50 歳以上	8	6	1	1	16	14 (87.5)	61.7～ 98.4
E2 2.0mg	50 歳未満	4	2	0	0	6	6 (100.0)	54.1～100.0
	50 歳以上	12	6	1	0	19	18 (94.7)	74.0～ 99.9

最終評価時（8 週後又は中止時）の全般改善度　総括報告書 No.B123, 表 11-4-16

表 22 全般改善度の層別解析（診断名による層別）

E2 用量群	診断名	全般改善度　被験者数				解析対象	中等度改善以上 被験者数(%)	95% 信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	更年期障害	6	8	3	0	17	14 (82.4)	56.6～ 96.2
	卵巣欠落症状	5	0	0	1	6	5 (83.3)	35.9～ 99.6
E2 1.0mg	更年期障害	12	6	0	0	18	18 (100.0)	81.5～100.0
	卵巣欠落症状	4	0	1	1	6	4 (66.7)	22.3～ 95.7
E2 2.0mg	更年期障害	14	5	1	0	20	19 (95.0)	75.1～ 99.9
	卵巣欠落症状	2	3	0	0	5	5 (100.0)	47.8～100.0

最終評価時（8 週後又は中止時）の全般改善度　総括報告書 No.B123, 表 11-4-16

表 23 全般改善度の層別解析（罹病期間による層別）

E2 用量群	罹病期間	全般改善度　被験者数				解析対象	中等度改善以上 被験者数(%)	95% 信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	3 年未満	10	7	1	0	18	17 (94.4)	72.7～ 99.9
	3 年以上	1	1	2	1	5	2 (40.0)	5.3～ 85.3
E2 1.0mg	3 年未満	11	4	1	0	16	15 (93.8)	69.8～ 99.8
	3 年以上	5	2	0	1	8	7 (87.5)	47.3～ 99.7
E2 2.0mg	3 年未満	13	5	1	0	19	18 (94.7)	74.0～ 99.9
	3 年以上	3	3	0	0	6	6 (100.0)	54.1～100.0

最終評価時（8 週後又は中止時）の全般改善度　総括報告書 No.B123, 表 11-4-16

表 24 全般改善度の層別解析（閉経後の期間による層別）

E2 用量群	閉経後期間	全般改善度　被験者数			解析対象	中等度改善以上被験者数(%)	95%信頼区間
		著明改善	中等度改善	軽度改善			
E2 0.5mg	3年未満	4	3	1	8	7 (87.5)	47.3～99.7
	3年以上	1	5	1	7	6 (85.7)	42.1～99.6
E2 1.0mg	3年未満	5	2	0	7	7 (100.0)	-
	3年以上	6	3	0	9	9 (100.0)	-
E2 2.0mg	3年未満	4	2	0	6	6 (100.0)	-
	3年以上	7	2	0	9	9 (100.0)	-

閉経時期が不明の被験者及び両卵巣摘出被験者は集計から除いた.

最終評価時（8週後又は中止時）の全般改善度　総括報告書No.B123，表11-4-16

表 25 全般改善度の層別解析（前治療薬有無による層別）

E2 用量群	前治療薬	全般改善度　被験者数				解析対象	中等度改善以上被験者数(%)	95%信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	無	8	4	3	1	16	12 (75.0)	47.6～ 92.7
	有	3	4	0	0	7	7 (100.0)	59.0～100.0
E2 1.0mg	無	12	4	1	0	17	16 (94.1)	71.3～ 99.9
	有	4	2	0	1	7	6 (85.7)	42.1～ 99.6
E2 2.0mg	無	11	4	1	0	16	15 (93.8)	69.8～ 99.8
	有	5	4	0	0	9	9 (100.0)	66.4～100.0

最終評価時（8週後又は中止時）の全般改善度　総括報告書No.B123，表11-4-16

表 26 全般改善度の層別解析（併用薬有無による層別）

E2 用量群	併用薬	全般改善度　被験者数				解析対象	中等度改善以上被験者数(%)	95%信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	無	11	4	2	0	17	15 (88.2)	63.6～ 98.5
	有	0	4	1	1	6	4 (66.7)	22.3～ 95.7
E2 1.0mg	無	10	4	1	1	16	14 (87.5)	61.7～ 98.4
	有	6	2	0	0	8	8 (100.0)	63.1～100.0
E2 2.0mg	無	14	5	1	0	20	19 (95.0)	75.1～ 99.9
	有	2	3	0	0	5	5 (100.0)	47.8～100.0

最終評価時（8週後又は中止時）の全般改善度　総括報告書No.B123，表11-4-16

表 27 全般改善度の層別解析（合併症有無による層別）

E2 用量群	合併症	全般改善度　被験者数				解析対象	中等度改善以上被験者数(%)	95%信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	無	11	3	2	0	16	14 (87.5)	61.7～ 98.4
	有	0	5	1	1	7	5 (71.4)	29.0～ 96.3
E2 1.0mg	無	13	4	1	1	19	17 (89.5)	66.9～ 98.7
	有	3	2	0	0	5	5 (100.0)	47.8～100.0
E2 2.0mg	無	14	5	1	0	20	19 (95.0)	75.1～ 99.9
	有	2	3	0	0	5	5 (100.0)	47.8～100.0

最終評価時（8週後又は中止時）の全般改善度　総括報告書No.B123，表11-4-16

表 28 全般改善度の層別解析（既往歴有無による層別）

E2 用量群	既往歴	全般改善度　被験者数				解析対象	中等度改善以上被験者数(%)	95%信頼区間
		著明改善	中等度改善	軽度改善	不変			
E2 0.5mg	無	3	4	2	0	9	7 (77.8)	40.0～ 97.2
	有	8	4	1	1	14	12 (85.7)	57.2～ 98.2
E2 1.0mg	無	4	3	0	0	7	7 (100.0)	59.0～100.0
	有	12	3	1	1	17	15 (88.2)	63.6～ 98.5
E2 2.0mg	無	6	3	0	0	9	9 (100.0)	66.4～100.0
	有	10	5	1	0	16	15 (93.8)	69.8～ 99.8

最終評価時（8週後又は中止時）の全般改善度　総括報告書No.B123，表11-4-16

試験番号　：300107（報告書 No.BC69）

治験の標題：自然閉経後の更年期障害及び両側卵巣摘出による卵巣欠落症状を有する患者を対象に連続 2 周期（8 週間）投与し，SH T 546（E2 のみを有効成分として含有する製剤）の至適用量を検討することを目的とした多施設共同，無作為化，二重盲検，プラセボ対照比較試験

1.　試験方法の概略

自然閉経後の更年期障害又は両側卵巣摘出による卵巣欠落症状を有する患者を対象に，多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験を行い，E2 の至適用量を検討した．ホットフラッシュを 1 日平均 3 回以上有し，その程度が中等度以上である患者 211 例（44～64 歳：平均 52.9 歳）が登録され，内訳は自然閉経後の更年期障害が 200 例，両側卵巣摘出による卵巣欠落症状が 11 例であった．E2 0.5mg 錠，E2 1.0mg 錠又はプラセボ錠を，それぞれ 1 日 1 回 1 錠，8 週間（2 周期）にわたって投与した（図 5 参照）．

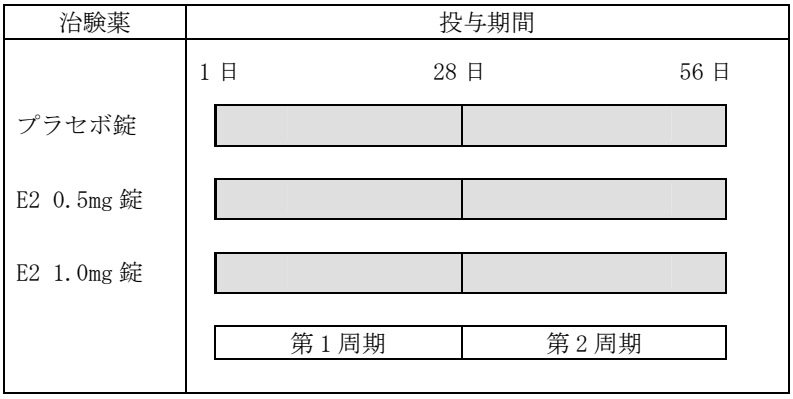

図 5 投与スケジュール

2.　試験対象集団

(1)　主要な組入れ・除外基準

1)　組入れ基準

更年期障害又は両側卵巣摘出による卵巣欠落症状と診断された患者で，下記の条件をすべて満たすものを対象とする．入院と外来の別は問わない．なお，患者は本治験に複数回組入れられてはならない．

1. 40 歳以上 65 歳未満の患者

2. 以下のいずれかを満たす患者

- 最終月経後 1 年以上経過している患者
- 最終月経後 6 箇月以上 1 年未満の患者で，来院 1（仮登録時）に測定した血清中 E2 濃度が 20pg/mL（ラジオイムノアッセイ（radio immunoassay：RIA 法））以下かつ FSH 濃度が 30mIU/mL（RIA 法）以上の患者
- 両側卵巣摘出後 1 箇月以上経過している患者
- 閉経前の子宮摘出により最終月経日不明の場合は来院 1 の血清中 E2 濃度が 20pg/mL（RIA 法）以下かつ FSH 濃度が 30mIU/mL（RIA 法）以上の患者

3. 投与開始前 7 日間（欠測日を除く 7 日間）で ホットフラッシュを 1 日平均 3 回以上有し，症状の程度が中等度以上の患者

2) 除外基準

1. 心理テスト（SDS）により，合計点数が 50 点以上の患者
2. 乳癌，子宮内膜癌又は子宮内膜増殖症を有する患者
3. 血栓症，塞栓症（脳血管障害，閉塞性動脈硬化症，静脈血栓症）又はその既往を有する患者
4. 5 分間安静にした後，坐位で測定し，収縮期血圧値が 160mmHg 又は拡張期血圧値が 100mmHg 以上の患者
5. 片頭痛又はてんかんを有する患者
6. インスリン治療を行っている糖尿病患者
7. エストロゲン製剤に対して過敏症の既往のある患者
8. 重篤な肝障害（活動性ウィルス性肝炎，肝硬変，急性アルコール性肝炎など）並びに腎障害（クレアチニン 2mg/dL 以上）を有する患者
9. 抗不整脈薬，抗狭心症薬，強心薬などによる治療を必要とする重篤な心疾患（不安定狭心症，心筋梗塞の既往，心不全など）を有する患者
10. 原因不明の不正出血を有する患者
11. 未治療の甲状腺機能障害（機能亢進症又は機能低下症）を有する患者
12. スクリーニング開始前 3 箇月以内に別の治験に参加していた患者
13. 抗精神病薬の投与を過去に受けたことがある又は投与を受けている患者．抗うつ薬又は副腎皮質ホルモン（経口又は注射剤）の投与を受けている患者
14. スクリーニング開始日以前の指定された下記期間に下記薬剤の投与を受けている患者

- スクリーニング開始日前 12 週間：

性ステロイドホルモンデポー剤（プリモジアン・デポー®（エナント酸テストステロン・吉草酸エストラジオール），エスジン・デポー®（エナント酸テストステロン・プロピオン酸テストステロン・プロピオン酸エストラジオール）など）

- スクリーニング開始日前 2 週間：

性ステロイドホルモンの経口／経皮／子宮内／腟内投与（プレマリン®（結合型エストロゲン），エストリール®（エストリオール），エストラダーム TTS®（エストラジオール），ドオルトン®（ノルゲストレル・エチニルエストラジオール），エデュレン®（エチニルエストラジオール・酢酸エチノジオール）など），漢方薬（「更年期障害」及び「血の道症」を治療目的とするもの）：当帰芍薬散，加味逍遥散，桂枝茯苓丸，温清飲など

- スクリーニング開始日前 1 週間：

自律神経調整薬：グランダキシン®（トフィソパム）など

睡眠薬：エバミール®（ロルメタゼパム），ネルボン®（ニトラゼパム），ベンザリン®（ニトラゼパム），ハルシオン®（トリアゾラム）など

抗不安薬：セルシン®（ジアゼパム），メイラックス®（ロフラゼブ酸エチル），デパス®（エチゾラム）など

15. 妊娠している可能性がある患者

16. 治験薬投与開始前の臨床検査において，臨床上問題と思われる異常値が認められた患者

(2) 解析対象集団

自然閉経後の更年期障害 200 例，両側卵巣摘出による卵巣欠落症状 11 例，合計 211 例を無作為に 3 群（プラセボ投与群，E2 0.5mg 投与群，E2 1.0mg 投与群）に割り付けた．全例に治験薬を投与し，そのうち子宮を有する被験者が 156 例，子宮を有さない被験者が 55 例であった．治療群ごとの被験者数，投与完了例数，中止例数及び中止理由の内訳を図 6に示す．7 例が治験薬の投与を中止した．中止理由は，同意の撤回（5 例）及び症状不変（2 例）であった．有害事象による中止はなかった．

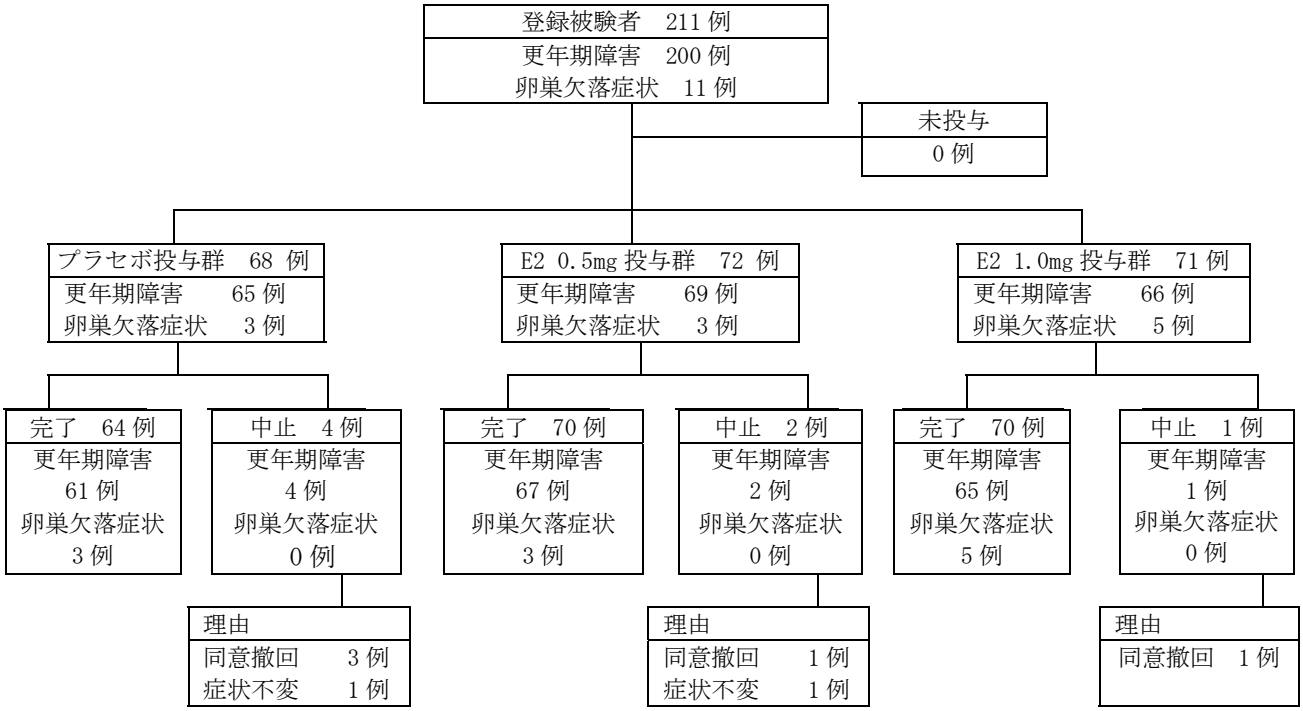

図 6 被験者の内訳

総括報告書 No.BC69 TF3 16.2.1

全登録被験者のうち 6 例に合計 6 件の治験実施計画書違反が認められた．治験実施計画書違反のあった被験者の要約を表 29に示す．違反の内訳はプラセボ投与群が 3 件，本剤（E2 0.5mg）投与群が 2 件，E2 1.0mg 投与群が 1 件であった．8 週後の来院が予定来院日から 7 日以上遅れた 3 件（プラセボ投与群 1 例 1 件，E2 0.5mg 投与群 2 例 2 件）は重大な違反と判定された．その他は軽微な違反と判定された．

表 29 治験実施計画書違反の内訳

違反の種類	被験者数	違反の内容
選択基準又は除外基準違反	0	
割付け違反	1	薬剤番号 124-2 に誤って 124-3 を割付けた
中止基準違反	0	
併用薬違反	0	
治療方法違反	1	最終来院日後も 5 日間治験薬を服用
検査観察時期の違反	3	最終来院日／投与日が予定より 1 週間以上遅延
検査観察方法の違反	1	安全性評価項目の検査を全く実施せず

総括報告書 No.BC69, TT3, 16.2.2

主要有効性変数の主たる解析対象集団は，FAS とした．副次的有効性変数及びその他の有効性解析項目についても FAS で解析を行った．また，主要有効性変数については参考として Valid case（VC）でも同じ解析を行った．

各解析対象集団は以下のように定義した．

[FAS]：全被験者の内，以下の被験者を除外した集団

- 組入れ規準に違反している被験者
- 除外基準に抵触している被験者
- 治験薬が全く投与されなかった被験者

[VC]：治験薬を投与した被験者のうち，以下の被験者を除外した集団

- 組入れ規準に違反している被験者
- 除外基準に抵触している被験者
- 服薬期間が 2 週間未満の被験者
- 服薬率が 2/3 未満の被験者
- 患者日誌を紛失した被験者
- 来院 3（4 週）の来院予定日から前後 2 週間までに有効性の評価や検査が実施されなかった被験者
- 来院 4（8 週）の来院予定日から前 2 週間から後 1 週間までに有効性の評価や検査が実施されなかった被験者
- 上記項目のほか，症例検討会で協議の上，除外とされた被験者

有効性及び安全性の解析に関する被験者の取扱いを症例検討会で決定した．解析対象集団の内訳を図 7に示す．全登録被験者 211 例を FAS 集団適格とした．重大な治験実施計画書違反のあった 3 例と，服薬が 2 週間未満であった 2 例，合計 5 例を VC から除外した．

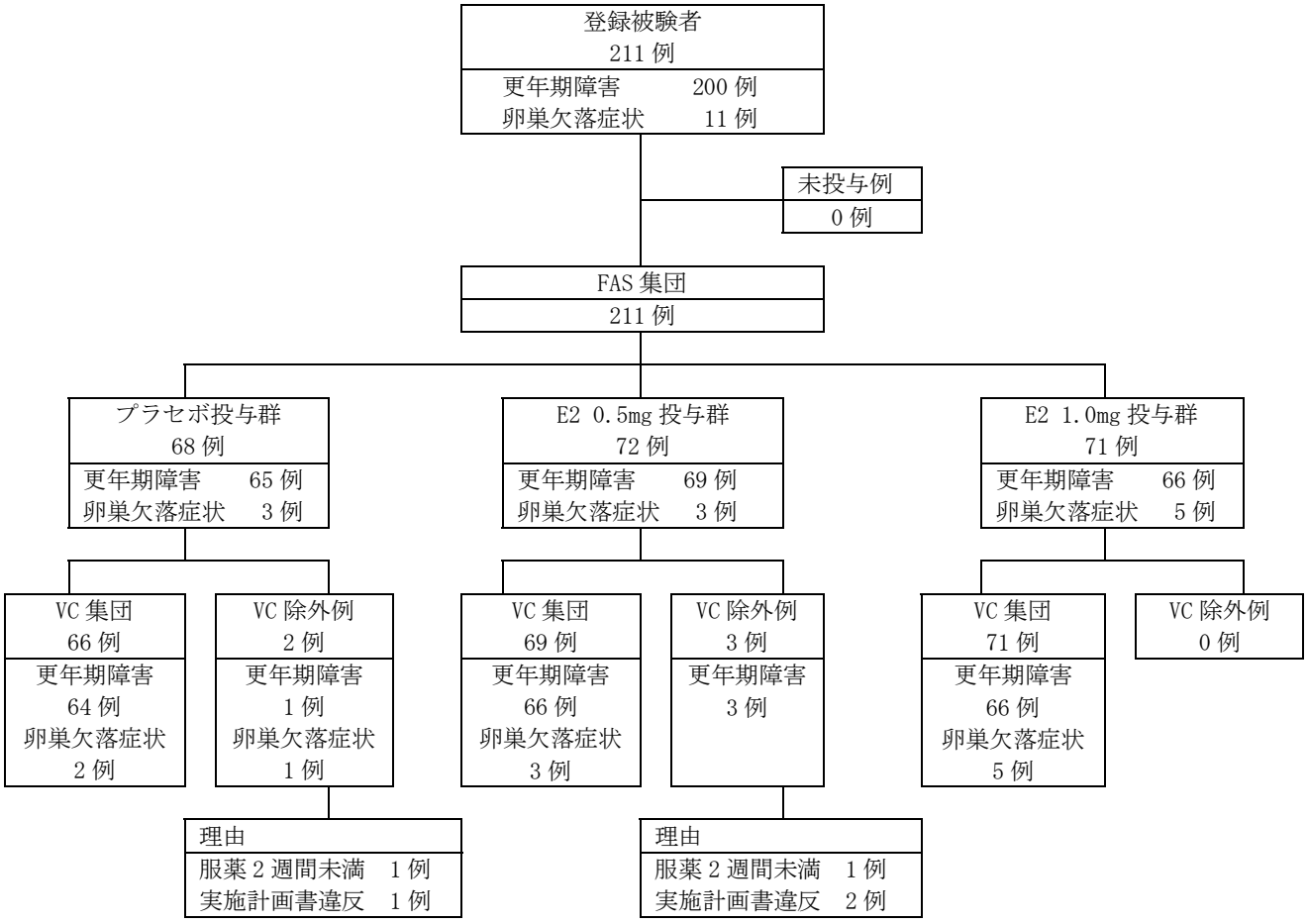

図 7 解析対象集団の内訳

総括報告書 No.BC69, TT4, 16.2.3

(3) 人口統計学的及び他の基準値の特性

有効性の主たる解析対象集団（FAS）の人口統計学的特性及びその他の基準値の特性を表 30に示す.

年齢，診断名，卵巣摘出術，子宮摘出術，SDS スコア合計及び閉経後の期間において投与群間の偏りは認められなかった．体容量指数（body mass index：BMI）については投与群間に有意差が認められた．投与前のホットフラッシュの回数と血中 E2 濃度に投与群間の明らかな差は認められなかった.

治験開始前 3 箇月以内の前治療薬使用歴が，プラセボ投与群で 47.1%，本剤（E2 0.5mg）投与群で 43.1%，E2 1.0mg 投与群で 53.5%の被験者に認められた．最も多かった前治療薬は CEE錠＊ ® であり，プラセボ投与群の 13.2%，本剤（E2 0.5mg）投与群の 19.4%，E2 1.0mg 投与群の 18.3%の被験者に使用歴があった．次いで[redacted] ®（酢酸メドロキシプロゲステロン）が多く，プラセボ投与群の 2.9%，本剤（E2 0.5mg）投与群の 4.2%，E2 1.0mg 投与群の 11.3%の被験者に使用歴があった.

＊新薬承認情報提供時に置き換え

表 30 人口統計学的特性及び他の基準値の特性（FAS）

項目		プラセボ N=68 被験者数(%)	E2 0.5mg N=72 被験者数(%)	E2 1.0mg N=71 被験者数(%)	検定
年齢	40～44 歳	1 (1.5)	0 (0.0)	1 (1.4)	χ^2検定
	45～49 歳	11 (16.2)	11 (15.3)	17 (23.9)	p=0.474
	50～54 歳	32 (47.1)	40 (55.6)	28 (39.4)	
	55～59 歳	22 (32.4)	17 (23.6)	19 (26.8)	
	60 歳以上	2 (2.9)	4 (5.6)	6 (8.5)	
	平均±SD	53.0±4.1	52.9±3.6	52.8±4.6	一元配置
	最小	44	46	44	分散分析
	最大	64	61	63	p=0.942
診断名	更年期障害	65 (95.6)	69 (95.8)	66 (93.0)	χ^2検定
	卵巣欠落症状	3 (4.4)	3 (4.2)	5 (7.0)	p=0.695
閉経後の期間（年）	平均±SD	4.55±4.32	4.80±5.16	4.80±3.89	一元配置
	最小	0.6	0.7	0.6	分散分析
	最大	25.3	36.6	16.4	p=0.941
ホットフラッシュの回数（/日）	平均±SD	6.02±3.25	5.65±3.02	5.65±2.91	実施せず
	最小	3.0	3.0	3.0	
	最大	19.7	21.3	20.3	
卵巣摘出術	なし	65 (95.6)	67 (93.1)	66 (93.0)	χ^2検定
	あり	3 (4.4)	5 (6.9)	5 (7.0)	p=0.767
子宮摘出術	なし	47 (69.1)	53 (73.6)	56 (78.9)	χ^2検定
	あり	21 (30.9)	19 (26.4)	15 (21.1)	p=0.423
BMI	平均±SD	22.32±2.88	21.67±2.76	23.03±3.45	一元配置
	最小	16.9	16.3	16.8	分散分析
	最大	33.2	29.6	32.8	p=0.030
SDS スコア合計	平均±SD	35.0±7.4	36.1±7.2	36.0±7.5	一元配置
	最小	22	23	24	分散分析
	最大	49	49	49	p=0.616
血中 E2 濃度（pg/mL）	平均±SD	2.32±6.78	3.10±8.63	2.25±4.67	実施せず
	最小	0.7	0.7	0.7	
	最大	56.2	66.0	30.9	

総括報告書 No.BC69, TT5, TT12, T102

3. 有効性の結果

(1) ホットフラッシュの回数

ホットフラッシュの回数の推移を表 31に，ホットフラッシュの回数減少率の推移を図 8及び表 32に示す．本剤（E2 0.5mg）投与群，E2 1.0mg 投与群の投与前におけるホットフラッシュの平均回数は，いずれも 5.65 回であった．最終評価時（8 週後又は中止時）にはそれぞれ 1.17 回，0.95 回まで減少した．ホットフラッシュの回数の平均減少率は本剤（E2 0.5mg）投与群，E2 1.0mg 投与群でそれぞれ 79.58%，82.49%であり，改善効果は顕著であった．プラセボ投与群では平均 6.02 回から平均 2.68 回まで減少し．平均減少率は 57.89%であった．

表 31 ホットフラッシュの回数の推移（FAS）

時期	投与群	被験者数	ホットフラッシュの回数			
			平均	SD	最小値	最大値
投与前	プラセボ	68	6.02	3.25	3.0	19.7
	E2 0.5mg	72	5.65	3.02	3.0	21.3
	E2 1.0mg	71	5.65	2.91	3.0	20.3
4 週後	プラセボ	65	2.97	2.18	0.0	9.4
	E2 0.5mg	71	2.25	2.41	0.0	12.1
	E2 1.0mg	71	1.74	1.99	0.0	9.6
8 週後	プラセボ	64	2.29	2.12	0.0	10.3
	E2 0.5mg	70	1.08	1.50	0.0	6.7
	E2 1.0mg	70	0.96	1.44	0.0	6.7
最終	プラセボ	68	2.68	3.06	0.0	20.4
	E2 0.5mg	72	1.17	1.66	0.0	7.4
	E2 1.0mg	71	0.95	1.43	0.0	6.7

総括報告書 No.BC69, TT12

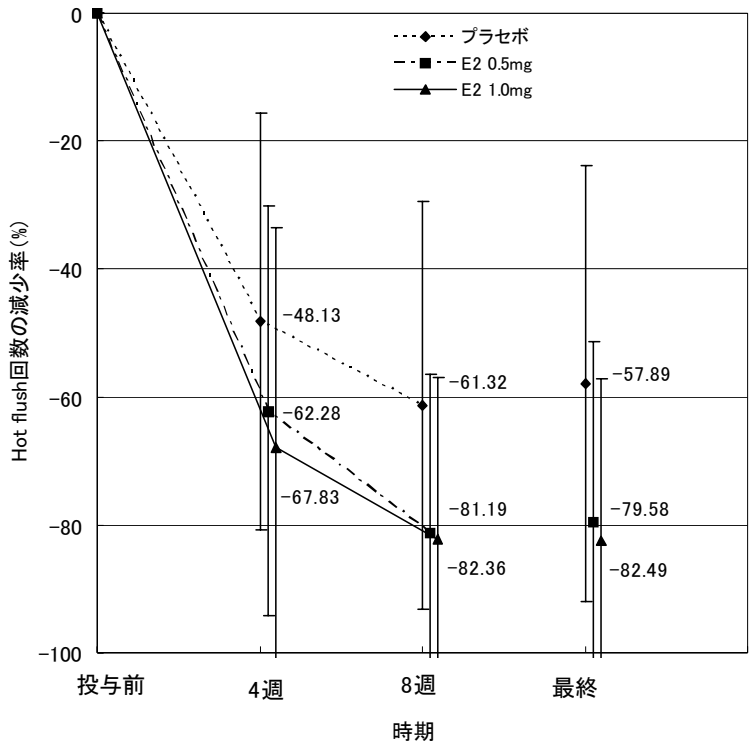

図 8 ホットフラッシュの回数減少率の推移（FAS）

平均と SD で示す．総括報告書 No.BC69　TT8, 12, 13, 15 から作図

最終評価時（8 週後又は中止時）のホットフラッシュの回数減少率を，本剤（E2 0.5mg）投与群とプラセボ投与群，E2 1.0mg 投与群とプラセボ投与群で比較した結果，いずれも有意な差が認められた（p＝0.000）．実薬群とプラセボ投与群との有意差は 4 週後，8 週後にも認められた．E2 用量

間の有意差は認められなかった（最終評価時）．本剤（E2 0.5mg）投与群と E2 1.0mg 投与群におけるホットフラッシュの回数減少率は，試験 010646 において観察された減少率と同程度であった．

表 32 ホットフラッシュの回数減少率の推移（FAS）

時期	投与群	被験者数	ホットフラッシュの回数減少率(%)				t 検定
			平均	SD	最小値	最大値	
4 週後	プラセボ	65	-48.13	32.65	-100.0	32.4	プラセボ対 E2 1.0mg：p=0.001(*)
	E2 0.5mg	71	-62.28	32.00	-100.0	26.9	プラセボ対 E2 0.5mg：p=0.013(*)
	E2 1.0mg	71	-67.83	34.24	-100.0	24.1	E2 0.5mg 対 E2 1.0mg：p=0.317(NS)
8 週後	プラセボ	64	-61.32	31.94	-100.0	18.9	プラセボ対 E2 1.0mg：p=0.000(*)
	E2 0.5mg	70	-81.19	24.72	-100.0	-2.1	プラセボ対 E2 0.5mg：p=0.000(*)
	E2 1.0mg	70	-82.36	25.47	-100.0	0.0	E2 0.5mg 対 E2 1.0mg：p=0.801(NS)
最終	プラセボ	68	-57.89	34.15	-100.0	20.0	プラセボ対 E2 1.0mg：p=0.000(*)
	E2 0.5mg	72	-79.58	28.29	-100.0	40.5	プラセボ対 E2 0.5mg：p=0.000(*)
	E2 1.0mg	71	-82.49	25.31	-100.0	0.0	E2 0.5mg 対 E2 1.0mg：p=0.555(NS)

総括報告書 No.BC69　TT8，10，13，14，15，16

プラセボ vs E2 1.0mg：t 検定

プラセボ vs E2 0.5mg，E2 0.5mg vs E2 1.0mg：Holm の方法により調整した t 検定

*：有意差あり，NS：有意差なし

VC 集団におけるホットフラッシュの回数の推移及び回数減少率の推移を表 33及び表 34に示す．VC 集団における結果は FAS 集団の結果と同様であった．最終評価時（8 週後又は中止時）のホットフラッシュの回数減少率を，本剤（E2 0.5mg）投与群とプラセボ投与群，E2 1.0mg 投与群とプラセボ投与群で比較した結果，いずれの差も有意であり，FAS 集団において得られた結論を支持する結果であった．

表 33 ホットフラッシュの回数の推移（VC）

時期	投与群	被験者数	ホットフラッシュの回数			
			平均	SD	最小値	最大値
投与前	プラセボ	66	6.06	3.29	3.0	19.7
	E2 0.5mg	69	5.60	3.04	3.0	21.3
	E2 1.0mg	71	5.65	2.91	3.0	20.3
4 週後	プラセボ	64	3.00	2.18	0.0	9.4
	E2 0.5mg	69	2.26	2.44	0.0	12.1
	E2 1.0mg	71	1.74	1.99	0.0	9.6
8 週後	プラセボ	63	2.32	2.12	0.0	10.3
	E2 0.5mg	69	1.08	1.51	0.0	6.7
	E2 1.0mg	70	0.96	1.44	0.0	6.7
最終	プラセボ	66	2.69	3.08	0.0	20.4
	E2 0.5mg	69	1.08	1.51	0.0	6.7
	E2 1.0mg	71	0.95	1.43	0.0	6.7

総括報告書 No.BC69，T39

表 34 ホットフラッシュの回数減少率の推移（VC）

時期	投与群	ホットフラッシュの回数減少率(%)					t 検定
		被験者数	平均	SD	最小値	最大値	
4 週後	プラセボ	64	-47.65	32.68	-100.0	32.4	プラセボ対 E2 0.5mg：p=0.015(*)
	E2 0.5mg	69	-61.71	32.25	-100.0	26.9	プラセボ対 E2 1.0mg：p=0.001(*)
	E2 1.0mg	71	-67.83	34.24	-100.0	24.1	E2 0.5mg 対 E2 1.0mg：p=0.275
8 週後	プラセボ	63	-60.75	31.86	-100.0	18.9	プラセボ対 E2 0.5mg：p=0.000(*)
	E2 0.5mg	69	-81.12	24.89	-100.0	-2.1	プラセボ対 E2 1.0mg：p=0.000(*)
	E2 1.0mg	70	-82.36	25.47	-100.0	0.0	E2 0.5mg 対 E2 1.0mg：p=0.790
最終	プラセボ	66	-58.47	32.93	-100.0	18.9	プラセボ対 E2 0.5mg：p=0.000(*)
	E2 0.5mg	69	-81.12	24.89	-100.0	-2.1	プラセボ対 E2 1.0mg：p=0.000(*)
	E2 1.0mg	71	-82.49	25.31	-100.0	0.0	E2 0.5mg 対 E2 1.0mg：p=0.771

総括報告書 No.BC69, TT9, 11, T40～T43

プラセボ対 E2 1.0mg ：t 検定

プラセボ対 E2 0.5mg , E2 0.5mg 対 E2 1.0mg：Holm の方法により調整した t 検定

*：有意差あり

(2) ホットフラッシュの程度

ホットフラッシュの程度別被験者の推移を投与群間で比較した結果を表 35及び図 9に示す．症状が消失した被験者は投与期間及び用量に依存して増加し，最終評価時（8 週時又は中止時）には，本剤（E2 0.5mg）投与群，E2 1.0mg 投与群及びプラセボ投与群のそれぞれ 29.2%（21/72 例），40.8%（29/71 例）及び 11.8%（8/68 例）を占めた．ホットフラッシュの程度は投与期間の経過とともに軽減し，その改善効果は用量に依存して優れる傾向が認められた．

投与前において，約 80%の被験者に中等度，約 20%の被験者に高度のホットフラッシュが認められた．本剤（E2 0.5mg）投与群では，8 週後に中等度の被験者が 11.4%（8/70 例）に減少し，高度の被験者は認められなかった．E2 1.0mg 投与群では 8 週後に中等度の被験者が 5.7%（4/70 例）まで減少し，高度の被験者は認められなかった．

各評価時期におけるホットフラッシュの程度別被験者の分布を Wilcoxon 検定を用いて評価した結果，8 週後及び最終評価時（8 週後又は中止時）に本剤（E2 0.5mg）投与群とプラセボ投与群の群間（8 週後：p＝0.007，最終評価時：p＝0.001），E2 1.0mg 投与群とプラセボ投与群の群間（8 週後：p=0.000，最終評価時：p＝0.000）にそれぞれ有意差が認められた．一方，4 週後では，E2 1.0mg 投与群とプラセボ投与群の群間にのみ有意差が認められ（p＝0.003），本剤（E2 0.5mg）投与群とプラセボ投与群の群間に有意差は認められなかった（p＝0.079）．すなわち，E2 1.0mg 投与群では本剤（E2 0.5mg）投与群と比較してホットフラッシュの改善効果が早く現れた（図 9 参照）．

E2 用量による有効性の違いをさらに検討するために，症状の程度が中等度以上であった被験者の割合を同様に比較した（表 36 参照）．中等度以上の症状を有する被験者の割合は，8 週後及び最終評価時（8 週後又は中止時）においてプラセボ投与群と比較して E2 1.0mg 投与群で有意に低かった（8 週後：p＝0.006，最終評価時：p＝0.000）．しかし，本剤（E2 0.5mg）投与群とプラセボ投与群の群間には有意差は認められなかった（8 週後：p＝0.110，最終評価時：p＝0.033）．

表 35 ホットフラッシュの程度の推移（FAS）

時期	投与群	被験者数(%)					Wilcoxon 検定
		合計	無	軽度	中等度	高度	
投与前	プラセボ	68 (100)	0 (0.0)	0 (0.0)	54 (79.4)	14 (20.6)	プラセボ対 E2 1.0mg p=0.438
	E2 0.5mg	72 (100)	0 (0.0)	0 (0.0)	56 (77.8)	16 (22.2)	プラセボ対 E2 0.5mg (検定せず)
	E2 1.0mg	71 (100)	0 (0.0)	0 (0.0)	60 (84.5)	11 (15.5)	E2 0.5mg 対 E2 1.0mg (検定せず)
4 週後	プラセボ	65 (100)	3 (4.6)	39 (60.0)	20 (30.8)	3 (4.6)	プラセボ対 E2 1.0mg p=0.003(*)
	E2 0.5mg	71 (100)	8 (11.3)	46 (64.8)	15 (21.1)	2 (2.8)	プラセボ対 E2 0.5mg p=0.079
	E2 1.0mg	71 (100)	15 (21.1)	42 (59.2)	12 (16.9)	2 (2.8)	E2 0.5mg 対 E2 1.0mg (NS)
8 週後	プラセボ	64 (100)	8 (12.5)	41 (64.1)	13 (20.3)	2 (3.1)	プラセボ対 E2 1.0mg p=0.000(*)
	E2 0.5mg	70 (100)	20 (28.6)	42 (60.0)	8 (11.4)	0 (0.0)	プラセボ対 E2 0.5mg p=0.007(*)
	E2 1.0mg	70 (100)	29 (41.4)	37 (52.9)	4 (5.7)	0 (0.0)	E2 0.5mg 対 E2 1.0mg p=0.066
最終	プラセボ	68 (100)	8 (11.8)	41 (60.3)	14 (20.6)	5 (7.4)	プラセボ対 E2 1.0mg p=0.000(*)
	E2 0.5mg	72 (100)	21 (29.2)	42 (58.3)	9 (12.5)	0 (0.0)	プラセボ対 E2 0.5mg p=0.001(*)
	E2 1.0mg	71 (100)	29 (40.8)	38 (53.5)	4 (5.6)	0 (0.0)	E2 0.5mg 対 E2 1.0mg p=0.072

総括報告書 No.BC69, T44～T47

プラセボ対 E2 1.0mg ：Wilcoxon 検定

プラセボ対 E2 0.5mg , E2 0.5mg 対 E2 1.0mg：Holm の方法により調整した Wilcoxon 検定

*：有意差あり, NS：有意差なし

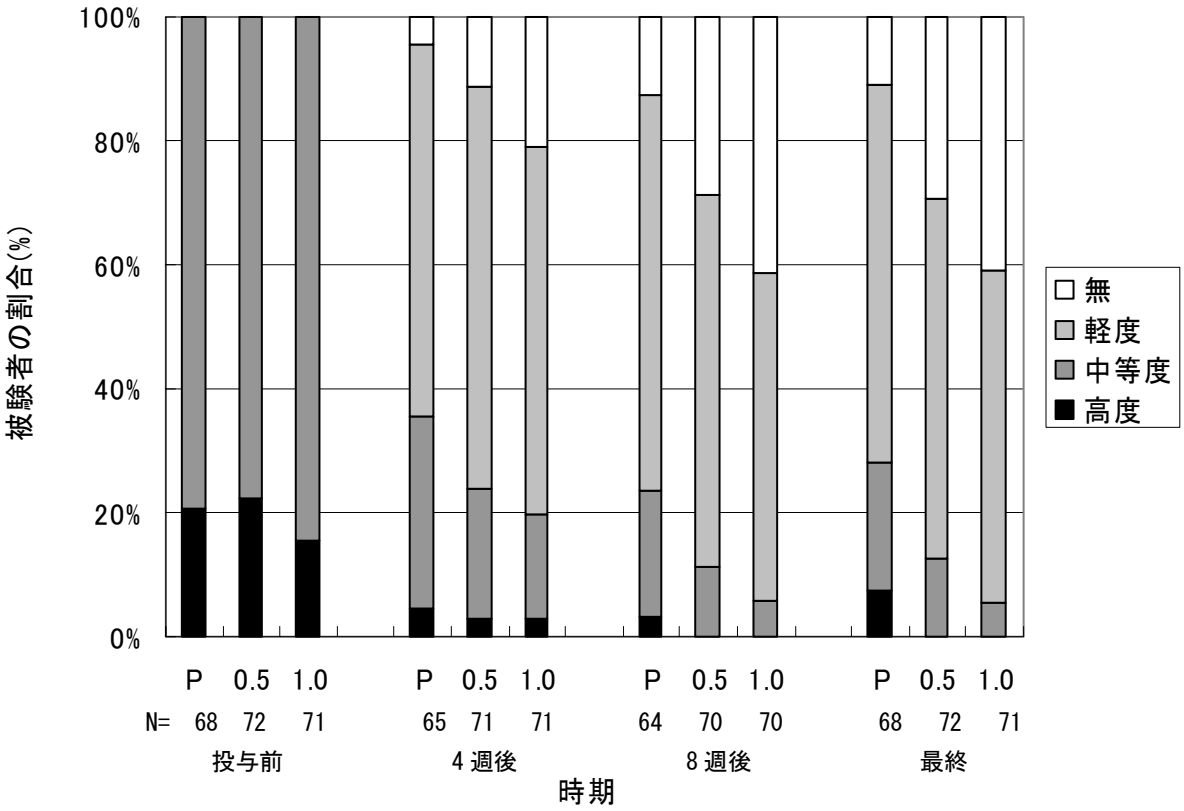

図 9 ホットフラッシュ の程度の推移（FAS）

総括報告書 No.BC69, T44-47 を元に作図

P: プラセボ投与群, 0.5：E2 0.5mg 投与群, 1.0：E2 1.0mg 投与群, N：被験者数

表 36 ホットフラッシュの程度の推移（中等度以上と中等度未満, FAS）

時期	症状の程度	被験者数(%)			Fisher の正確確率検定
		プラセボ	E2 0.5mg	E2 1.0mg	
投与前	なし又は軽度	0 (0)	0 (0)	0 (0)	(検定せず)
	中等度以上	68 (100.0)	72 (100.0)	71 (100.0)	
4週後	なし又は軽度	45 (66.2)	55 (76.4)	57 (80.3)	プラセボ 対 E2 1.0mg：p=0.084 プラセボ 対 E2 0.5mg：(検定せず) E2 0.5mg 対 E2 1.0mg：(検定せず)
	中等度以上	23 (33.8)	17 (23.6)	14 (19.7)	
8週後	なし又は軽度	53 (77.9)	64 (88.9)	67 (94.4)	プラセボ 対 E2 1.0mg：p=0.006(*) プラセボ 対 E2 0.5mg：p=0.110 E2 0.5mg 対 E2 1.0mg：(NS)
	中等度以上	15 (22.1)	8 (11.1)	4 (5.6)	
最終	なし又は軽度	49 (72.1)	63 (87.5)	67 (94.4)	プラセボ 対 E2 1.0mg：p=0.000(*) プラセボ 対 E2 0.5mg：p=0.033 E2 0.5mg 対 E2 1.0mg：(NS)
	中等度以上	19 (27.9)	9 (12.5)	4 (5.6)	

総括報告書 No.BC69, T76-79

プラセボ対 E2 1.0mg ：Fisher の正確確率検定

プラセボ対 E2 0.5mg , E2 0.5mg 対 E2 1.0mg：Holm の方法により調整した Fisher の正確確率検定

*：有意差あり, NS：有意差なし

(3)　発汗

発汗の程度の推移を表 37及び図 10に示す．症状が消失した被験者は投与期間及び用量に依存して増加し，最終評価時（8 週後又は中止時）には，本剤（E2 0.5mg）投与群，E2 1.0mg 投与群及びプラセボ投与群のそれぞれ 61.1%（44/72 例），70.4%（50/71 例）及び 36.8%（25/68 例）を占めた．発汗の程度は投与期間の経過とともに軽減し，その改善効果には用量に依存して優れる傾向が認められた．

90%以上の被験者が投与前に発汗を症状として有しており，各投与群とも中等度の症状を有する被験者が最も多く（約 50%），軽度，高度の症状を有する被験者の割合はそれぞれ約 20%であった．プラセボ投与群では中等度の症状を有する被験者の割合が 8 週後までに 18.8%（12/64 例）に減少した．一方，　本剤（E2 0.5mg）投与群，E2 1.0mg 投与群では 8 週後にそれぞれ 8.6%（6/70 例），2.9%（2/70 例）まで減少し，E2 1.0mg 投与群では高度の発汗を有する被験者は認められなかった．

各評価時期における発汗の程度別被験者の分布を Wilcoxon 検定を用いて評価した結果，8 週後及び最終評価時（8 週後又は中止時）に本剤（E2 0.5mg）投与群とプラセボ投与群の群間（8 週後：p＝0.002，最終評価時：p＝0.001），E2 1.0mg 投与群とプラセボ投与群の群間（8 週後：p＝0.000，最終評価時：p＝0.000）にそれぞれ有意差が認められた．E2 用量間に有意差は認められなかった．一方，4 週後では，E2 1.0mg 投与群とプラセボ投与群の群間にのみ有意差が認められ（p＝0.008），本剤（E2 0.5mg）投与群とプラセボ投与群の群間に有意差は認められなかった．

表 37 発汗の程度の推移 (FAS)

時期	投与群	被験者数(%)					Wilcoxon 検定
		合計	無	軽度	中等度	高度	
投与前	プラセボ	68 (100)	5 (7.4)	15 (22.1)	32 (47.1)	16 (23.5)	プラセボ対 E2 1.0mg p=0.668
	E2 0.5mg	72 (100)	4 (5.6)	12 (16.7)	38 (52.8)	18 (25.0)	プラセボ対 E2 0.5mg (検定せず)
	E2 1.0mg	71 (100)	5 (7.0)	15 (21.1)	39 (54.9)	12 (16.9)	E2 0.5mg 対 E2 1.0mg (検定せず)
4 週後	プラセボ	65 (100)	20 (30.8)	26 (40.0)	14 (21.5)	5 (7.7)	プラセボ対 E2 1.0mg p=0.008(*)
	E2 0.5mg	71 (100)	26 (36.6)	26 (36.6)	16 (22.5)	3 (4.2)	プラセボ対 E2 0.5mg (NS)
	E2 1.0mg	71 (100)	35 (49.3)	27 (38.0)	6 (8.5)	3 (4.2)	E2 0.5mg 対 E2 1.0mg p=0.051
8 週後	プラセボ	64 (100)	25 (39.1)	25 (39.1)	12 (18.8)	2 (3.1)	プラセボ対 E2 1.0mg p=0.000(*)
	E2 0.5mg	70 (100)	44 (62.9)	19 (27.1)	6 (8.6)	1 (1.4)	プラセボ対 E2 0.5mg p=0.002(*)
	E2 1.0mg	70 (100)	49 (70.0)	19 (27.1)	2 (2.9)	0 (0.0)	E2 0.5mg 対 E2 1.0mg p=0.258
最終	プラセボ	68 (100)	25 (36.8)	25 (36.8)	13 (19.1)	5 (7.4)	プラセボ対 E2 1.0mg p=0.000(*)
	E2 0.5mg	72 (100)	44 (61.1)	20 (27.8)	6 (8.3)	2 (2.8)	プラセボ対 E2 0.5mg p=0.001(*)
	E2 1.0mg	71 (100)	50 (70.4)	19 (26.8)	2 (2.8)	0 (0.0)	E2 0.5mg 対 E2 1.0mg p=0.152

総括報告書 No.BC69, T48～T51

プラセボ投与群対 E2 1.0mg 投与群：Wilcoxon 検定

プラセボ投与群対 E2 0.5mg 投与群及び E2 0.5mg 投与群対 E2 1.0mg 投与群：Holm の方法により調整した Wilcoxon 検定

*：有意差あり，NS：有意差なし

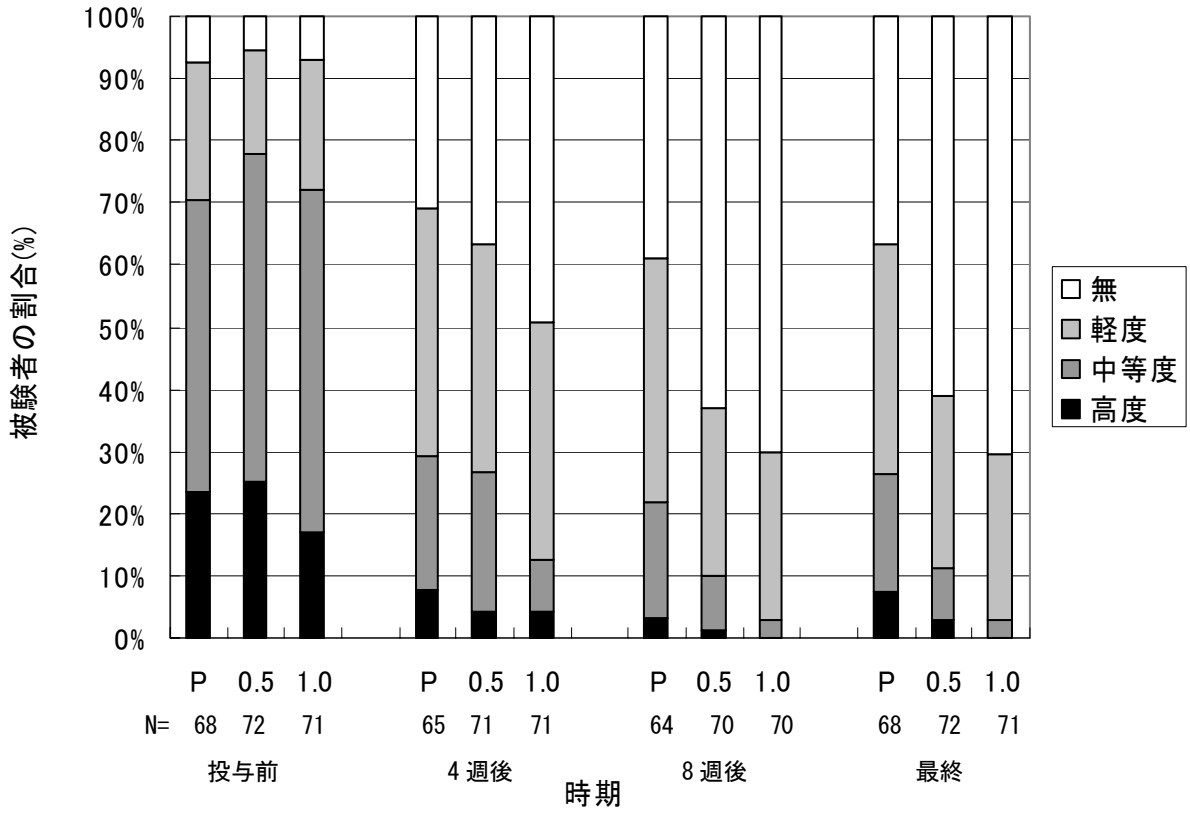

図 10 発汗の程度の推移（FAS）

総括報告書 No.BC69，T48-51 を元に作図
P：プラセボ投与群，0.5：E2 0.5mg 投与群，1.0：E2 1.0mg 投与群，N：被験者数

E2 用量による有効性の違いをさらに検討するために，発汗の程度が中等度以上であった被験者の割合を同様に比較した（表 38 参照）．中等度以上の症状を有する被験者の割合は，いずれの評価時期でも， E2 1.0mg 投与群においてプラセボ投与群と比較して有意に低かった（4 週後：p＝0.034，8 週後：p＝0.001，最終：p＝0.000）．しかし，いずれの評価時期にも本剤（E2 0.5mg）投与群とプラセボ投与群との間に有意差は認められなかった（4 週後：有意差なし，8 週後：p＝0.097，最終：p＝0.029）．

表 38 発汗の程度の推移（中等度以上と中等度未満，FAS）

時期	症状の程度	被験者数(%)			Fisher の正確確率検定
		プラセボ	E2 0.5mg	E2 1.0mg	
投与前	なし又は軽度	20 (29.4)	16 (22.2)	20 (28.2)	プラセボ 対 E2 1.0mg：p=1.000 プラセボ 対 E2 0.5mg：(検定せず) E2 0.5mg 対 E2 1.0mg：(検定せず)
	中等度以上	48 (70.6)	56 (77.8)	51 (71.8)	
4 週後	なし又は軽度	49 (72.1)	53 (73.6)	62 (87.3)	プラセボ 対 E2 1.0mg：p=0.034(*) プラセボ 対 E2 0.5mg：(NS) E2 0.5mg 対 E2 1.0mg：P=0.057
	中等度以上	19 (27.9)	19 (26.4)	9 (12.7)	
8 週後	なし又は軽度	54 (79.4)	65 (90.3)	69 (97.2)	プラセボ 対 E2 1.0mg：p=0.001(*) プラセボ 対 E2 0.5mg：p=0.097 E2 0.5mg 対 E2 1.0mg：(NS)
	中等度以上	14 (20.6)	7 (9.7)	2 (2.8)	
最終	なし又は軽度	50 (73.5)	64 (88.9)	69 (97.2)	プラセボ 対 E2 1.0mg：p=0.000(*) プラセボ 対 E2 0.5mg：p=0.029 E2 0.5mg 対 E2 1.0mg：(NS)
	中等度以上	18 (26.5)	8 (11.1)	2 (2.8)	

総括報告書 No.BC69，T80～T83

プラセボ投与群対 E2 1.0mg 投与群：Fisher の正確確率検定

プラセボ投与群対 E2 0.5mg 投与群及び E2 0.5mg 投与群対 E2 1.0mg 投与群：Holm の方法により調整した Fisher の正確確率検定

＊：有意差あり，NS：有意差なし

(4) 腟乾燥感

腟乾燥感の有無の推移を表 39及び図 11に示す．投与前には約 30%の被験者が腟乾燥感を訴えていた．腟乾燥感に対する改善効果はプラセボ投与群より実薬群において顕著であった．プラセボ投与群では 4 週後において症状の改善が認められたものの，8 週後にはそれ以上の改善が認められず，最終評価時（8 週後又は中止時）には腟乾燥感「有」の被験者が 20.6%（14/68 例）に認められた．一方，実薬群では，8 週後まで症状の改善が継続し，最終評価時（8 週後又は中止時）に腟乾燥感「有」の被験者の割合は本剤（E2 0.5mg）投与群で 4.2%（3/72 例），E2 1.0mg 投与群で 7.0%（5/71 例）であった．8 週後及び最終評価時（8 週後又は中止時）における腟乾燥感の有無について，本剤（E2 0.5mg）投与群とプラセボ投与群の間（8 週後：p＝0.006，最終評価時：p＝0.004），E2 1.0mg 投与群とプラセボ投与群の群間（8 週後：p＝0.040，最終評価時：p＝0.026）に有意差が認められたものの，E2 用量間に有意差は認められなかった．

表 39 腟乾燥感の有無の推移（FAS）

時期	投与群	被験者数(%)			Fisher の正確確率検定
		合計	無	有	
投与前	プラセボ	68 (100)	47 (69.1)	21 (30.9)	プラセボ対 E2 1.0mg：p=0.721
	E2 0.5mg	72 (100)	51 (70.8)	21 (29.2)	プラセボ対 E2 0.5mg：(検定せず)
	E2 1.0mg	71 (100)	47 (66.2)	24 (33.8)	E2 0.5mg 対 E2 1.0mg：(検定せず)
4 週後	プラセボ	65 (100)	52 (80.0)	13 (20.0)	プラセボ対 E2 1.0mg：p=0.372
	E2 0.5mg	71 (100)	64 (90.1)	7 (9.9)	プラセボ対 E2 0.5mg：(検定せず)
	E2 1.0mg	71 (100)	61 (85.9)	10 (14.1)	E2 0.5mg 対 E2 1.0mg：(検定せず)
8 週後	プラセボ	64 (100)	51 (79.7)	13 (20.3)	プラセボ対 E2 1.0mg：p=0.040(*)
	E2 0.5mg	70 (100)	67 (95.7)	3 (4.3)	プラセボ対 E2 0.5mg：p=0.006(*)
	E2 1.0mg	70 (100)	65 (92.9)	5 (7.1)	E2 0.5mg 対 E2 1.0mg：p=0.718
最終	プラセボ	68 (100)	54 (79.4)	14 (20.6)	プラセボ対 E2 1.0mg：p=0.026(*)
	E2 0.5mg	72 (100)	69 (95.8)	3 (4.2)	プラセボ対 E2 0.5mg：p=0.004(*)
	E2 1.0mg	71 (100)	66 (93.0)	5 (7.0)	E2 0.5mg 対 E2 1.0mg：p=0.494

総括報告書 No.BC69, T56～T59

プラセボ投与群対 E2 1.0mg 投与群： Fisher の正確確率検定

プラセボ投与群対 E2 0.5mg 投与群及び E2 0.5mg 投与群対 E2 1.0mg 投与群：Holm の方法で調整した Fisher の正確確率検定

*：有意差あり

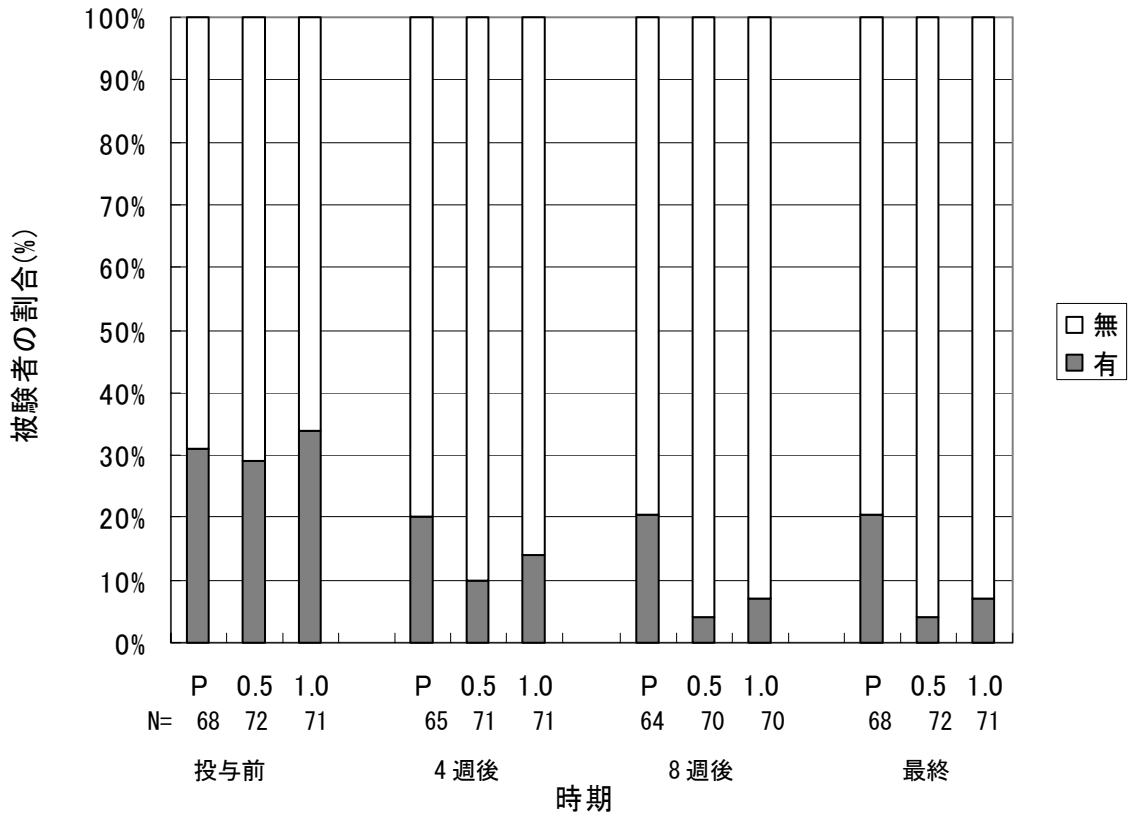

図 11 膣乾燥感の有無の推移

総括報告書 No.BC69，T56～T59 を元に作図
P：プラセボ投与群，0.5：E2 0.5mg 投与群，1.0：E2 1.0mg 投与群，N：被験者数

(5) 不眠

不眠の程度の推移を表 40に示す．投与前には 51～57%の被験者が不眠の症状を有しており，主に中等度から軽度の症状であった．プラセボ投与群では症状の改善が 4 週後に認められ，8 週後にはそれ以上の改善は認められなかった．一方，実薬群では 8 週後まで症状の改善が継続した．8 週後及び最終評価時（8 週後又は中止時）に無症状となった被験者の割合は実薬群に多く，本剤（E2 0.5mg）投与群，E2 1.0mg 投与群及びプラセボ投与群でそれぞれ，投与前より 38.8%，39.4%及び 23.6%増加した．実薬群とプラセボ投与群の間に有意な差は認められなかったものの，最終評価時（8 週後又は中止時）にはプラセボ投与群と比較して E2 1.0mg 投与群における不眠の改善が優れる傾向が認められた．E2 用量間の差異は認められなかった．

表 40 不眠の程度の推移（FAS）

時期	投与群	被験者数(%)					群間比較
		合計	無	軽度	中等度	高度	
投与前	プラセボ	68 (100)	33 (48.5)	21 (30.9)	12 (17.6)	2 (2.9)	プラセボ対 E2 1.0mg p=0.206 プラセボ対 E2 0.5mg (検定せず) E2 0.5mg 対 E2 1.0mg (検定せず)
	E2 0.5mg	72 (100)	31 (43.1)	18 (25.0)	21 (29.2)	2 (2.8)	
	E2 1.0mg	71 (100)	32 (45.1)	13 (18.3)	21 (29.6)	5 (7.0)	
4週後	プラセボ	65 (100)	49 (75.4)	12 (18.5)	3 (4.6)	1 (1.5)	プラセボ対 E2 1.0mg p=0.738 プラセボ対 E2 0.5mg (検定せず) E2 0.5mg 対 E2 1.0mg (検定せず)
	E2 0.5mg	71 (100)	49 (69.0)	14 (19.7)	7 (9.9)	1 (1.4)	
	E2 1.0mg	71 (100)	52 (73.2)	13 (18.3)	5 (7.0)	1 (1.4)	
8週後	プラセボ	64 (100)	49 (76.6)	11 (17.2)	3 (4.7)	1 (1.6)	プラセボ対 E2 1.0mg p=0.261 プラセボ対 E2 0.5mg (検定せず) E2 0.5mg 対 E2 1.0mg (検定せず)
	E2 0.5mg	70 (100)	59 (84.3)	8 (11.4)	2 (2.9)	1 (1.4)	
	E2 1.0mg	70 (100)	59 (84.3)	8 (11.4)	3 (4.3)	0 (0.0)	
最終	プラセボ	68 (100)	49 (72.1)	13 (19.1)	4 (5.9)	2 (2.9)	プラセボ対 E2 1.0mg p=0.070 プラセボ対 E2 0.5mg (検定せず) E2 0.5mg 対 E2 1.0mg (検定せず)
	E2 0.5mg	72 (100)	59 (81.9)	9 (12.5)	3 (4.2)	1 (1.4)	
	E2 1.0mg	71 (100)	60 (84.5)	8 (11.3)	3 (4.2)	0 (0.0)	

総括報告書 No.BC69, T52～T55

プラセボ対 E2 1.0mg：Wilcoxon 検定

プラセボ対 E2 0.5mg ，E2 0.5mg 対 E2 1.0mg：Holm の方法により調整した Wilcoxon 検定

(6) 血中 E2 濃度

血中 E2 濃度の推移を表 41に，血中 FSH 濃度の推移を表 42に示す．最終評価時（8 週後又は中止時）の平均血中 E2 濃度は本剤（E2 0.5mg）投与群で 21.41pg/mL，E2 1.0mg 投与群で 44.95pg/mL であり，いずれも閉経前女性の卵胞初期濃度（20～60pg/mL）に達していた．血中 FSH 濃度は E2 投与量に依存して減少する傾向を示した．

表 41 血中 E2 濃度（pg/mL）の推移（FAS）

時期	投与群	被験者数	平均	SD	最小値	中央値	最大値
投与前	プラセボ	68	2.32	6.78	0.7	1.10	56.2
	E2 0.5mg	72	3.10	8.63	0.7	1.00	66.0
	E2 1.0mg	71	2.25	4.67	0.7	1.00	30.9
最終	プラセボ	67	6.37	28.19	0.7	1.40	227.4
	E2 0.5mg	72	21.41	25.36	0.7	15.35	173.5
	E2 1.0mg	71	44.95	45.46	1.1	31.90	233.4

総括報告書 No.BC69, T102

表 42 血中 FSH 濃度（mIU/mL）の推移（FAS）

時期	投与群	被験者数	平均	SD	最小値	中央値	最大値
投与前	プラセボ	68	78.74	35.09	23.0	73.35	293.0
	E2 0.5mg	72	78.71	23.40	34.0	76.00	144.4
	E2 1.0mg	71	79.19	23.17	20.9	77.80	147.9
最終	プラセボ	67	75.48	26.32	6.7	71.60	176.0
	E2 0.5mg	72	62.33	22.42	12.9	60.05	135.7
	E2 1.0mg	71	49.76	19.94	4.8	45.40	100.6

総括報告書 No.BC69, T102

(7) 部分集団における結果の比較

解析対象集団の特性のうち BMI に関してのみ投与群間の有意な偏りが認められたため，BMI と用量を要因とする二元配置分散分析により交互作用を検討し（FAS，N=211），BMI（22.0 以上／未満）で区分した部分集団について，主要有効性変数であるホットフラッシュの回数の平均減少率の解析を行った．BMI と用量の間に交互作用は認められなかった（p＝0.345）．最終評価時（8 週後又は中止時）のホットフラッシュの回数の平均減少率には，BMI の違いによる有意な差が認められた（p＝0.036）．BMI によるホットフラッシュの回数の平均減少率の違いが主解析の結論に及ぼす影響を評価するため，BMI 区分及び用量を説明変数とする多重回帰モデルを用いて調整したホットフラッシュの回数の平均減少率を FAS 集団の投与群間で比較したところ（Tukey 検定），調整前の結果と同じであった．したがって，主解析の結論に BMI の投与群間の偏りによる影響はないと考える．

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2.7.6.4.2　　試験別の有害事象発現率

表 2.7.6.4- 1　試験 010561：有害事象発現率（例数，%） 2

表 2.7.6.4- 2　試験 305044：有害事象発現率（例数，%） 3

表 2.7.6.4- 3　試験 308560：重症度別の有害事象発現率（例数，%） 5

表 2.7.6.4- 4　試験 308560：治験薬との関連性判定別の有害事象発現率（例数，%） 8

表 2.7.6.4- 5　試験 300107：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%） 11

表 2.7.6.4- 6　試験 300107：AE コード用語の対比表（MedDRA ver 7.1 基本語 vs MedDRA ver 3.0 基本語） 53

表 2.7.6.4- 7　試験 300103：重症度別の有害事象発現率（例数，%） 57

表 2.7.6.4- 8　試験 300103：治験薬との関連性判定別の有害事象発現率（例数，%） 232

表 2.7.6.4- 9　試験 300103：AE コード用語の対比表（MedDRA ver 7.1 基本語 vs MedDRA ver 6.1 基本語） 407

表 2.7.6.4- 10　試験 010646：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%） 417

表 2.7.6.4- 11　試験 010730：重症度別の有害事象発現率（例数，%） 419

表 2.7.6.4- 12　試験 010731：重症度別の有害事象発現率（例数，%） 422

表 2.7.6.4- 13　試験 010568：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%） 425

表 2.7.6.4- 14　試験 [redacted]216：有害事象例数 429

表 2.7.6.4- 15　試験 [redacted]216 の 1 年延長試験：有害事象発現例数..... 431

表 2.7.6.4- 16　試験 [redacted]065：有害事象発現率（例数，%） 433

表 2.7.6.4- 1　　試験 010561：有害事象発現率（例数，%）

総括報告書 B868，表Ⅶ-25 より引用

表Ⅶ－25　症状別自覚症状発現症例数

＜エストラジオール単剤投与群＞

自覚症状	ｴｽﾄﾗｼﾞｵｰﾙ：1mg　（n＝9）		ｴｽﾄﾗｼﾞｵｰﾙ：2mg　（n＝10）	
	発現例数(%)	症例番号	発現例数(%)	症例番号
下腹部膨満感	－		3　(30)	2-3, 2-8, 2-10
乳頭痛	2　(22)	1-3, 1-10	2　(20)	2-3, 2-10
帯下	2　(22)	1-3, 1-9	2　(20)	2-9, 2-12
腰痛	－		1　(10)	2-3

自覚症状の程度は全て軽度

＜エストラジオール＋レボノルゲストレル併用投与群＞

自覚症状	ｴｽﾄﾗｼﾞｵｰﾙ：1mg＋ ﾚﾎﾞﾉﾙｹﾞｽﾄﾚﾙ：40μg (N=10)		ｴｽﾄﾗｼﾞｵｰﾙ：2mg＋ ﾚﾎﾞﾉﾙｹﾞｽﾄﾚﾙ：80μg (n＝10)	
	発現例数(%)	症例番号	発現例数(%)	症例番号
下腹部膨満感	1　(10)	3-4	－	
乳頭痛	－		4　(40)	4-1, 4-4, 4-5, 4-7
帯下	1　(10)	3-7	2　(20)	4-4, 4-7
下肢浮腫	1　(10)	3-6	－	
下肢倦怠感	1　(10)	3-10	－	

自覚症状の程度は全て軽度

表 2.7.6.4- 2 試験 305044：有害事象発現率（例数，%）

総括報告書 A06581 14 項，T10 より引用

T 10: Number (%) of volunteers with any AE during the entire study by MedDRA term - full analysis set

Events	caucasian	asian
ANY EVENT	22/32 (68.8%)	30/32 (93.8%)
EYE DISORDERS		
ANY EVENT	1/32 (3.1%)	0/32 (0.0%)
CHEMOSIS	1/32 (3.1%)	0/32 (0.0%)
GASTROINTESTINAL DISORDERS		
ANY EVENT	3/32 (9.4%)	7/32 (21.9%)
ABDOMEN ENLARGED FEELING OF	0/32 (0.0%)	3/32 (9.4%)
ABDOMINAL PAIN LOWER	0/32 (0.0%)	2/32 (6.3%)
CONSTIPATION	0/32 (0.0%)	1/32 (3.1%)
DIARRHEA	0/32 (0.0%)	1/32 (3.1%)
NAUSEA	2/32 (6.3%)	0/32 (0.0%)
PHARYNX STRANGE SENSATION OF	0/32 (0.0%)	1/32 (3.1%)
SINGULTUS	1/32 (3.1%)	0/32 (0.0%)
VOMITING	1/32 (3.1%)	0/32 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
ANY EVENT	2/32 (6.3%)	2/32 (6.3%)
ABDOMINAL PAIN	0/32 (0.0%)	1/32 (3.1%)
PELVIC PAIN	1/32 (3.1%)	0/32 (0.0%)
TENDERNESS	0/32 (0.0%)	1/32 (3.1%)
WEAKNESS	1/32 (3.1%)	0/32 (0.0%)
INFECTIONS AND INFESTATIONS		
ANY EVENT	4/32 (12.5%)	0/32 (0.0%)
COMMON COLD SYNDROME	4/32 (12.5%)	0/32 (0.0%)
SINUSITIS	1/32 (3.1%)	0/32 (0.0%)

Note:events are given as Adverse event MEDDRA MSDECODE / Adverse event
Note:Events are given as MedDRA system organ class and lowest level term.
Number of volunteers with events / total number of volunteers (%)
Each episode of AE was counted as 1 AE: in some volunteers, multiple episodes of AE were recorded.

Biometry Europe Identifier: 305044 - ae - 27 - 21NOV02

(Continued)

Events	caucasian	asian
INVESTIGATIONS		
ANY EVENT	5/32 (15.6%)	4/32 (12.5%)
TRIGLYCERIDE DECREASED	0/32 (0.0%)	1/32 (3.1%)
TRIGLYCERIDE INCREASED	0/32 (0.0%)	2/32 (6.3%)
WBC DEC	0/32 (0.0%)	1/32 (3.1%)
WEIGHT GAIN	5/32 (15.6%)	0/32 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
ANY EVENT	1/32 (3.1%)	2/32 (6.3%)
ARTHRALGIA MULTIPLE	1/32 (3.1%)	0/32 (0.0%)
OSTEOARTHRITIS KNEES	0/32 (0.0%)	1/32 (3.1%)
PAIN OF LOWER EXTREMITIES	0/32 (0.0%)	1/32 (3.1%)
STIFFNESS SHOULDER	0/32 (0.0%)	1/32 (3.1%)
NERVOUS SYSTEM DISORDERS		
ANY EVENT	12/32 (37.5%)	1/32 (3.1%)
DIZZINESS	1/32 (3.1%)	0/32 (0.0%)
HEADACHE	11/32 (34.4%)	1/32 (3.1%)
MIGRAINE	1/32 (3.1%)	0/32 (0.0%)

Note:events are given as Adverse event MEDDRA MSDECODE / Adverse event
Note:Events are given as MedDRA system organ class and lowest level term.
Number of volunteers with events / total number of volunteers (%)
Each episode of AE was counted as 1 AE: in some volunteers, multiple episodes of AE were recorded.

Biometry Europe Identifier: 305044 - ae - 27 - 21NOV02
(Continued)

Events	caucasian	asian
REPRODUCTIVE SYSTEM AND BREAST DISORDERS		
ANY EVENT	9/32 (28.1%)	30/32 (93.8%)
BREAST ENLARGEMENT	3/32 (9.4%)	0/32 (0.0%)
BREAST PAIN	0/32 (0.0%)	3/32 (9.4%)
BREAST SWELLING	0/32 (0.0%)	13/32 (40.6%)
CERVICAL POLYP	0/32 (0.0%)	2/32 (6.3%)
HOT FLUSHES,MENOPAUSAL	1/32 (3.1%)	0/32 (0.0%)
LEUKORRHEA	2/32 (6.3%)	10/32 (31.3%)
NIPPLE PAIN	0/32 (0.0%)	9/32 (28.1%)
SPOTTING VAGINAL	5/32 (15.6%)	0/32 (0.0%)
VAGINAL BLEEDING	0/32 (0.0%)	17/32 (53.1%)
VULVAL ITCHING	0/32 (0.0%)	1/32 (3.1%)
RESPIRATORY,THORACIC AND MEDIASTINAL DISORDERS		
ANY EVENT	1/32 (3.1%)	0/32 (0.0%)
RHINITIS	1/32 (3.1%)	0/32 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS		
ANY EVENT	1/32 (3.1%)	0/32 (0.0%)
SKIN PIGMENTATION	1/32 (3.1%)	0/32 (0.0%)

Note:events are given as Adverse event MEDDRA MSDECODE / Adverse event
Note:Events are given as MedDRA system organ class and lowest level term.
Number of volunteers with events / total number of volunteers (%)
Each episode of AE was counted as 1 AE: in some volunteers, multiple episodes of AE were recorded.

Biometry Europe Identifier: 305044 - ae - 27 - 21NOV02

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表 2.7.6.4- 3　　試験 308560：重症度別の有害事象発現率（例数，%）

総括報告書 A20152 14 項，table59 より引用

Table 59: Number of volunteers with adverse events by maximum intensity - FAS.

Preferred Term	Maximum intensity	E2, 0.100 mg, fasted state N (%)	E2, 0.190 mg, fasted state N (%)	E2, 0.190 mg, fed state N (%)
ANY SYSTEM				
ANY EVENT	mild	3/24 (12.5%)	1/24 (4.2%)	4/24 (16.7%)
	moderate	1/24 (4.2%)	2/24 (8.3%)	0/24 (0.0%)
	TOTAL	4/24 (16.7%)	3/24 (12.5%)	4/24 (16.7%)
GASTROINTESTINAL DISORDERS				
ANY EVENT	mild	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
Nausea	mild	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
ANY EVENT	mild	0/24 (0.0%)	0/24 (0.0%)	2/24 (8.3%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	2/24 (8.3%)
Venipuncture site haemorrhage	mild	0/24 (0.0%)	0/24 (0.0%)	2/24 (8.3%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	2/24 (8.3%)
INFECTIONS AND INFESTATIONS				
ANY EVENT	moderate	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
Herpes simplex	moderate	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Table 59: Number of volunteers with adverse events by maximum intensity - FAS. (cont.)

Preferred Term	Maximum intensity	E2, 0.100 mg, fasted state N (%)	E2, 0.190 mg, fasted state N (%)	E2, 0.190 mg, fed state N (%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS				
ANY EVENT	mild	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
Traumatic haematoma	mild	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
	TOTAL	0/24 (0.0%)	0/24 (0.0%)	1/24 (4.2%)
NERVOUS SYSTEM DISORDERS				
ANY EVENT	mild	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	moderate	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	1/24 (4.2%)	0/24 (0.0%)
Headache	mild	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	moderate	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	1/24 (4.2%)	0/24 (0.0%)
PSYCHIATRIC DISORDERS				
ANY EVENT	mild	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
Sleep disorder	mild	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS				
ANY EVENT	mild	1/24 (4.2%)	1/24 (4.2%)	0/24 (0.0%)
	moderate	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Table 59: Number of volunteers with adverse events by maximum intensity - FAS. (cont.)

Preferred Term	Maximum intensity	E2, 0.100 mg, fasted state N (%)	E2, 0.190 mg, fasted state N (%)	E2, 0.190 mg, fed state N (%)
ANY EVENT	TOTAL	1/24 (4.2%)	2/24 (8.3%)	0/24 (0.0%)
Menopausal symptoms	mild	1/24 (4.2%)	0/24 (0.0%)	0/24 (0.0%)
	moderate	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)
	TOTAL	1/24 (4.2%)	1/24 (4.2%)	0/24 (0.0%)
Metrorrhagia	mild	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)
	TOTAL	0/24 (0.0%)	1/24 (4.2%)	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Nihon Schering K.K.

表 2.7.6.4- 4　　試験 308560：治験薬との関連性判定別の有害事象発現率（例数，%）

総括報告書 A20152 14 項，table 66 より引用

Table 66: Number of volunteers and event counts by study drug relationship - FAS.

Preferred Term	Study drug relationship	E2, 0.100 mg, fasted state Events	N (%)	E2, 0.190 mg, fasted state Events	N (%)	E2, 0.190 mg, fed state Events	N (%)
ANY SYSTEM							
ANY EVENT	no	0	0/24 (0.0%)	0	0/24 (0.0%)	3	3/24 (12.5%)
	unlikely	3	3/24 (12.5%)	2	2/24 (8.3%)	1	1/24 (4.2%)
	possible	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
	TOTAL	4	4/24 (16.7%)	3	3/24 (12.5%)	4	4/24 (16.7%)
GASTROINTESTINAL DISORDERS							
ANY EVENT	unlikely	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
Nausea	unlikely	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS							
ANY EVENT	no	0	0/24 (0.0%)	0	0/24 (0.0%)	2	2/24 (8.3%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	2	2/24 (8.3%)
Venipuncture site haemorrhage	no	0	0/24 (0.0%)	0	0/24 (0.0%)	2	2/24 (8.3%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	2	2/24 (8.3%)
INFECTIONS AND INFESTATIONS							
ANY EVENT	unlikely	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
Herpes simplex	unlikely	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Table 66: Number of volunteers and event counts by study drug relationship - FAS. (cont.)

Preferred Term	Study drug relationship	E2, 0.100 mg, fasted state Events	N (%)	E2, 0.190 mg, fasted state Events	N (%)	E2, 0.190 mg, fed state Events	N (%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS							
ANY EVENT	no	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
Traumatic haematoma	no	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
	TOTAL	0	0/24 (0.0%)	0	0/24 (0.0%)	1	1/24 (4.2%)
NERVOUS SYSTEM DISORDERS							
ANY EVENT	possible	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
Headache	possible	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
PSYCHIATRIC DISORDERS							
ANY EVENT	unlikely	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
Sleep disorder	unlikely	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	0	0/24 (0.0%)	0	0/24 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS							
ANY EVENT	unlikely	1	1/24 (4.2%)	2	2/24 (8.3%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	2	2/24 (8.3%)	0	0/24 (0.0%)
Menopausal symptoms	unlikely	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)
	TOTAL	1	1/24 (4.2%)	1	1/24 (4.2%)	0	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Table 66: Number of volunteers and event counts by study drug relationship - FAS. (cont.)

Preferred Term	Study drug relationship	E2, 0.100 mg, fasted state Events	N (%)	E2, 0.190 mg, fasted state Events	N (%)	E2, 0.190 mg, fed state Events	N (%)
Metrorrhagia	unlikely	0	0/24 (0.0%)	1	1/24 (4.2%)	0	0/24 (0.0%)
	TOTAL	0	0/24 (0.0%)	1	1/24 (4.2%)	0	0/24 (0.0%)

Note: N is the number of volunteers with respective event / number of volunteers at risk.
Study 308560 / final / t_ae.sas / BIAS / 12APR05

Nihon Schering K.K.

表 2.7.6.4- 5　試験 300107：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%）

総括報告書 B69，14.3.1 項　T93 より引用

T 93　No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
ANY EVENT	mild	no	16/68 (23.5%)	9/72 (12.5%)	12/71 (16.9%)	37/211 (17.5%)
		unlikely	3/68 (4.4%)	1/72 (1.4%)	2/71 (2.8%)	6/211 (2.8%)
		possible	2/68 (2.9%)	6/72 (8.3%)	4/71 (5.6%)	12/211 (5.7%)
		probable	5/68 (7.4%)	6/72 (8.3%)	9/71 (12.7%)	20/211 (9.5%)
		definite	1/68 (1.5%)	2/72 (2.8%)	3/71 (4.2%)	6/211 (2.8%)
	moderate	no	4/68 (5.9%)	5/72 (6.9%)	4/71 (5.6%)	13/211 (6.2%)
		unlikely	2/68 (2.9%)	0/72 (0.0%)	3/71 (4.2%)	5/211 (2.4%)
		possible	1/68 (1.5%)	1/72 (1.4%)	0/71 (0.0%)	2/211 (0.9%)
		probable	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		definite	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
	severe	no	0/68 (0.0%)	3/72 (4.2%)	1/71 (1.4%)	4/211 (1.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		34/68 (50.0%)	34/72 (47.2%)	40/71 (56.3%)	108/211 (51.2%)
Abdominal distension	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	2/68 (2.9%)	0/72 (0.0%)	0/71 (0.0%)	2/211 (0.9%)
		possible	0/68 (0.0%)	3/72 (4.2%)	2/71 (2.8%)	5/211 (2.4%)
		probable	0/68 (0.0%)	2/72 (2.8%)	0/71 (0.0%)	2/211 (0.9%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	5/72 (6.9%)	2/71 (2.8%)	9/211 (4.3%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Abdominal pain lower	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	1/72 (1.4%)	2/71 (2.8%)	3/211 (1.4%)
		probable	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		definite	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	2/72 (2.8%)	6/71 (8.5%)	9/211 (4.3%)
Abdominal pain NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Abdominal pain upper	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Alanine aminotransferase increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Appetite decreased NOS	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Aspartate aminotransferase increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Asthma NOS	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
Back pain	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	2/72 (2.8%)	0/71 (0.0%)	3/211 (1.4%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Biopsy endometrium abnormal	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
Blood alkaline phosphatase NOS increas	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Blood cholesterol increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Blood glucose decreased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Blood lactate dehydrogenase increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
Blood pressure increased	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Blood triglycerides increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Breast engorgement	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	2/68 (2.9%)	0/72 (0.0%)	2/71 (2.8%)	4/211 (1.9%)
		probable	2/68 (2.9%)	1/72 (1.4%)	3/71 (4.2%)	6/211 (2.8%)
		definite	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		4/68 (5.9%)	3/72 (4.2%)	6/71 (8.5%)	13/211 (6.2%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Breast pain	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
		definite	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	3/71 (4.2%)	4/211 (1.9%)
Bronchitis NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Cervical polyp	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Chest pain NEC	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Chest pressure sensation	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Cholelithiasis	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Constipation	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		3/68 (4.4%)	1/72 (1.4%)	0/71 (0.0%)	4/211 (1.9%)
Cough	mild	no	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Cystitis NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
Diarrhoea NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Dizziness (exc vertigo)	mild	no	2/68 (2.9%)	0/72 (0.0%)	2/71 (2.8%)	4/211 (1.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	1/72 (1.4%)	3/71 (4.2%)	6/211 (2.8%)
Ecchymosis	mild	no	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Eczema NOS	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	1/72 (1.4%)	0/71 (0.0%)	2/211 (0.9%)
Endometrial cancer stage IV	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Epistaxis	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Fatigue	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	1/72 (1.4%)	0/71 (0.0%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Feeling cold	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Fibrocystic breast disease	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	2/68 (2.9%)	0/72 (0.0%)	0/71 (0.0%)	2/211 (0.9%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	0/72 (0.0%)	0/71 (0.0%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Formication	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Gamma-glutamyltransferase increased	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Genital pruritus female	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Headache NOS	mild	no	8/68 (11.8%)	0/72 (0.0%)	5/71 (7.0%)	13/211 (6.2%)
		unlikely	1/68 (1.5%)	1/72 (1.4%)	0/71 (0.0%)	2/211 (0.9%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	2/71 (2.8%)	3/211 (1.4%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		9/68 (13.2%)	2/72 (2.8%)	7/71 (9.9%)	18/211 (8.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Heart rate increased	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Hoarseness	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Hyperventilation	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Hypoaesthesia	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Hypotension NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Influenza	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Joint stiffness	mild	no	1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	1/72 (1.4%)	2/71 (2.8%)	5/211 (2.4%)
Low density lipoprotein increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Malaise	mild	no	1/68 (1.5%)	1/72 (1.4%)	1/71 (1.4%)	3/211 (1.4%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	1/72 (1.4%)	1/71 (1.4%)	4/211 (1.9%)
Metastases to lymph nodes	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Nail disorder NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Nasal congestion	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Nasal dryness	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Nasopharyngitis	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Nausea	mild	no	1/68 (1.5%)	0/72 (0.0%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	1/72 (1.4%)	2/71 (2.8%)	4/211 (1.9%)
Neck pain	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Nipple pain	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Ocular hyperaemia	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Oedema NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
Palpitations	mild	no	1/68 (1.5%)	0/72 (0.0%)	2/71 (2.8%)	3/211 (1.4%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	3/71 (4.2%)	4/211 (1.9%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Paronychia	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
Periodontitis	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Pharyngitis NOS	mild	no	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	2/72 (2.8%)	2/71 (2.8%)	4/211 (1.9%)
Pruritus NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	2/71 (2.8%)	3/211 (1.4%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Pyrexia	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	2/72 (2.8%)	0/71 (0.0%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	3/72 (4.2%)	0/71 (0.0%)	3/211 (1.4%)
Rhinitis allergic NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Rhinitis NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Rhinorrhoea	mild	no	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	2/71 (2.8%)	3/211 (1.4%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Sore throat NOS	mild	no	1/68 (1.5%)	2/72 (2.8%)	2/71 (2.8%)	5/211 (2.4%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	2/72 (2.8%)	0/71 (0.0%)	2/211 (0.9%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	4/72 (5.6%)	2/71 (2.8%)	7/211 (3.3%)
Spinal disorder NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Sputum increased	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
Stomatitis	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Tendonitis	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
Tinea pedis	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Tinnitus	mild	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Toothache	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Upper respiratory tract infection NOS	mild	no	1/68 (1.5%)	2/72 (2.8%)	0/71 (0.0%)	3/211 (1.4%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	2/72 (2.8%)	1/71 (1.4%)	4/211 (1.9%)
Urticaria NOS	mild	no	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Uterine haemorrhage	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	1/68 (1.5%)	0/72 (0.0%)	2/71 (2.8%)	3/211 (1.4%)
		probable	0/68 (0.0%)	1/72 (1.4%)	1/71 (1.4%)	2/211 (0.9%)
		definite	1/68 (1.5%)	1/72 (1.4%)	1/71 (1.4%)	3/211 (1.4%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		2/68 (2.9%)	2/72 (2.8%)	4/71 (5.6%)	8/211 (3.8%)
Vaginal discharge	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	4/72 (5.6%)	5/71 (7.0%)	9/211 (4.3%)
		probable	2/68 (2.9%)	7/72 (9.7%)	5/71 (7.0%)	14/211 (6.6%)
		definite	0/68 (0.0%)	1/72 (1.4%)	0/71 (0.0%)	1/211 (0.5%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	2/71 (2.8%)	2/211 (0.9%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		3/68 (4.4%)	12/72 (16.7%)	12/71 (16.9%)	27/211 (12.8%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Vaginitis bacterial NOS	mild	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		0/68 (0.0%)	0/72 (0.0%)	1/71 (1.4%)	1/211 (0.5%)
Myalgia aggravated	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : SO04OT.sas)

(Continued)

Nihon Schering K.K.

T 93 No. and (%) of patients with one or more adverse events by intensity and relation to study medication per treatment group (FAS) (continued)

EVENT(MedDRA)	Maximum AE intensity	Maximum AE study drug relation	placebo	E2, 0.5 mg	E2, 1.0 mg	Overall
(System Organ Class continued from previous page)						
Gingival oedema	mild	no	1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	moderate	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	severe	no	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		unlikely	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		possible	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		probable	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
		definite	0/68 (0.0%)	0/72 (0.0%)	0/71 (0.0%)	0/211 (0.0%)
	Total		1/68 (1.5%)	0/72 (0.0%)	0/71 (0.0%)	1/211 (0.5%)

Note: events are given as System Organ Class / Adverse event MedDRA preferred term code
(Order No. : S0040T.sas)

表 2.7.6.4- 6 試験 300107：AE コード用語の対比表（MedDRA ver 7.1 基本語 vs MedDRA ver 3.0 基本語）

CTD 統合解析の AE コード語		総括報告書中の AE コード語		CRF 中の記載
MedDRA_SOC 分類名（日本語，Ver7.1）	MedDRA_PT 用語（日本語，Ver7.1）	MedDRA_SOC 用語（英語，Ver3.0）	MedDRA_PT 用語（英語，Ver3.0）	医師報告用語（日本語）
胃腸障害	悪心	Gastrointestinal disorders	Nausea	嘔気
	下腹部痛	Gastrointestinal disorders	Abdominal pain lower	下腹部痛
	下痢	Gastrointestinal disorders	Diarrhoea NOS	下痢
	口内炎	Gastrointestinal disorders	Stomatitis	口内炎
	歯痛	Gastrointestinal disorders	Toothache	歯痛
	歯肉腫脹	Gastrointestinal disorders	Gingival oedema	歯肉の腫脹
	上腹部痛	General disorders and administration site conditions	Abdominal pain upper	胃痛
	腹痛	Gastrointestinal disorders	Abdominal pain NOS	腹痛
	腹部不快感	Gastrointestinal disorders	Abdominal distension	下腹部重圧感
	腹部不快感	General disorders and administration site conditions	Abdominal pain lower	下腹部違和感
	腹部膨満	Gastrointestinal disorders	Abdominal distension	下腹部の張った感じ，下腹部緊満感，下腹部膨満感
	便秘	Gastrointestinal disorders	Constipation	便秘，便秘症
感染症および寄生虫症	インフルエンザ	Respiratory, thoracic and mediastinal disorders	Influenza	インフルエンザ
	咽頭炎	Infections and infestations	Pharyngitis NOS	咽頭炎
	気管支炎	Infections and infestations	Bronchitis NOS	気管支炎（感冒）
	細菌性膣炎	Infections and infestations	Vaginitis bacterial NOS	細菌性膣炎
	歯根膜感染	Infections and infestations	Periodontitis	歯根炎症
	上気道感染	Infections and infestations	Upper respiratory tract infection NOS	上気道炎
	足部白癬	Skin & subcutaneous tissue disorders	Tinea pedis	白癬（足）
	爪囲炎	Skin & subcutaneous tissue disorders	Paronychia	左第３指爪根部炎症（手）
	爪感染	Skin & subcutaneous tissue disorders	Nail disorder NOS	右足親指ツメ化膿
	鼻咽頭炎	Respiratory, thoracic and mediastinal disorders	Cough	咳（感冒），感冒（咳嗽）
	鼻咽頭炎	General disorders and administration site conditions	Malaise	感冒による倦怠感，倦怠感（感冒）
	鼻咽頭炎	Respiratory, thoracic and mediastinal disorders	Nasal congestion	鼻づまり（感冒）
	鼻咽頭炎	Infections and infestations	Nasopharyngitis	感冒症候群
	鼻咽頭炎	Infections and infestations	Pharyngitis NOS	感冒（咽頭炎）
	鼻咽頭炎	General disorders and administration site conditions	Pyrexia	感冒による発熱

CTD 統合解析の AE コード語		総括報告書中の AE コード語		CRF 中の記載
MedDRA_SOC 分類名（日本語，Ver7.1）	MedDRA_PT 用語（日本語，Ver7.1）	MedDRA_SOC 用語（英語，Ver3.0）	MedDRA_PT 用語（英語，Ver3.0）	医師報告用語（日本語）
	鼻咽頭炎	Respiratory, thoracic and mediastinal disorders	Rhinitis NOS	（風邪）鼻炎
	鼻咽頭炎	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	感冒（鼻汁）
	鼻咽頭炎	Infections and infestations	Sore throat NOS	感冒（咽頭痛），感冒による咽頭痛
	鼻咽頭炎	Respiratory, thoracic and mediastinal disorders	Sputum increased	感冒（喀痰）
	膀胱炎	Renal and urinary disorders	Cystitis NOS	膀胱炎
肝胆道系障害	胆石症	Hepato-biliary disorders	Cholelithiasis	胆石
眼障害	眼充血	Eye disorders	Ocular hyperaemia	右眼充血
筋骨格系および結合組織障害	筋骨格硬直	Musculoskeletal, connective tissue and bone disorders	Joint stiffness	肩こり，肩こり（首すじ）
	筋痛	Musculoskeletal, connective tissue and bone disorders	Myalgia aggravated	筋肉痛（両腕）
	頚部痛	Musculoskeletal, connective tissue and bone disorders	Neck pain	頸部痛
	重感	General disorders and administration site conditions	Fatigue	身体が重い
	脊椎靭帯骨化症	Musculoskeletal, connective tissue and bone disorders	Spinal disorder NOS	胸椎黄色靭帯骨化症（下肢痛）
	背部痛	Musculoskeletal, connective tissue and bone disorders	Back pain	腰痛，背部痛
	腱炎	Musculoskeletal, connective tissue and bone disorders	Tendonitis	足底部腱膜炎
血管障害	低血圧	Vascular disorders	Hypotension NOS	低血圧症
呼吸器、胸郭および縦隔障害	アレルギー性鼻炎	Immune system disorders	Rhinitis allergic NOS	アレルギー性鼻炎
	咽喉頭疼痛	Infections and infestations	Sore throat NOS	咽頭痛
	過換気	Respiratory, thoracic and mediastinal disorders	Hyperventilation	過呼吸発作
	湿性咳嗽	Respiratory, thoracic and mediastinal disorders	Sputum increased	喀痰
	鼻乾燥	Respiratory, thoracic and mediastinal disorders	Nasal dryness	鼻がかわく
	鼻出血	Vascular disorders	Epistaxis	鼻出血
	鼻漏	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	鼻汁
	喘息	Respiratory, thoracic and mediastinal disorders	Asthma NOS	喘息
	嗄声	Respiratory, thoracic and mediastinal disorders	Hoarseness	嗄声
耳および迷路障害	耳鳴	Nervous system disorders	Tinnitus	耳なり
傷害、中毒および処置合併症	挫傷	Skin & subcutaneous tissue disorders	Ecchymosis	打ち身，打撲（右肩、顔、胸部）
心臓障害	動悸	Cardiac disorders	Palpitations	動悸
神経系障害	感覚減退	Nervous system disorders	Hypoaesthesia	左手しびれ
	蟻走感	Nervous system disorders	Formication	皮膚の蟻走感

CTD 統合解析の AE コード語		総括報告書中の AE コード語		CRF 中の記載
MedDRA_SOC 分類名（日本語，Ver7.1）	MedDRA_PT 用語（日本語，Ver7.1）	MedDRA_SOC 用語（英語，Ver3.0）	MedDRA_PT 用語（英語，Ver3.0）	医師報告用語（日本語）
	頭痛	Nervous system disorders	Headache NOS	後頭部痛，頭重感，頭痛
	浮動性めまい	Nervous system disorders	Dizziness (exc vertigo)	めまい
生殖系および乳房障害	子宮頚管ポリープ	Reproductive system and breast disorders	Cervical polyp	子宮頸管ポリープ
	子宮出血	Reproductive system and breast disorders	Uterine haemorrhage	子宮出血
	女性陰部そう痒症	Reproductive system and breast disorders	Genital pruritus female	外陰掻痒
	性器出血	Reproductive system and breast disorders	Uterine haemorrhage	性器出血，不正出血
	性器分泌物	Reproductive system and breast disorders	Vaginal discharge	おりもの
	性器分泌物	Reproductive system and breast disorders	Vaginal discharge	帯下，帯下（黄色），帯下（乳白色），帯下感
	線維嚢胞性乳腺疾患	Neoplasms benign and malignant (including cysts and polyps)	Fibrocystic breast disease	乳腺症
	乳頭痛	Reproductive system and breast disorders	Nipple pain	乳頭痛
	乳房腫脹	Reproductive system and breast disorders	Breast engorgement	乳房の張った感じ，乳房緊満，乳房緊満感
	乳房痛	Reproductive system and breast disorders	Breast pain	乳房圧痛
	乳房痛	Reproductive system and breast disorders	Breast pain	乳房圧痛感
	乳房痛	Reproductive system and breast disorders	Breast pain	乳房痛
全身障害および投与局所様態	胸痛	General disorders and administration site conditions	Chest pain NEC	胸痛
	胸部不快感	Cardiac disorders	Chest pressure sensation	胸部圧迫感
	倦怠感	General disorders and administration site conditions	Malaise	倦怠感，全身倦怠感
	発熱	General disorders and administration site conditions	Pyrexia	発熱
	疲労	General disorders and administration site conditions	Fatigue	疲労
	末梢性浮腫	General disorders and administration site conditions	Oedema NOS	下肢浮腫
	冷感	General disorders and administration site conditions	Feeling cold	寒気
代謝および栄養障害	食欲減退	Metabolism and nutrition disorders	Appetite decreased NOS	食欲減退
皮膚および皮下組織障害	そう痒症	Skin & subcutaneous tissue disorders	Pruritus NOS	掻痒（心窩部），皮膚掻痒（腋下、足のつけね）
	湿疹	Skin & subcutaneous tissue disorders	Eczema NOS	湿疹
	全身性そう痒症	Skin & subcutaneous tissue disorders	Pruritus NOS	全身掻痒感
	蕁麻疹	Skin & subcutaneous tissue disorders	Urticaria NOS	蕁麻疹
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	リンパ節転移	Neoplasms benign and malignant (including cysts and polyps)	Metastases to lymph nodes	左頚部リンパ節転移
	子宮内膜癌第４期	Neoplasms benign and malignant (including cysts and polyps)	Endometrial cancer stage IV	子宮内膜腺癌（Stage Ⅳb）
臨床検査	アスパラギン酸アミノトランスフェラーゼ増加	Investigations	Aspartate aminotransferase increased	GOT 上昇

CTD 統合解析の AE コード語		総括報告書中の AE コード語		CRF 中の記載
MedDRA_SOC 分類名（日本語，Ver7.1）	MedDRA_PT 用語（日本語，Ver7.1）	MedDRA_SOC 用語（英語，Ver3.0）	MedDRA_PT 用語（英語，Ver3.0）	医師報告用語（日本語）
	アラニン・アミノトランスフェラーゼ増加	Investigations	Alanine aminotransferase increased	GPT 上昇
	γ－グルタミルトランスフェラーゼ増加	Investigations	Gamma-glutamyltransferase increased	γ－GTP 上昇，γGTP 上昇
	血圧上昇	Investigations	Blood pressure increased	血圧上昇
	血中アルカリホスファターゼ増加	Investigations	Blood alkaline phosphatase NOS increased	Al－P 上昇
	血中コレステロール増加	Investigations	Blood cholesterol increased	T－cho 上昇
	血中トリグリセリド増加	Investigations	Blood triglycerides increased	TG 上昇
	血中ブドウ糖減少	Investigations	Blood glucose decreased	血糖値低下
	血中乳酸脱水素酵素増加	Investigations	Blood lactate dehydrogenase increased	LDH の上昇，LDH 上昇
	子宮内膜生検異常	Investigations	Biopsy endometrium abnormal	子宮内膜細胞診悪化（ClassⅤ）
	心拍数増加	Investigations	Heart rate increased	脈拍数増加
	低比重リポ蛋白増加	Investigations	Low density lipoprotein increased	LDL－cho 上昇

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表 2.7.6.4- 7　　試験 300103：重症度別の有害事象発現率（例数，%）

総括報告書 A23185　表 14-3-1-5（1 年間投与），表 14-3-1-6（2 年間投与）より引用

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	9/20 (45.0%)	6/20 (30.0%)	1/20 (5.0%)	16/20 (80.0%)
Blood and lymphatic system disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypochromic anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cardiac disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Angina pectoris	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arrhythmia	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Palpitations	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Supraventricular extrasystoles	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deafness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Meniere's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinnitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endocrine disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Goitre	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroid cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroiditis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

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Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abnormal sensation in eye	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthenopia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blepharitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Conjunctival haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctivitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Corneal dystrophy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eye pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lacrimation increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open angle glaucoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periorbital haematoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pterygium	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Retinal detachment	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vitreous floaters	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	2/20 (10.0%)	4/20 (20.0%)	0/20 (0.0%)	6/20 (30.0%)
Abdominal distension	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abdominal pain	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain lower	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Abdominal pain upper	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorectal disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Constipation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diarrhoea	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Dyspepsia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epigastric discomfort	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastritis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastritis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastroenteritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastrointestinal pain	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastrointestinal upset	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glossitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Haemorrhoids	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal ischaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal obstruction	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritable bowel syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lip dry	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nausea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pancreatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Reflux oesophagitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Stomach discomfort	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Stomatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Tongue ulceration	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Toothache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vomiting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

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Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	3/20 (15.0%)	1/20 (5.0%)	0/20 (0.0%)	4/20 (20.0%)
Chest discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Feeling cold	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Feeling hot	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Malaise	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Oedema peripheral	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Thirst	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hepatobiliary disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cholecystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic function abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Immune system disorders				
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Dermatitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Seasonal allergy	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	6/20 (30.0%)	3/20 (15.0%)	0/20 (0.0%)	9/20 (45.0%)
Bronchiolitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chronic sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Groin abscess	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes simplex	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Herpes zoster	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Laryngopharyngitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nasopharyngitis	4/20 (20.0%)	2/20 (10.0%)	0/20 (0.0%)	6/20 (30.0%)
Otitis media	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngitis	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Tinea pedis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tonsillitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract infection	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Injury, poisoning and procedural complications				
ANY EVENT	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Arthropod sting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Contusion	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Haemarthrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open wound	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Blood glucose increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Blood thyroid stimulating hormone decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood thyroid stimulating hormone increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood triglycerides increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gamma-glutamyltransferase increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipids increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Liver function test abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Low density lipoprotein increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Protein urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Smear cervix abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sputum test	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urine output decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Weight increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
White blood cell count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Metabolism and nutrition disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorexia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diabetes mellitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypercholesterolaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperlipidaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	2/20 (10.0%)	2/20 (10.0%)	0/20 (0.0%)	4/20 (20.0%)
Arthralgia	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Arthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Back pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Buttock pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint swelling	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Limb discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Localised osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle cramp	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Musculoskeletal stiffness	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Myalgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck, shoulder and arm syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nodal osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pain in extremity	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Radius fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rib fracture	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Sensation of heaviness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Spondylosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tenosynovitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric cancer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipoma	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Metastases to lymph nodes	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Autonomic nervous system imbalance	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dizziness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysgeusia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Facial nerve disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Headache	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hypoaesthesia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intercostal neuralgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neuropathy peripheral	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parosmia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sciatica	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tension headache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vertigo	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Psychiatric disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depressive symptom	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysphoria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Insomnia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritability	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sleep disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Bladder malposition acquired	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Micturition disorder	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Urge incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urinary incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	2/20 (10.0%)	1/20 (5.0%)	0/20 (0.0%)	3/20 (15.0%)
Breast discomfort	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Breast disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast engorgement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast fibrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast pain	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Cervical polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cervicitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysmenorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibrocystic breast disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital discharge	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Genital haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital pruritus female	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hot flush	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Menopausal symptoms	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Nipple pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Uterine malposition	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginal candidiasis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulval oedema	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvovaginal discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngolaryngeal pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharynx discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Productive cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract inflammation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	3/20 (15.0%)	1/20 (5.0%)	0/20 (0.0%)	4/20 (20.0%)
Acne	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Body tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cheilitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermal cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dermatitis contact	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dry skin	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eczema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Eczema asteatotic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Erythema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Excoriation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Face oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hyperkeratosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pruritus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash papular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash pustular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin papilloma	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Urticaria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail avulsion	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vascular disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Atherosclerosis obliterans	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure fluctuation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deep vein thrombosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypertension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypotension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral vascular disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	28/59 (47.5%)	18/59 (30.5%)	1/59 (1.7%)	47/59 (79.7%)
Blood and lymphatic system disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypochromic anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cardiac disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Angina pectoris	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arrhythmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Palpitations	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Supraventricular extrasystoles	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Deafness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Meniere's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinnitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Endocrine disorders				
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Goitre	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Thyroid cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thyroiditis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Abnormal sensation in eye	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Asthenopia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blepharitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctival haemorrhage	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Corneal dystrophy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eye pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lacrimation increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open angle glaucoma	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Periorbital haematoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pterygium	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinal detachment	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vitreous floaters	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	6/59 (10.2%)	3/59 (5.1%)	0/59 (0.0%)	9/59 (15.3%)
Abdominal distension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain lower	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain upper	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anorectal disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Constipation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Diarrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspepsia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epigastric discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric ulcer	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Gastritis	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastritis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastroenteritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Gastrointestinal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastrointestinal upset	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Glossitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemorrhoids	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal ischaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal obstruction	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Irritable bowel syndrome	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lip dry	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nausea	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Pancreatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Reflux oesophagitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomach discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomatitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tongue ulceration	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Toothache	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vomiting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	4/59 (6.8%)	3/59 (5.1%)	0/59 (0.0%)	7/59 (11.9%)
Chest discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest pain	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fatigue	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Feeling cold	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Feeling hot	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Malaise	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Oedema peripheral	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Thirst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatobiliary disorders				
ANY EVENT	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Cholecystitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic function abnormal	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Immune system disorders				
ANY EVENT	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Dermatitis allergic	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Rhinitis allergic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Seasonal allergy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	11/59 (18.6%)	6/59 (10.2%)	0/59 (0.0%)	17/59 (28.8%)
Bronchiolitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bronchitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bronchitis acute	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Chronic sinusitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cystitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Cystitis acute	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Groin abscess	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes simplex	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes zoster	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Laryngopharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nasopharyngitis	8/59 (13.6%)	4/59 (6.8%)	0/59 (0.0%)	12/59 (20.3%)
Otitis media	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinea pedis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tonsillitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract infection	2/59 (3.4%)	1/59 (1.7%)	0/59 (0.0%)	3/59 (5.1%)
Injury, poisoning and procedural complications				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arthropod sting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Contusion	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemarthrosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open wound	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Blood glucose increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood thyroid stimulating hormone decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood thyroid stimulating hormone increased	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood triglycerides increased	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gamma-glutamyltransferase increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipids increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Liver function test abnormal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Low density lipoprotein increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Protein urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Smear cervix abnormal	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sputum test	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urine output decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Weight increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
White blood cell count decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metabolism and nutrition disorders				
ANY EVENT	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Anorexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Diabetes mellitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hypercholesterolaemia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hyperlipidaemia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	6/59 (10.2%)	4/59 (6.8%)	1/59 (1.7%)	11/59 (18.6%)
Arthralgia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Arthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Back pain	2/59 (3.4%)	3/59 (5.1%)	0/59 (0.0%)	5/59 (8.5%)
Buttock pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint swelling	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Limb discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Localised osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle cramp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Musculoskeletal stiffness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Myalgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck, shoulder and arm syndrome	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nodal osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pain in extremity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Radius fracture	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)
Rib fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sensation of heaviness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Spondylosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tenosynovitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric cancer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metastases to lymph nodes	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	3/59 (5.1%)	2/59 (3.4%)	0/59 (0.0%)	5/59 (8.5%)
Autonomic nervous system imbalance	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dizziness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysgeusia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Facial nerve disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Headache	0/59 (0.0%)	2/59 (3.4%)	0/59 (0.0%)	2/59 (3.4%)
Hypoaesthesia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intercostal neuralgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neuropathy peripheral	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Parosmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sciatica	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tension headache	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vertigo	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Psychiatric disorders				
ANY EVENT	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Depressive symptom	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysphoria	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Insomnia	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Irritability	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sleep disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bladder malposition acquired	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysuria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Micturition disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urge incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urinary incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	10/59 (16.9%)	3/59 (5.1%)	0/59 (0.0%)	13/59 (22.0%)
Breast discomfort	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Breast disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast engorgement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast fibrosis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Breast pain	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Cervical polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cervicitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysmenorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibrocystic breast disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Genital discharge	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Genital haemorrhage	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Genital pruritus female	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hot flush	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Menopausal symptoms	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nipple pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Uterine malposition	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vaginal candidiasis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulval oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvovaginal discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Asthma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngolaryngeal pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Pharynx discomfort	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Productive cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract inflammation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	4/59 (6.8%)	1/59 (1.7%)	0/59 (0.0%)	5/59 (8.5%)
Acne	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Body tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cheilitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Dermal cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis contact	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dry skin	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eczema	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Eczema asteatotic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Erythema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Excoriation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Face oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hyperkeratosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pruritus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rash	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash papular	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash pustular	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin papilloma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urticaria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nail avulsion	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Vascular disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Atherosclerosis obliterans	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure fluctuation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Deep vein thrombosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypertension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypotension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral vascular disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	6/16 (37.5%)	5/16 (31.3%)	2/16 (12.5%)	13/16 (81.3%)
Blood and lymphatic system disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypochromic anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cardiac disorders				
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Angina pectoris	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arrhythmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Palpitations	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Supraventricular extrasystoles	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deafness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Meniere's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinnitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endocrine disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Goitre	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thyroid cyst	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Thyroiditis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abnormal sensation in eye	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Asthenopia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blepharitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctival haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Corneal dystrophy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eye pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lacrimation increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open angle glaucoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periorbital haematoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pterygium	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinal detachment	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vitreous floaters	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	5/16 (31.3%)	1/16 (6.3%)	1/16 (6.3%)	7/16 (43.8%)
Abdominal distension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abdominal pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain lower	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain upper	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	3/16 (18.8%)
Abdominal rigidity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anorectal disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Constipation	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Diarrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dyspepsia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Epigastric discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastritis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastroenteritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal upset	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glossitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemorrhoids	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal ischaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal obstruction	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Irritable bowel syndrome	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Lip dry	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nausea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pancreatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Reflux oesophagitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Stomach discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Stomatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tongue ulceration	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Toothache	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vomiting	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Chest discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling cold	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling hot	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Malaise	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Oedema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Oedema peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thirst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatobiliary disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cholecystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic function abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Immune system disorders				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Dermatitis allergic	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Rhinitis allergic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Seasonal allergy	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	3/16 (18.8%)	1/16 (6.3%)	0/16 (0.0%)	4/16 (25.0%)
Bronchiolitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chronic sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Groin abscess	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes simplex	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes zoster	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Laryngopharyngitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nasopharyngitis	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Otitis media	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Tinea pedis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tonsillitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Upper respiratory tract infection	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Injury, poisoning and procedural complications				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arthropod sting	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Contusion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemarthrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open wound	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Blood glucose increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood pressure increased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood thyroid stimulating hormone decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood thyroid stimulating hormone increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood triglycerides increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gamma-glutamyltransferase increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipids increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Liver function test abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Low density lipoprotein increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Protein urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Smear cervix abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sputum test	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urine output decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Weight increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
White blood cell count decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Metabolism and nutrition disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Anorexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Diabetes mellitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypercholesterolaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperlipidaemia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	3/16 (18.8%)	3/16 (18.8%)	0/16 (0.0%)	6/16 (37.5%)
Arthralgia	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Arthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Back pain	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	3/16 (18.8%)
Buttock pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint swelling	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Limb discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Localised osteoarthritis	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Muscle cramp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle rigidity	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Musculoskeletal stiffness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Myalgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck, shoulder and arm syndrome	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nodal osteoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pain in extremity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Radius fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rib fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sensation of heaviness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Spondylosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tenosynovitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric cancer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Metastases to lymph nodes	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	4/16 (25.0%)	1/16 (6.3%)	0/16 (0.0%)	5/16 (31.3%)
Autonomic nervous system imbalance	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dizziness	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Dysgeusia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Facial nerve disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Hypoaesthesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intercostal neuralgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neuropathy peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parosmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sciatica	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Tension headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vertigo	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Psychiatric disorders				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Depressive symptom	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dysphoria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Insomnia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Irritability	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sleep disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bladder malposition acquired	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Micturition disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urge incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urinary incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	4/16 (25.0%)	1/16 (6.3%)	0/16 (0.0%)	5/16 (31.3%)
Breast discomfort	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Breast disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast engorgement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast fibrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Cervical polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cervicitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysmenorrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibrocystic breast disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital discharge	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Genital haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital pruritus female	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hot flush	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Menopausal symptoms	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nipple pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Uterine malposition	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginal candidiasis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulval oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvovaginal discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)	2/16 (12.5%)
Asthma	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)
Cough	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Pharyngolaryngeal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharynx discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Productive cough	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinorrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Upper respiratory tract inflammation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Acne	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Body tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cheilitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermal cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis contact	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dry skin	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eczema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Eczema asteatotic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Erythema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Excoriation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Face oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperkeratosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pruritus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash papular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash pustular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin papilloma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urticaria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail avulsion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vascular disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Atherosclerosis obliterans	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure fluctuation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deep vein thrombosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypertension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypotension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral vascular disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	24/57 (42.1%)	15/57 (26.3%)	3/57 (5.3%)	42/57 (73.7%)
Blood and lymphatic system disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypochromic anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cardiac disorders				
ANY EVENT	1/57 (1.8%)	1/57 (1.8%)	1/57 (1.8%)	3/57 (5.3%)
Angina pectoris	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Arrhythmia	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Palpitations	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Supraventricular extrasystoles	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Ear and labyrinth disorders				
ANY EVENT	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Deafness	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Meniere's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinnitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endocrine disorders				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Goitre	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thyroid cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thyroiditis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abnormal sensation in eye	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Asthenopia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blepharitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctival haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Corneal dystrophy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eye pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lacrimation increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Open angle glaucoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periorbital haematoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pterygium	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinal detachment	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vitreous floaters	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	7/57 (12.3%)	1/57 (1.8%)	1/57 (1.8%)	9/57 (15.8%)
Abdominal distension	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abdominal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal pain lower	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal pain upper	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal rigidity	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anorectal disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Constipation	5/57 (8.8%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Diarrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dyspepsia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epigastric discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric ulcer	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis atrophic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastroenteritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal upset	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Glossitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Haemorrhoids	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intestinal ischaemia	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Intestinal obstruction	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Irritable bowel syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lip dry	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nausea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pancreatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Reflux oesophagitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Stomach discomfort	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Stomatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tongue ulceration	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Toothache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vomiting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Chest discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chest pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fatigue	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Feeling cold	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling hot	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Malaise	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Oedema peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thirst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hepatobiliary disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cholecystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic function abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Immune system disorders				
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Dermatitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Seasonal allergy	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	11/57 (19.3%)	4/57 (7.0%)	0/57 (0.0%)	15/57 (26.3%)
Bronchiolitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis acute	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Chronic sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis acute	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Groin abscess	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes simplex	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes zoster	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Laryngopharyngitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nasopharyngitis	6/57 (10.5%)	2/57 (3.5%)	0/57 (0.0%)	8/57 (14.0%)
Otitis media	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pharyngitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tinea pedis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tonsillitis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Upper respiratory tract infection	5/57 (8.8%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Injury, poisoning and procedural complications				
ANY EVENT	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Arthropod sting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Contusion	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Haemarthrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Open wound	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	6/57 (10.5%)	1/57 (1.8%)	0/57 (0.0%)	7/57 (12.3%)
Blood glucose increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood triglycerides increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gamma-glutamyltransferase increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Lipids increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Liver function test abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Low density lipoprotein increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Protein urine present	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Smear cervix abnormal	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Sputum test	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Urine output decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Weight increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
White blood cell count decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metabolism and nutrition disorders				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Anorexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Diabetes mellitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypercholesterolaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperlipidaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	9/57 (15.8%)	2/57 (3.5%)	0/57 (0.0%)	11/57 (19.3%)
Arthralgia	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Arthritis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Back pain	5/57 (8.8%)	1/57 (1.8%)	0/57 (0.0%)	6/57 (10.5%)
Buttock pain	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Joint swelling	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Limb discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Localised osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle cramp	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle rigidity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Musculoskeletal stiffness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Myalgia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck, shoulder and arm syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nodal osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pain in extremity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Radius fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rib fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sensation of heaviness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Spondylosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tenosynovitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric cancer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lipoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metastases to lymph nodes	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	5/57 (8.8%)	2/57 (3.5%)	0/57 (0.0%)	7/57 (12.3%)
Autonomic nervous system imbalance	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dizziness	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Dysgeusia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Facial nerve disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Headache	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hypoaesthesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intercostal neuralgia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Neuropathy peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parosmia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sciatica	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tension headache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vertigo	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Psychiatric disorders				
ANY EVENT	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Depressive symptom	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysphoria	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Insomnia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Irritability	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sleep disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bladder malposition acquired	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Micturition disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urge incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urinary incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	19/57 (33.3%)	5/57 (8.8%)	0/57 (0.0%)	24/57 (42.1%)
Breast discomfort	8/57 (14.0%)	0/57 (0.0%)	0/57 (0.0%)	8/57 (14.0%)
Breast disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast engorgement	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Breast fibrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast pain	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Cervical polyp	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Cervicitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dysmenorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibrocystic breast disease	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Genital discharge	6/57 (10.5%)	0/57 (0.0%)	0/57 (0.0%)	6/57 (10.5%)
Genital haemorrhage	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Genital pruritus female	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Hot flush	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Menopausal symptoms	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nipple pain	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Uterine malposition	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vaginal candidiasis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Vulval oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvovaginal discomfort	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	5/57 (8.8%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Asthma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cough	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Pharyngolaryngeal pain	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Pharynx discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Productive cough	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Upper respiratory tract inflammation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	8/57 (14.0%)	1/57 (1.8%)	1/57 (1.8%)	10/57 (17.5%)
Acne	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Body tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cheilitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermal cyst	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis contact	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dry skin	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eczema	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Eczema asteatotic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Erythema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Excoriation	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Face oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperkeratosis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nail disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pruritus	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash papular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash pustular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin papilloma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urticaria	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Surgical and medical procedures				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nail avulsion	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vascular disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Atherosclerosis obliterans	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure fluctuation	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Deep vein thrombosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypertension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypotension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Peripheral vascular disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	15/40 (37.5%)	12/40 (30.0%)	2/40 (5.0%)	29/40 (72.5%)
Blood and lymphatic system disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypochromic anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cardiac disorders				
ANY EVENT	1/40 (2.5%)	2/40 (5.0%)	0/40 (0.0%)	3/40 (7.5%)
Angina pectoris	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Arrhythmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Palpitations	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Supraventricular extrasystoles	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Deafness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Meniere's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinnitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endocrine disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Goitre	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroid cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroiditis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	4/40 (10.0%)	1/40 (2.5%)	0/40 (0.0%)	5/40 (12.5%)
Abnormal sensation in eye	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Asthenopia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blepharitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctival haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Corneal dystrophy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eye pain	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Lacrimation increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open angle glaucoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periorbital haematoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pterygium	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Retinal detachment	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vitreous floaters	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	4/40 (10.0%)	5/40 (12.5%)	0/40 (0.0%)	9/40 (22.5%)
Abdominal distension	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain lower	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain upper	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Abdominal rigidity	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anorectal disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Constipation	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Diarrhoea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Dyspepsia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epigastric discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastritis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastroenteritis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Gastrointestinal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastrointestinal upset	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glossitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Haemorrhoids	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Intestinal ischaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Intestinal obstruction	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Irritable bowel syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lip dry	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nausea	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Pancreatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Reflux oesophagitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Stomach discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Stomatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tongue ulceration	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Toothache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vomiting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	5/40 (12.5%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Chest discomfort	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chest pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fatigue	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling cold	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling hot	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Malaise	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Oedema peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thirst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatobiliary disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Cholecystitis	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Hepatic function abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Immune system disorders				
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Dermatitis allergic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis allergic	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Seasonal allergy	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	8/40 (20.0%)	3/40 (7.5%)	0/40 (0.0%)	11/40 (27.5%)
Bronchiolitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chronic sinusitis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Cystitis	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Cystitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Groin abscess	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes simplex	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes zoster	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Laryngopharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nasopharyngitis	4/40 (10.0%)	1/40 (2.5%)	0/40 (0.0%)	5/40 (12.5%)
Otitis media	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinea pedis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tonsillitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Upper respiratory tract infection	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	3/40 (7.5%)
Injury, poisoning and procedural complications				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Arthropod sting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Contusion	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Haemarthrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open wound	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	7/40 (17.5%)	0/40 (0.0%)	0/40 (0.0%)	7/40 (17.5%)
Blood glucose increased	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Blood pressure decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood thyroid stimulating hormone decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood thyroid stimulating hormone increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood triglycerides increased	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gamma-glutamyltransferase increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipids increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Liver function test abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Low density lipoprotein increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Protein urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Smear cervix abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sputum test	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urine output decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Weight increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
White blood cell count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metabolism and nutrition disorders				
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Anorexia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diabetes mellitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypercholesterolaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperlipidaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	11/40 (27.5%)	1/40 (2.5%)	0/40 (0.0%)	12/40 (30.0%)
Arthralgia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Arthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Back pain	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Buttock pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint swelling	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Limb discomfort	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Localised osteoarthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Muscle cramp	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle rigidity	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Musculoskeletal stiffness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Myalgia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Neck pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neck, shoulder and arm syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nodal osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pain in extremity	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Radius fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rib fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sensation of heaviness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Spondylosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tenosynovitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric cancer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metastases to lymph nodes	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	9/40 (22.5%)	0/40 (0.0%)	0/40 (0.0%)	9/40 (22.5%)
Autonomic nervous system imbalance	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dizziness	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Dysgeusia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Facial nerve disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Headache	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Hypoaesthesia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intercostal neuralgia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neuropathy peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parosmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sciatica	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tension headache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vertigo	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Psychiatric disorders				
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Depressive symptom	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysphoria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Insomnia	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Irritability	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sleep disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Renal and urinary disorders				
ANY EVENT	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Bladder malposition acquired	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysuria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Micturition disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urge incontinence	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Urinary incontinence	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	15/40 (37.5%)	3/40 (7.5%)	0/40 (0.0%)	18/40 (45.0%)
Breast discomfort	9/40 (22.5%)	0/40 (0.0%)	0/40 (0.0%)	9/40 (22.5%)
Breast disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast engorgement	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Breast fibrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast pain	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Cervical polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cervicitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysmenorrhoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibrocystic breast disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Genital discharge	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Genital haemorrhage	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Genital pruritus female	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hot flush	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Menopausal symptoms	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nipple pain	5/40 (12.5%)	1/40 (2.5%)	0/40 (0.0%)	6/40 (15.0%)
Uterine malposition	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vaginal candidiasis	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Vulval oedema	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vulvitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulvovaginal discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Asthma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngolaryngeal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharynx discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Productive cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinorrhoea	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Upper respiratory tract inflammation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Acne	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Body tinea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cheilitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermal cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis contact	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dry skin	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eczema	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Eczema asteatotic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Erythema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Excoriation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Face oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperkeratosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Nail disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pruritus	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash papular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rash pustular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin papilloma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urticaria	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Surgical and medical procedures				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail avulsion	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vascular disorders				
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Atherosclerosis obliterans	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure fluctuation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Deep vein thrombosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypertension	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypotension	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral vascular disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	49/117 (41.9%)	48/117 (41.0%)	5/117 (4.3%)	102/117 (87.2%)
Blood and lymphatic system disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	3/117 (2.6%)
Anaemia	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Hypochromic anaemia	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Cardiac disorders				
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Angina pectoris	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arrhythmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Palpitations	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Supraventricular extrasystoles	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Deafness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Meniere's disease	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Tinnitus	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Endocrine disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Goitre	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thyroid cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thyroiditis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	4/117 (3.4%)
Abnormal sensation in eye	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Asthenopia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blepharitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Conjunctival haemorrhage	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Conjunctivitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Corneal dystrophy	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eye pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lacrimation increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open angle glaucoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Periorbital haematoma	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Pterygium	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinal detachment	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vitreous floaters	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	19/117 (16.2%)	8/117 (6.8%)	0/117 (0.0%)	27/117 (23.1%)
Abdominal distension	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Abdominal pain	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Abdominal pain lower	5/117 (4.3%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Abdominal pain upper	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Abdominal rigidity	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Anorectal disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Constipation	2/117 (1.7%)	5/117 (4.3%)	0/117 (0.0%)	7/117 (6.0%)
Diarrhoea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dyspepsia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Epigastric discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastric ulcer	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Gastritis	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Gastritis atrophic	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastroenteritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastrointestinal pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastrointestinal upset	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Glossitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Haemorrhoids	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal ischaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal obstruction	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Irritable bowel syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lip dry	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nausea	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pancreatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Reflux oesophagitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomach discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tongue ulceration	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Toothache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vomiting	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	8/117 (6.8%)	0/117 (0.0%)	0/117 (0.0%)	8/117 (6.8%)
Chest discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Chest pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fatigue	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling cold	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling hot	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Malaise	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Oedema	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Oedema peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thirst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatobiliary disorders				
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cholecystitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic function abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Immune system disorders				
ANY EVENT	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	6/117 (5.1%)
Dermatitis allergic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinitis allergic	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Seasonal allergy	4/117 (3.4%)	1/117 (0.9%)	0/117 (0.0%)	5/117 (4.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	18/117 (15.4%)	9/117 (7.7%)	1/117 (0.9%)	28/117 (23.9%)
Bronchiolitis	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Bronchitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chronic sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cystitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cystitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Groin abscess	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Herpes simplex	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Herpes zoster	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Laryngopharyngitis	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Nasopharyngitis	12/117 (10.3%)	4/117 (3.4%)	0/117 (0.0%)	16/117 (13.7%)
Otitis media	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Pharyngitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tinea pedis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tonsillitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Upper respiratory tract infection	6/117 (5.1%)	2/117 (1.7%)	0/117 (0.0%)	8/117 (6.8%)
Injury, poisoning and procedural complications				
ANY EVENT	4/117 (3.4%)	2/117 (1.7%)	0/117 (0.0%)	6/117 (5.1%)
Arthropod sting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Contusion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Haemarthrosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Injury	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	2/117 (1.7%)
Open wound	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	9/117 (7.7%)	4/117 (3.4%)	0/117 (0.0%)	13/117 (11.1%)
Blood glucose increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood pressure decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure increased	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	5/117 (4.3%)
Blood thyroid stimulating hormone decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood thyroid stimulating hormone increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood triglycerides increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gamma-glutamyltransferase increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lipids increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Liver function test abnormal	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Low density lipoprotein increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Protein urine present	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Smear cervix abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sputum test	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urine output decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Weight increased	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
White blood cell count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Metabolism and nutrition disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Anorexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Diabetes mellitus	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypercholesterolaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperlipidaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	14/117 (12.0%)	7/117 (6.0%)	1/117 (0.9%)	22/117 (18.8%)
Arthralgia	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	4/117 (3.4%)
Arthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Back pain	7/117 (6.0%)	4/117 (3.4%)	1/117 (0.9%)	12/117 (10.3%)
Buttock pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Joint swelling	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Limb discomfort	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Localised osteoarthritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Muscle cramp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle rigidity	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Musculoskeletal stiffness	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Myalgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neck pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck, shoulder and arm syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nodal osteoarthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pain in extremity	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Radius fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rib fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sensation of heaviness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Spondylosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tenosynovitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Gastric cancer	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Lipoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Metastases to lymph nodes	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	7/117 (6.0%)	2/117 (1.7%)	1/117 (0.9%)	10/117 (8.5%)
Autonomic nervous system imbalance	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dizziness	1/117 (0.9%)	1/117 (0.9%)	1/117 (0.9%)	3/117 (2.6%)
Dysgeusia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Facial nerve disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Headache	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	6/117 (5.1%)
Hypoaesthesia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intercostal neuralgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neuropathy peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parosmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sciatica	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tension headache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vertigo	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Psychiatric disorders				
ANY EVENT	7/117 (6.0%)	1/117 (0.9%)	0/117 (0.0%)	8/117 (6.8%)
Depressive symptom	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysphoria	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Insomnia	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	6/117 (5.1%)
Irritability	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Sleep disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Renal and urinary disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Bladder malposition acquired	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysuria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Micturition disorder	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urge incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urinary incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	48/117 (41.0%)	20/117 (17.1%)	0/117 (0.0%)	68/117 (58.1%)
Breast discomfort	25/117 (21.4%)	1/117 (0.9%)	0/117 (0.0%)	26/117 (22.2%)
Breast disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Breast engorgement	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Breast fibrosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Breast pain	16/117 (13.7%)	3/117 (2.6%)	0/117 (0.0%)	19/117 (16.2%)
Cervical polyp	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Cervicitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysmenorrhoea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fibrocystic breast disease	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Genital discharge	14/117 (12.0%)	0/117 (0.0%)	0/117 (0.0%)	14/117 (12.0%)
Genital haemorrhage	9/117 (7.7%)	10/117 (8.5%)	0/117 (0.0%)	19/117 (16.2%)
Genital pruritus female	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Hot flush	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Menopausal symptoms	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nipple pain	4/117 (3.4%)	4/117 (3.4%)	0/117 (0.0%)	8/117 (6.8%)
Uterine malposition	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vaginal candidiasis	2/117 (1.7%)	3/117 (2.6%)	0/117 (0.0%)	5/117 (4.3%)
Vulval oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulvitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vulvovaginal discomfort	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	6/117 (5.1%)	4/117 (3.4%)	0/117 (0.0%)	10/117 (8.5%)
Asthma	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Cough	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Pharyngolaryngeal pain	4/117 (3.4%)	2/117 (1.7%)	0/117 (0.0%)	6/117 (5.1%)
Pharynx discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Productive cough	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Rhinorrhoea	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	2/117 (1.7%)
Upper respiratory tract inflammation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	17/117 (14.5%)	2/117 (1.7%)	0/117 (0.0%)	19/117 (16.2%)
Acne	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Body tinea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cheilitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermal cyst	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis contact	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dry skin	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eczema	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Eczema asteatotic	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Erythema	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Excoriation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Face oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperkeratosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nail disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pruritus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Rash	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Rash papular	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rash pustular	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin papilloma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urticaria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Surgical and medical procedures				
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail avulsion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vascular disorders				
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	1/117 (0.9%)	3/117 (2.6%)
Atherosclerosis obliterans	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Blood pressure fluctuation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Deep vein thrombosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypertension	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypotension	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Peripheral vascular disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
ANY EVENT	131/309 (42.4%)	104/309 (33.7%)	14/309 (4.5%)	249/309 (80.6%)
Blood and lymphatic system disorders				
ANY EVENT	2/309 (0.6%)	0/309 (0.0%)	1/309 (0.3%)	3/309 (1.0%)
Anaemia	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hypochromic anaemia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Cardiac disorders				
ANY EVENT	2/309 (0.6%)	4/309 (1.3%)	2/309 (0.6%)	8/309 (2.6%)
Angina pectoris	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Arrhythmia	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)	2/309 (0.6%)
Palpitations	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	4/309 (1.3%)
Supraventricular extrasystoles	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Ear and labyrinth disorders				
ANY EVENT	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	4/309 (1.3%)
Deafness	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Meniere's disease	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Tinnitus	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Endocrine disorders				
ANY EVENT	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Goitre	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroid cyst	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroiditis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	10/309 (3.2%)	3/309 (1.0%)	0/309 (0.0%)	13/309 (4.2%)
Abnormal sensation in eye	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Asthenopia	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Blepharitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctival haemorrhage	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctivitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Corneal dystrophy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eye pain	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Lacrimation increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open angle glaucoma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Periorbital haematoma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Pterygium	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinal detachment	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vitreous floaters	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	43/309 (13.9%)	22/309 (7.1%)	2/309 (0.6%)	67/309 (21.7%)
Abdominal distension	7/309 (2.3%)	1/309 (0.3%)	0/309 (0.0%)	8/309 (2.6%)
Abdominal pain	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	4/309 (1.3%)
Abdominal pain lower	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal pain upper	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal rigidity	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Anorectal disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Constipation	8/309 (2.6%)	6/309 (1.9%)	0/309 (0.0%)	14/309 (4.5%)
Diarrhoea	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Dyspepsia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epigastric discomfort	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Gastric ulcer	0/309 (0.0%)	3/309 (1.0%)	0/309 (0.0%)	3/309 (1.0%)
Gastritis	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Gastritis atrophic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastroenteritis	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	4/309 (1.3%)
Gastrointestinal pain	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Gastrointestinal upset	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Glossitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Haemorrhoids	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Intestinal ischaemia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Intestinal obstruction	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Irritable bowel syndrome	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lip dry	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nausea	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	3/309 (1.0%)
Pancreatitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Reflux oesophagitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Stomach discomfort	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Stomatitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Tongue ulceration	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Toothache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vomiting	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
General disorders and administration site conditions				
ANY EVENT	24/309 (7.8%)	4/309 (1.3%)	0/309 (0.0%)	28/309 (9.1%)
Chest discomfort	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Chest pain	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fatigue	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Feeling cold	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Feeling hot	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Malaise	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Oedema	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Oedema peripheral	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Thirst	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Hepatobiliary disorders				
ANY EVENT	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	2/309 (0.6%)
Cholecystitis	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Hepatic function abnormal	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Immune system disorders				
ANY EVENT	13/309 (4.2%)	3/309 (1.0%)	0/309 (0.0%)	16/309 (5.2%)
Dermatitis allergic	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Rhinitis allergic	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Seasonal allergy	10/309 (3.2%)	2/309 (0.6%)	0/309 (0.0%)	12/309 (3.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	57/309 (18.4%)	26/309 (8.4%)	1/309 (0.3%)	84/309 (27.2%)
Bronchiolitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Bronchitis	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Bronchitis acute	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Chronic sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cystitis	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Cystitis acute	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Groin abscess	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Herpes simplex	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Herpes zoster	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Laryngopharyngitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nasopharyngitis	35/309 (11.3%)	14/309 (4.5%)	0/309 (0.0%)	49/309 (15.9%)
Otitis media	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Pharyngitis	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Tinea pedis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tonsillitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Upper respiratory tract infection	17/309 (5.5%)	4/309 (1.3%)	0/309 (0.0%)	21/309 (6.8%)
Injury, poisoning and procedural complications				
ANY EVENT	4/309 (1.3%)	4/309 (1.3%)	1/309 (0.3%)	9/309 (2.9%)
Arthropod sting	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Contusion	0/309 (0.0%)	2/309 (0.6%)	1/309 (0.3%)	3/309 (1.0%)
Haemarthrosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Injury	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)
Open wound	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Investigations				
ANY EVENT	32/309 (10.4%)	5/309 (1.6%)	0/309 (0.0%)	37/309 (12.0%)
Blood glucose increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood pressure decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood pressure increased	8/309 (2.6%)	2/309 (0.6%)	0/309 (0.0%)	10/309 (3.2%)
Blood thyroid stimulating hormone decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood thyroid stimulating hormone increased	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Blood triglycerides increased	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Gamma-glutamyltransferase increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lipids increased	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Liver function test abnormal	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Low density lipoprotein increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Protein urine present	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Smear cervix abnormal	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Sputum test	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urine output decreased	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Weight increased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
White blood cell count decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Metabolism and nutrition disorders				
ANY EVENT	9/309 (2.9%)	0/309 (0.0%)	0/309 (0.0%)	9/309 (2.9%)
Anorexia	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Diabetes mellitus	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hypercholesterolaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperlipidaemia	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	45/309 (14.6%)	19/309 (6.1%)	2/309 (0.6%)	66/309 (21.4%)
Arthralgia	10/309 (3.2%)	3/309 (1.0%)	0/309 (0.0%)	13/309 (4.2%)
Arthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Back pain	18/309 (5.8%)	9/309 (2.9%)	1/309 (0.3%)	28/309 (9.1%)
Buttock pain	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Joint swelling	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Limb discomfort	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	3/309 (1.0%)
Localised osteoarthritis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Muscle cramp	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Muscle rigidity	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Musculoskeletal stiffness	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Myalgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neck pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neck, shoulder and arm syndrome	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nodal osteoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pain in extremity	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Radius fracture	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Rib fracture	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Sensation of heaviness	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Spondylosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tenosynovitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Gastric cancer	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Lipoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Metastases to lymph nodes	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Nervous system disorders				
ANY EVENT	30/309 (9.7%)	7/309 (2.3%)	1/309 (0.3%)	38/309 (12.3%)
Autonomic nervous system imbalance	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dizziness	6/309 (1.9%)	3/309 (1.0%)	1/309 (0.3%)	10/309 (3.2%)
Dysgeusia	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Facial nerve disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Headache	12/309 (3.9%)	3/309 (1.0%)	0/309 (0.0%)	15/309 (4.9%)
Hypoaesthesia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Intercostal neuralgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neuropathy peripheral	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Parosmia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sciatica	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tension headache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vertigo	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Psychiatric disorders				
ANY EVENT	17/309 (5.5%)	3/309 (1.0%)	0/309 (0.0%)	20/309 (6.5%)
Depressive symptom	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysphoria	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Insomnia	11/309 (3.6%)	2/309 (0.6%)	0/309 (0.0%)	13/309 (4.2%)
Irritability	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sleep disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Renal and urinary disorders				
ANY EVENT	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Bladder malposition acquired	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysuria	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Micturition disorder	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Urge incontinence	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urinary incontinence	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	98/309 (31.7%)	33/309 (10.7%)	0/309 (0.0%)	131/309 (42.4%)
Breast discomfort	50/309 (16.2%)	1/309 (0.3%)	0/309 (0.0%)	51/309 (16.5%)
Breast disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Breast engorgement	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Breast fibrosis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Breast pain	26/309 (8.4%)	4/309 (1.3%)	0/309 (0.0%)	30/309 (9.7%)
Cervical polyp	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Cervicitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dysmenorrhoea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fibrocystic breast disease	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)
Genital discharge	27/309 (8.7%)	1/309 (0.3%)	0/309 (0.0%)	28/309 (9.1%)
Genital haemorrhage	12/309 (3.9%)	11/309 (3.6%)	0/309 (0.0%)	23/309 (7.4%)
Genital pruritus female	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Hot flush	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Menopausal symptoms	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	3/309 (1.0%)
Nipple pain	12/309 (3.9%)	6/309 (1.9%)	0/309 (0.0%)	18/309 (5.8%)
Uterine malposition	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vaginal candidiasis	4/309 (1.3%)	4/309 (1.3%)	0/309 (0.0%)	8/309 (2.6%)
Vulval oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvovaginal discomfort	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	15/309 (4.9%)	5/309 (1.6%)	1/309 (0.3%)	21/309 (6.8%)
Asthma	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	2/309 (0.6%)
Cough	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Pharyngolaryngeal pain	7/309 (2.3%)	2/309 (0.6%)	0/309 (0.0%)	9/309 (2.9%)
Pharynx discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Productive cough	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinorrhoea	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	4/309 (1.3%)
Upper respiratory tract inflammation	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.5: Adverse Events - Number (%) of Patients by Maximum Intensity - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	37/309 (12.0%)	5/309 (1.6%)	1/309 (0.3%)	43/309 (13.9%)
Acne	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Body tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cheilitis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Dermal cyst	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dermatitis contact	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dry skin	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eczema	11/309 (3.6%)	1/309 (0.3%)	0/309 (0.0%)	12/309 (3.9%)
Eczema asteatotic	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Erythema	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Excoriation	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Face oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperkeratosis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Nail disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pruritus	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Rash	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Rash papular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rash pustular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin papilloma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Urticaria	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Surgical and medical procedures				
ANY EVENT	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nail avulsion	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Vascular disorders				
ANY EVENT	3/309 (1.0%)	1/309 (0.3%)	1/309 (0.3%)	5/309 (1.6%)
Atherosclerosis obliterans	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Blood pressure fluctuation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Deep vein thrombosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypertension	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypotension	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Peripheral vascular disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0020T)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	9/20 (45.0%)	6/20 (30.0%)	2/20 (10.0%)	17/20 (85.0%)
Blood and lymphatic system disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypochromic anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Iron deficiency anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cardiac disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Angina pectoris	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arrhythmia	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Palpitations	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Supraventricular extrasystoles	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deafness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Meniere's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinnitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endocrine disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Goitre	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroid cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroiditis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abnormal sensation in eye	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthenopia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blepharitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Cataract	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctival haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctivitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Corneal dystrophy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis eyelid	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eye pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hordeolum	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Keratoconjunctivitis sicca	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lacrimation increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open angle glaucoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periorbital haematoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Posterior capsule opacification	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pterygium	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Retinal detachment	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Retinopathy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vitreous floaters	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	3/20 (15.0%)	4/20 (20.0%)	0/20 (0.0%)	7/20 (35.0%)
Abdominal distension	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abdominal pain	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain lower	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain upper	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorectal disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Constipation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diarrhoea	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Diverticulum intestinal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Duodenal ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dyspepsia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epigastric discomfort	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastritis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastritis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastroenteritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastrointestinal pain	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastrointestinal upset	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gingivitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glossitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Haemorrhoids	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal ischaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal obstruction	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritable bowel syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lip dry	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nausea	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pancreatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Parotid gland enlargement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periodontal disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periodontitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Reflux oesophagitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Stomach discomfort	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Stomatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Tongue ulceration	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vomiting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
General disorders and administration site conditions				
ANY EVENT	3/20 (15.0%)	2/20 (10.0%)	0/20 (0.0%)	5/20 (25.0%)
Asthenia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Axillary pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Feeling cold	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Feeling hot	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Malaise	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Oedema peripheral	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Pyrexia	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Thirst	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hepatobiliary disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cholecystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic function abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatitis B	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatitis C	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Immune system disorders				
ANY EVENT	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	3/20 (15.0%)
Allergy to plants	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
House dust allergy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Seasonal allergy	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	3/20 (15.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	7/20 (35.0%)	5/20 (25.0%)	0/20 (0.0%)	12/20 (60.0%)
Bronchiolitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chronic sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dental caries	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Groin abscess	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes dermatitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes simplex	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Herpes zoster	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Influenza	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Laryngopharyngitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nasopharyngitis	6/20 (30.0%)	2/20 (10.0%)	0/20 (0.0%)	8/20 (40.0%)
Otitis media	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Otitis media chronic	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Paronychia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngitis	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Pneumonia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinea pedis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tonsillitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract infection	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Animal bite	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arthropod sting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Contusion	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Haemarthrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypothermia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Mouth injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open wound	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	5/20 (25.0%)	0/20 (0.0%)	0/20 (0.0%)	5/20 (25.0%)
Activated partial thromboplastin time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Antithrombin III decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood bilirubin increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood creatinine increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood fibrinogen decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood glucose increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure increased	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Blood thyroid stimulating hormone decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood thyroid stimulating hormone increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood triglycerides increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Coagulation time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eosinophil count increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eosinophil percentage increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gamma-glutamyltransferase increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glucose urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipids increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Liver function test abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Low density lipoprotein increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lymphocyte percentage decreased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Neutrophil percentage increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Platelet count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Protein urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Prothrombin time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Smear cervix abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sputum test	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urine output decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Weight increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
White blood cell count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorexia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Decreased appetite	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diabetes mellitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypercholesterolaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperlipidaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	3/20 (15.0%)	2/20 (10.0%)	1/20 (5.0%)	6/20 (30.0%)
Arthralgia	2/20 (10.0%)	1/20 (5.0%)	0/20 (0.0%)	3/20 (15.0%)
Arthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Back pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Buttock pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Foot fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hand fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint sprain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint swelling	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Limb discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Localised osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Monoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle cramp	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle rigidity	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle twitching	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Musculoskeletal stiffness	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Myalgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Neck, shoulder and arm syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nodal osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pain in extremity	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Radius fracture	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Rib fracture	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Sensation of heaviness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Spondylosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tenosynovitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thoracic vertebral fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Traumatic fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Wrist fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Colonic polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibroadenoma of breast	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibroma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastric cancer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic cancer metastatic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipoma	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Metastases to lymph nodes	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ovarian neoplasm	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nervous system disorders				
ANY EVENT	4/20 (20.0%)	0/20 (0.0%)	0/20 (0.0%)	4/20 (20.0%)
Autonomic nervous system imbalance	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Depressed level of consciousness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dizziness	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Dizziness postural	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysgeusia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Facial nerve disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Headache	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hypoaesthesia	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Intercostal neuralgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neuropathy peripheral	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parkinson's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parosmia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sciatica	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tension headache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vertigo	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Amnesia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depression	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depressive symptom	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysphoria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Insomnia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritability	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neurosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sleep disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Bladder malposition acquired	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Micturition disorder	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Nocturia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pollakiuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urge incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urinary incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	4/20 (20.0%)	2/20 (10.0%)	0/20 (0.0%)	6/20 (30.0%)
Breast discomfort	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Breast disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast engorgement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast fibrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast hyperplasia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast pain	2/20 (10.0%)	1/20 (5.0%)	0/20 (0.0%)	3/20 (15.0%)
Cervical polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cervicitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysmenorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endometrial hyperplasia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibrocystic breast disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital discharge	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Genital haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital pruritus female	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital rash	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hot flush	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Menopausal symptoms	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Nipple pain	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Uterine leiomyoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Uterine malposition	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginal candidiasis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginitis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulval oedema	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvovaginal discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Asthma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dyspnoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epistaxis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngolaryngeal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pharynx discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Productive cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Rhinorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract inflammation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	3/20 (15.0%)	1/20 (5.0%)	0/20 (0.0%)	4/20 (20.0%)
Acne	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Body tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cheilitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermal cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dermatitis contact	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dry skin	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eczema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Eczema asteatotic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Erythema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Excoriation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Face oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Folliculitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperkeratosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Milia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pruritus	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Rash	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash papular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash pustular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin papilloma	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Urticaria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail avulsion	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Atherosclerosis obliterans	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure fluctuation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chillblains	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deep vein thrombosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypertension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypotension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral coldness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral vascular disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	22/59 (37.3%)	29/59 (49.2%)	2/59 (3.4%)	53/59 (89.8%)
Blood and lymphatic system disorders				
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Anaemia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Hypochromic anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Iron deficiency anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cardiac disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Angina pectoris	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arrhythmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Palpitations	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Supraventricular extrasystoles	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Deafness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Meniere's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinnitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Endocrine disorders				
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Goitre	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Thyroid cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thyroiditis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	2/59 (3.4%)	2/59 (3.4%)	0/59 (0.0%)	4/59 (6.8%)
Abnormal sensation in eye	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Asthenopia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blepharitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cataract	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Conjunctival haemorrhage	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Corneal dystrophy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis eyelid	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eye pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hordeolum	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Keratoconjunctivitis sicca	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lacrimation increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open angle glaucoma	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Periorbital haematoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Posterior capsule opacification	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pterygium	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinal detachment	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinopathy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vitreous floaters	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	14/59 (23.7%)	3/59 (5.1%)	0/59 (0.0%)	17/59 (28.8%)
Abdominal distension	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Abdominal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain lower	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain upper	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Abdominal rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anorectal disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Constipation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diarrhoea	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diverticulum intestinal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Duodenal ulcer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspepsia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epigastric discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric ulcer	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Gastritis	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastritis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastroenteritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Gastrointestinal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastrointestinal upset	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gingivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Glossitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemorrhoids	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Intestinal ischaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal obstruction	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Irritable bowel syndrome	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lip dry	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nausea	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Pancreatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Parotid gland enlargement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Periodontal disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Periodontitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Reflux oesophagitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomach discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomatitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tongue ulceration	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vomiting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
General disorders and administration site conditions				
ANY EVENT	5/59 (8.5%)	4/59 (6.8%)	0/59 (0.0%)	9/59 (15.3%)
Asthenia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Axillary pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest pain	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fatigue	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Feeling cold	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Feeling hot	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Malaise	3/59 (5.1%)	1/59 (1.7%)	0/59 (0.0%)	4/59 (6.8%)
Oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Oedema peripheral	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pyrexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thirst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatobiliary disorders				
ANY EVENT	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Cholecystitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic function abnormal	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Hepatitis B	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatitis C	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Immune system disorders				
ANY EVENT	1/59 (1.7%)	2/59 (3.4%)	0/59 (0.0%)	3/59 (5.1%)
Allergy to plants	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dermatitis allergic	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
House dust allergy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinitis allergic	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Seasonal allergy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	17/59 (28.8%)	9/59 (15.3%)	0/59 (0.0%)	26/59 (44.1%)
Bronchiolitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bronchitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bronchitis acute	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Chronic sinusitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cystitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Cystitis acute	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dental caries	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Groin abscess	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes dermatitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Herpes simplex	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes zoster	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Influenza	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Laryngopharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nasopharyngitis	12/59 (20.3%)	8/59 (13.6%)	0/59 (0.0%)	20/59 (33.9%)
Otitis media	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Otitis media chronic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Paronychia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pneumonia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sinusitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tinea pedis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tonsillitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract infection	2/59 (3.4%)	1/59 (1.7%)	0/59 (0.0%)	3/59 (5.1%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Animal bite	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arthropod sting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Contusion	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Haemarthrosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypothermia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Mouth injury	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Open wound	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	14/59 (23.7%)	0/59 (0.0%)	0/59 (0.0%)	14/59 (23.7%)
Activated partial thromboplastin time prolonged	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Antithrombin III decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood bilirubin increased	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood creatinine increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood fibrinogen decreased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blood glucose increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure increased	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood thyroid stimulating hormone decreased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blood thyroid stimulating hormone increased	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Blood triglycerides increased	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Coagulation time prolonged	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eosinophil count increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Eosinophil percentage increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gamma-glutamyltransferase increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Glucose urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipids increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Liver function test abnormal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Low density lipoprotein increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lymphocyte percentage decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neutrophil percentage increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Platelet count decreased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Protein urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Prothrombin time prolonged	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Smear cervix abnormal	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sputum test	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urine output decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Weight increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
White blood cell count decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Anorexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Decreased appetite	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diabetes mellitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hypercholesterolaemia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hyperlipidaemia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	10/59 (16.9%)	6/59 (10.2%)	2/59 (3.4%)	18/59 (30.5%)
Arthralgia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Arthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Back pain	4/59 (6.8%)	5/59 (8.5%)	0/59 (0.0%)	9/59 (15.3%)
Buttock pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Foot fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hand fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint sprain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint swelling	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Limb discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Localised osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Monoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle cramp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle fatigue	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle rigidity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Muscle twitching	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Musculoskeletal stiffness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Myalgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck, shoulder and arm syndrome	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nodal osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pain in extremity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Radius fracture	0/59 (0.0%)	1/59 (1.7%)	2/59 (3.4%)	3/59 (5.1%)
Rib fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sensation of heaviness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Spondylosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tenosynovitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Thoracic vertebral fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Traumatic fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Wrist fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Colonic polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibroadenoma of breast	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibroma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric cancer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic cancer metastatic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metastases to lymph nodes	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ovarian neoplasm	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nervous system disorders				
ANY EVENT	5/59 (8.5%)	5/59 (8.5%)	0/59 (0.0%)	10/59 (16.9%)
Autonomic nervous system imbalance	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Depressed level of consciousness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dizziness	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dizziness postural	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysgeusia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Facial nerve disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Headache	1/59 (1.7%)	3/59 (5.1%)	0/59 (0.0%)	4/59 (6.8%)
Hypoaesthesia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Intercostal neuralgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neuropathy peripheral	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Parkinson's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Parosmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sciatica	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tension headache	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vertigo	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Amnesia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Depression	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Depressive symptom	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysphoria	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Insomnia	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Irritability	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neurosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sleep disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Renal and urinary disorders				
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bladder malposition acquired	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysuria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Micturition disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nocturia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pollakiuria	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Urge incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urinary incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	22/59 (37.3%)	12/59 (20.3%)	0/59 (0.0%)	34/59 (57.6%)
Breast discomfort	16/59 (27.1%)	3/59 (5.1%)	0/59 (0.0%)	19/59 (32.2%)
Breast disorder	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Breast engorgement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast fibrosis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Breast hyperplasia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast pain	5/59 (8.5%)	2/59 (3.4%)	0/59 (0.0%)	7/59 (11.9%)
Cervical polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cervicitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysmenorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Endometrial hyperplasia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibrocystic breast disease	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Genital discharge	6/59 (10.2%)	0/59 (0.0%)	0/59 (0.0%)	6/59 (10.2%)
Genital haemorrhage	2/59 (3.4%)	6/59 (10.2%)	0/59 (0.0%)	8/59 (13.6%)
Genital pruritus female	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Genital rash	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hot flush	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Menopausal symptoms	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nipple pain	4/59 (6.8%)	1/59 (1.7%)	0/59 (0.0%)	5/59 (8.5%)
Uterine leiomyoma	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Uterine malposition	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vaginal candidiasis	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Vaginitis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulval oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvovaginal discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	5/59 (8.5%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Asthma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspnoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epistaxis	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pharyngolaryngeal pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Pharynx discomfort	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Productive cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract inflammation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	8/59 (13.6%)	1/59 (1.7%)	0/59 (0.0%)	9/59 (15.3%)
Acne	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Body tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cheilitis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Dermal cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis contact	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dry skin	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eczema	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Eczema asteatotic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Erythema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Excoriation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Face oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Folliculitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hyperkeratosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Milia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pruritus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rash	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Rash papular	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash pustular	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin papilloma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urticaria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Nail avulsion	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Atherosclerosis obliterans	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure fluctuation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chillblains	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Deep vein thrombosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypertension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypotension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral coldness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral vascular disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	6/16 (37.5%)	6/16 (37.5%)	2/16 (12.5%)	14/16 (87.5%)
Blood and lymphatic system disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypochromic anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Iron deficiency anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cardiac disorders				
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Angina pectoris	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arrhythmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Palpitations	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Supraventricular extrasystoles	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deafness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Meniere's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinnitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endocrine disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Goitre	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thyroid cyst	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Thyroiditis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abnormal sensation in eye	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Asthenopia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blepharitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cataract	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctival haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Corneal dystrophy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis eyelid	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eye pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hordeolum	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Keratoconjunctivitis sicca	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lacrimation increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open angle glaucoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periorbital haematoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Posterior capsule opacification	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pterygium	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinal detachment	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinopathy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vitreous floaters	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	7/16 (43.8%)	1/16 (6.3%)	1/16 (6.3%)	9/16 (56.3%)
Abdominal distension	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain lower	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain upper	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	3/16 (18.8%)
Abdominal rigidity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anorectal disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Constipation	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Diarrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Diverticulum intestinal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Duodenal ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dyspepsia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Epigastric discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastritis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastroenteritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastrointestinal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal upset	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gingivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glossitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemorrhoids	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal ischaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal obstruction	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Irritable bowel syndrome	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Lip dry	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nausea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pancreatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parotid gland enlargement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periodontal disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periodontitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Reflux oesophagitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Stomach discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Stomatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tongue ulceration	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vomiting	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)
General disorders and administration site conditions				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Asthenia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Axillary pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling cold	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling hot	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Malaise	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Oedema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Oedema peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pyrexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thirst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatobiliary disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cholecystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic function abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatitis B	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatitis C	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Immune system disorders				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Allergy to plants	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis allergic	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
House dust allergy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinitis allergic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Seasonal allergy	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	6/16 (37.5%)	1/16 (6.3%)	0/16 (0.0%)	7/16 (43.8%)
Bronchiolitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chronic sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dental caries	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Groin abscess	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes simplex	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes zoster	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Influenza	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Laryngopharyngitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nasopharyngitis	3/16 (18.8%)	1/16 (6.3%)	0/16 (0.0%)	4/16 (25.0%)
Otitis media	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Otitis media chronic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Paronychia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Pneumonia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinea pedis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tonsillitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Upper respiratory tract infection	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Animal bite	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arthropod sting	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Contusion	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Haemarthrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypothermia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Mouth injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open wound	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	4/16 (25.0%)	0/16 (0.0%)	0/16 (0.0%)	4/16 (25.0%)
Activated partial thromboplastin time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Antithrombin III decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood bilirubin increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood creatinine increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood fibrinogen decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood glucose increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood pressure increased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood thyroid stimulating hormone decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood thyroid stimulating hormone increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood triglycerides increased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Coagulation time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eosinophil count increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eosinophil percentage increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gamma-glutamyltransferase increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glucose urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipids increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Liver function test abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Low density lipoprotein increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lymphocyte percentage decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neutrophil percentage increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Platelet count decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Protein urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Prothrombin time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Smear cervix abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sputum test	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urine output decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Weight increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
White blood cell count decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Anorexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Decreased appetite	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Diabetes mellitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypercholesterolaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperlipidaemia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	4/16 (25.0%)	3/16 (18.8%)	0/16 (0.0%)	7/16 (43.8%)
Arthralgia	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	3/16 (18.8%)
Arthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Back pain	3/16 (18.8%)	1/16 (6.3%)	0/16 (0.0%)	4/16 (25.0%)
Buttock pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Foot fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hand fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint sprain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint swelling	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Limb discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Localised osteoarthritis	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Monoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle cramp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle rigidity	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Muscle twitching	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Musculoskeletal stiffness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Myalgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck, shoulder and arm syndrome	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nodal osteoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pain in extremity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Radius fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rib fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sensation of heaviness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Spondylosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tenosynovitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thoracic vertebral fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Traumatic fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Wrist fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Colonic polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibroadenoma of breast	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibroma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric cancer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic cancer metastatic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Metastases to lymph nodes	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ovarian neoplasm	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nervous system disorders				
ANY EVENT	3/16 (18.8%)	2/16 (12.5%)	0/16 (0.0%)	5/16 (31.3%)
Autonomic nervous system imbalance	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depressed level of consciousness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dizziness	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Dizziness postural	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysgeusia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Facial nerve disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Hypoaesthesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intercostal neuralgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neuropathy peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parkinson's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parosmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sciatica	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Tension headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vertigo	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Amnesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depression	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depressive symptom	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dysphoria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Insomnia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Irritability	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neurosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sleep disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bladder malposition acquired	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Micturition disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nocturia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pollakiuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urge incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urinary incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	6/16 (37.5%)	1/16 (6.3%)	0/16 (0.0%)	7/16 (43.8%)
Breast discomfort	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Breast disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast engorgement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast fibrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast hyperplasia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast pain	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Cervical polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cervicitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysmenorrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endometrial hyperplasia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibrocystic breast disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital discharge	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Genital haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital pruritus female	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hot flush	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Menopausal symptoms	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Nipple pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Uterine leiomyoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Uterine malposition	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginal candidiasis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginitis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulval oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vulvovaginal discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	1/16 (6.3%)	3/16 (18.8%)
Asthma	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)
Cough	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dyspnoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Epistaxis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngolaryngeal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharynx discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Productive cough	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Rhinorrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Upper respiratory tract inflammation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Acne	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Body tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cheilitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermal cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis contact	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dry skin	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eczema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Eczema asteatotic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Erythema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Excoriation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Face oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Folliculitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperkeratosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Milia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pruritus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash papular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash pustular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin papilloma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urticaria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Surgical and medical procedures				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail avulsion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Atherosclerosis obliterans	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure fluctuation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chillblains	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deep vein thrombosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypertension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypotension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral coldness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral vascular disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	20/57 (35.1%)	23/57 (40.4%)	6/57 (10.5%)	49/57 (86.0%)
Blood and lymphatic system disorders				
ANY EVENT	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypochromic anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Iron deficiency anaemia	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Cardiac disorders				
ANY EVENT	1/57 (1.8%)	1/57 (1.8%)	1/57 (1.8%)	3/57 (5.3%)
Angina pectoris	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Arrhythmia	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Palpitations	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Supraventricular extrasystoles	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Ear and labyrinth disorders				
ANY EVENT	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Deafness	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Meniere's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinnitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endocrine disorders				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Goitre	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thyroid cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thyroiditis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abnormal sensation in eye	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Asthenopia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blepharitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cataract	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Conjunctival haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Corneal dystrophy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis eyelid	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eye pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hordeolum	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Keratoconjunctivitis sicca	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lacrimation increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Open angle glaucoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periorbital haematoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Posterior capsule opacification	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pterygium	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinal detachment	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinopathy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vitreous floaters	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	14/57 (24.6%)	2/57 (3.5%)	1/57 (1.8%)	17/57 (29.8%)
Abdominal distension	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abdominal pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abdominal pain lower	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abdominal pain upper	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Abdominal rigidity	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anorectal disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Constipation	6/57 (10.5%)	1/57 (1.8%)	0/57 (0.0%)	7/57 (12.3%)
Diarrhoea	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Diverticulum intestinal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Duodenal ulcer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dyspepsia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epigastric discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric ulcer	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Gastritis atrophic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastroenteritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal upset	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gingivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Glossitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Haemorrhoids	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Intestinal ischaemia	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Intestinal obstruction	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Irritable bowel syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lip dry	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nausea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pancreatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parotid gland enlargement	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periodontal disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periodontitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Reflux oesophagitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Stomach discomfort	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Stomatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tongue ulceration	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vomiting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
General disorders and administration site conditions				
ANY EVENT	6/57 (10.5%)	1/57 (1.8%)	0/57 (0.0%)	7/57 (12.3%)
Asthenia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Axillary pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chest discomfort	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Chest pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fatigue	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling cold	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling hot	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Malaise	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Oedema peripheral	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pyrexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thirst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hepatobiliary disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cholecystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic cyst	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic function abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatitis B	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatitis C	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Immune system disorders				
ANY EVENT	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Allergy to plants	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
House dust allergy	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rhinitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Seasonal allergy	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	15/57 (26.3%)	9/57 (15.8%)	1/57 (1.8%)	25/57 (43.9%)
Bronchiolitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis acute	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Chronic sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis acute	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Dental caries	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Groin abscess	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes simplex	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes zoster	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Influenza	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Laryngopharyngitis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Nail tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nasopharyngitis	10/57 (17.5%)	5/57 (8.8%)	1/57 (1.8%)	16/57 (28.1%)
Otitis media	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Otitis media chronic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Paronychia	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Pharyngitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pneumonia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinea pedis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tonsillitis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Upper respiratory tract infection	7/57 (12.3%)	1/57 (1.8%)	0/57 (0.0%)	8/57 (14.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	3/57 (5.3%)
Animal bite	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Arthropod sting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Contusion	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Haemarthrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypothermia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Mouth injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Open wound	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin injury	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	9/57 (15.8%)	3/57 (5.3%)	0/57 (0.0%)	12/57 (21.1%)
Activated partial thromboplastin time prolonged	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Antithrombin III decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood bilirubin increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood creatinine increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood fibrinogen decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood glucose increased	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Blood pressure decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure increased	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Blood thyroid stimulating hormone decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood triglycerides increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Coagulation time prolonged	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eosinophil count increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eosinophil percentage increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gamma-glutamyltransferase increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Glucose urine present	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Lipids increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Liver function test abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Low density lipoprotein increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lymphocyte percentage decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neutrophil percentage increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Platelet count decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Protein urine present	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Prothrombin time prolonged	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Smear cervix abnormal	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	3/57 (5.3%)
Sputum test	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Urine output decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Weight increased	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
White blood cell count decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Anorexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Decreased appetite	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Diabetes mellitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypercholesterolaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperlipidaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	9/57 (15.8%)	4/57 (7.0%)	1/57 (1.8%)	14/57 (24.6%)
Arthralgia	4/57 (7.0%)	0/57 (0.0%)	0/57 (0.0%)	4/57 (7.0%)
Arthritis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Back pain	5/57 (8.8%)	1/57 (1.8%)	0/57 (0.0%)	6/57 (10.5%)
Buttock pain	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Foot fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hand fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Joint sprain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Joint swelling	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Limb discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Localised osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Monoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle cramp	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle fatigue	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle rigidity	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Muscle twitching	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Musculoskeletal stiffness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Myalgia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck, shoulder and arm syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nodal osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pain in extremity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Radius fracture	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Rib fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sensation of heaviness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Spondylosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tenosynovitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thoracic vertebral fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Traumatic fracture	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Wrist fracture	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)	2/57 (3.5%)
Colonic polyp	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)	2/57 (3.5%)
Fibroadenoma of breast	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibroma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric cancer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic cancer metastatic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lipoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metastases to lymph nodes	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Ovarian neoplasm	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nervous system disorders				
ANY EVENT	7/57 (12.3%)	3/57 (5.3%)	0/57 (0.0%)	10/57 (17.5%)
Autonomic nervous system imbalance	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depressed level of consciousness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dizziness	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Dizziness postural	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysgeusia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Facial nerve disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Headache	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Hypoaesthesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intercostal neuralgia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Neuropathy peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parkinson's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parosmia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sciatica	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tension headache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vertigo	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	3/57 (5.3%)	2/57 (3.5%)	0/57 (0.0%)	5/57 (8.8%)
Amnesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depression	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depressive symptom	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysphoria	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Insomnia	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Irritability	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neurosis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sleep disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Renal and urinary disorders				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bladder malposition acquired	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Micturition disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nocturia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pollakiuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urge incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urinary incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	22/57 (38.6%)	6/57 (10.5%)	0/57 (0.0%)	28/57 (49.1%)
Breast discomfort	8/57 (14.0%)	0/57 (0.0%)	0/57 (0.0%)	8/57 (14.0%)
Breast disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast engorgement	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Breast fibrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast hyperplasia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast pain	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Cervical polyp	3/57 (5.3%)	1/57 (1.8%)	0/57 (0.0%)	4/57 (7.0%)
Cervicitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dysmenorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endometrial hyperplasia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibrocystic breast disease	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Genital discharge	8/57 (14.0%)	0/57 (0.0%)	0/57 (0.0%)	8/57 (14.0%)
Genital haemorrhage	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Genital pruritus female	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Genital rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hot flush	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Menopausal symptoms	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Nipple pain	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Uterine leiomyoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Uterine malposition	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vaginal candidiasis	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	3/57 (5.3%)
Vaginitis atrophic	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Vulval oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvovaginal discomfort	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	5/57 (8.8%)	1/57 (1.8%)	0/57 (0.0%)	6/57 (10.5%)
Asthma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cough	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Dyspnoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epistaxis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pharyngolaryngeal pain	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
Pharynx discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Productive cough	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rhinorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Upper respiratory tract inflammation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	11/57 (19.3%)	2/57 (3.5%)	1/57 (1.8%)	14/57 (24.6%)
Acne	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Body tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cheilitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermal cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis contact	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dry skin	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eczema	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Eczema asteatotic	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Erythema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Excoriation	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Face oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Folliculitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperkeratosis	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Milia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nail disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pruritus	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash papular	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rash pustular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin papilloma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urticaria	3/57 (5.3%)	2/57 (3.5%)	0/57 (0.0%)	5/57 (8.8%)
Surgical and medical procedures				
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nail avulsion	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Atherosclerosis obliterans	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure fluctuation	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chillblains	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Deep vein thrombosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypertension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypotension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Peripheral coldness	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Peripheral vascular disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	18/40 (45.0%)	14/40 (35.0%)	3/40 (7.5%)	35/40 (87.5%)
Blood and lymphatic system disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypochromic anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Iron deficiency anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cardiac disorders				
ANY EVENT	1/40 (2.5%)	2/40 (5.0%)	0/40 (0.0%)	3/40 (7.5%)
Angina pectoris	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Arrhythmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Palpitations	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Supraventricular extrasystoles	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Deafness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Meniere's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinnitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endocrine disorders				
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Goitre	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroid cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroiditis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	4/40 (10.0%)	1/40 (2.5%)	0/40 (0.0%)	5/40 (12.5%)
Abnormal sensation in eye	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Asthenopia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blepharitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cataract	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctival haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Corneal dystrophy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis eyelid	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eye pain	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Hordeolum	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Keratoconjunctivitis sicca	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lacrimation increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open angle glaucoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periorbital haematoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Posterior capsule opacification	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pterygium	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Retinal detachment	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Retinopathy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vitreous floaters	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	6/40 (15.0%)	5/40 (12.5%)	0/40 (0.0%)	11/40 (27.5%)
Abdominal distension	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain lower	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain upper	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Abdominal rigidity	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anorectal disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Constipation	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Diarrhoea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diverticulum intestinal	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Duodenal ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dyspepsia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epigastric discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastritis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastroenteritis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Gastrointestinal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastrointestinal upset	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gingivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glossitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Haemorrhoids	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Intestinal ischaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Intestinal obstruction	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Irritable bowel syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lip dry	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nausea	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Pancreatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parotid gland enlargement	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periodontal disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periodontitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Reflux oesophagitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Stomach discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Stomatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tongue ulceration	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vomiting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
General disorders and administration site conditions				
ANY EVENT	6/40 (15.0%)	0/40 (0.0%)	0/40 (0.0%)	6/40 (15.0%)
Asthenia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Axillary pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chest discomfort	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chest pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fatigue	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling cold	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling hot	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Malaise	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Oedema peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pyrexia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Thirst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatobiliary disorders				
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)	2/40 (5.0%)
Cholecystitis	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Hepatic cyst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatic function abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hepatitis B	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hepatitis C	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Immune system disorders				
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Allergy to plants	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis allergic	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
House dust allergy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis allergic	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Seasonal allergy	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	13/40 (32.5%)	3/40 (7.5%)	0/40 (0.0%)	16/40 (40.0%)
Bronchiolitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chronic sinusitis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Cystitis	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Cystitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dental caries	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Groin abscess	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes simplex	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes zoster	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Influenza	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Laryngopharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail tinea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Nasopharyngitis	8/40 (20.0%)	1/40 (2.5%)	0/40 (0.0%)	9/40 (22.5%)
Otitis media	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Otitis media chronic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Paronychia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pneumonia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sinusitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinea pedis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tonsillitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Upper respiratory tract infection	3/40 (7.5%)	1/40 (2.5%)	0/40 (0.0%)	4/40 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)	2/40 (5.0%)
Animal bite	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Arthropod sting	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Contusion	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Haemarthrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypothermia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Mouth injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open wound	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	11/40 (27.5%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Activated partial thromboplastin time prolonged	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Antithrombin III decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood bilirubin increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood creatinine increased	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Blood fibrinogen decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood glucose increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood pressure decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure increased	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Blood thyroid stimulating hormone decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood thyroid stimulating hormone increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood triglycerides increased	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Coagulation time prolonged	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Eosinophil count increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eosinophil percentage increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gamma-glutamyltransferase increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glucose urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipids increased	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Liver function test abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Low density lipoprotein increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lymphocyte percentage decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neutrophil percentage increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Platelet count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Protein urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Prothrombin time prolonged	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Smear cervix abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sputum test	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urine output decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Weight increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
White blood cell count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Anorexia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Decreased appetite	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Diabetes mellitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypercholesterolaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperlipidaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	13/40 (32.5%)	2/40 (5.0%)	1/40 (2.5%)	16/40 (40.0%)
Arthralgia	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Arthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Back pain	4/40 (10.0%)	1/40 (2.5%)	1/40 (2.5%)	6/40 (15.0%)
Buttock pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Foot fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hand fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint sprain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint swelling	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Limb discomfort	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Localised osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Monoarthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Muscle cramp	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle fatigue	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle rigidity	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Muscle twitching	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Musculoskeletal stiffness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Myalgia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Neck pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neck, shoulder and arm syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nodal osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pain in extremity	3/40 (7.5%)	1/40 (2.5%)	1/40 (2.5%)	5/40 (12.5%)
Radius fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rib fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sensation of heaviness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Spondylosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tenosynovitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thoracic vertebral fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Traumatic fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Wrist fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	2/40 (5.0%)
Colonic polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibroadenoma of breast	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibroma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric cancer	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Hepatic cancer metastatic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metastases to lymph nodes	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ovarian neoplasm	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Nervous system disorders				
ANY EVENT	11/40 (27.5%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Autonomic nervous system imbalance	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Depressed level of consciousness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dizziness	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Dizziness postural	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysgeusia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Facial nerve disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Headache	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Hypoaesthesia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intercostal neuralgia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neuropathy peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parkinson's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parosmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sciatica	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tension headache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vertigo	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Amnesia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Depression	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Depressive symptom	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysphoria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Insomnia	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Irritability	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neurosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sleep disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Renal and urinary disorders				
ANY EVENT	4/40 (10.0%)	1/40 (2.5%)	0/40 (0.0%)	5/40 (12.5%)
Bladder malposition acquired	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysuria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Micturition disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nocturia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pollakiuria	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Urge incontinence	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Urinary incontinence	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	14/40 (35.0%)	5/40 (12.5%)	0/40 (0.0%)	19/40 (47.5%)
Breast discomfort	11/40 (27.5%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Breast disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast engorgement	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Breast fibrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast hyperplasia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast pain	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Cervical polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cervicitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysmenorrhoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endometrial hyperplasia	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Fibrocystic breast disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Genital discharge	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Genital haemorrhage	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Genital pruritus female	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Genital rash	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hot flush	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Menopausal symptoms	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nipple pain	5/40 (12.5%)	1/40 (2.5%)	0/40 (0.0%)	6/40 (15.0%)
Uterine leiomyoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Uterine malposition	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vaginal candidiasis	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Vaginitis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulval oedema	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vulvitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulvovaginal discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	2/40 (5.0%)
Asthma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dyspnoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epistaxis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngolaryngeal pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pharynx discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Productive cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinorrhoea	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Upper respiratory tract inflammation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	5/40 (12.5%)	1/40 (2.5%)	0/40 (0.0%)	6/40 (15.0%)
Acne	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Body tinea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cheilitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermal cyst	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis contact	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dry skin	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eczema	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Eczema asteatotic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Erythema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Excoriation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Face oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Folliculitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperkeratosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Milia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pruritus	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash papular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rash pustular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin papilloma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urticaria	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Surgical and medical procedures				
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail avulsion	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Atherosclerosis obliterans	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure fluctuation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chillblains	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Deep vein thrombosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypertension	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypotension	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral coldness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral vascular disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	49/117 (41.9%)	49/117 (41.9%)	10/117 (8.5%)	108/117 (92.3%)
Blood and lymphatic system disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	3/117 (2.6%)
Anaemia	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Hypochromic anaemia	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Iron deficiency anaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cardiac disorders				
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Angina pectoris	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arrhythmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Palpitations	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Supraventricular extrasystoles	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Ear and labyrinth disorders				
ANY EVENT	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	4/117 (3.4%)
Deafness	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Meniere's disease	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Tinnitus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Endocrine disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Goitre	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thyroid cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thyroiditis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	8/117 (6.8%)	1/117 (0.9%)	0/117 (0.0%)	9/117 (7.7%)
Abnormal sensation in eye	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Asthenopia	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Blepharitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cataract	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Conjunctival haemorrhage	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Conjunctivitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Corneal dystrophy	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis eyelid	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eye pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hordeolum	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Keratoconjunctivitis sicca	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lacrimation increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open angle glaucoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Periorbital haematoma	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Posterior capsule opacification	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pterygium	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinal detachment	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinopathy	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vitreous floaters	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	30/117 (25.6%)	11/117 (9.4%)	0/117 (0.0%)	41/117 (35.0%)
Abdominal distension	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Abdominal pain	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Abdominal pain lower	5/117 (4.3%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Abdominal pain upper	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	4/117 (3.4%)
Abdominal rigidity	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Anorectal disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Constipation	6/117 (5.1%)	6/117 (5.1%)	0/117 (0.0%)	12/117 (10.3%)
Diarrhoea	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Diverticulum intestinal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Duodenal ulcer	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dyspepsia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Epigastric discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastric ulcer	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Gastritis	4/117 (3.4%)	1/117 (0.9%)	0/117 (0.0%)	5/117 (4.3%)
Gastritis atrophic	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastroenteritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastrointestinal pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastrointestinal upset	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Gingivitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Glossitis	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Haemorrhoids	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Intestinal ischaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal obstruction	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Irritable bowel syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lip dry	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nausea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pancreatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parotid gland enlargement	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Periodontal disease	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Periodontitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Reflux oesophagitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomach discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomatitis	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Tongue ulceration	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vomiting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
General disorders and administration site conditions				
ANY EVENT	12/117 (10.3%)	0/117 (0.0%)	0/117 (0.0%)	12/117 (10.3%)
Asthenia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Axillary pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Chest discomfort	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Chest pain	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fatigue	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Feeling cold	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling hot	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Malaise	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Oedema	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Oedema peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pyrexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thirst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatobiliary disorders				
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Cholecystitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic function abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatitis B	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hepatitis C	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Immune system disorders				
ANY EVENT	8/117 (6.8%)	1/117 (0.9%)	0/117 (0.0%)	9/117 (7.7%)
Allergy to plants	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dermatitis allergic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
House dust allergy	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinitis allergic	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Seasonal allergy	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	6/117 (5.1%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	30/117 (25.6%)	11/117 (9.4%)	1/117 (0.9%)	42/117 (35.9%)
Bronchiolitis	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Bronchitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chronic sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cystitis	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Cystitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dental caries	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Groin abscess	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Herpes dermatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Herpes simplex	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Herpes zoster	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Influenza	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Laryngopharyngitis	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Nail tinea	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nasopharyngitis	20/117 (17.1%)	5/117 (4.3%)	0/117 (0.0%)	25/117 (21.4%)
Otitis media	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Otitis media chronic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Paronychia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pharyngitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pneumonia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tinea pedis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tonsillitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Upper respiratory tract infection	10/117 (8.5%)	2/117 (1.7%)	0/117 (0.0%)	12/117 (10.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	4/117 (3.4%)	3/117 (2.6%)	0/117 (0.0%)	7/117 (6.0%)
Animal bite	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arthropod sting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Contusion	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Haemarthrosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypothermia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Injury	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	2/117 (1.7%)
Mouth injury	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open wound	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin injury	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	13/117 (11.1%)	5/117 (4.3%)	0/117 (0.0%)	18/117 (15.4%)
Activated partial thromboplastin time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Antithrombin III decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood bilirubin increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood creatinine increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood fibrinogen decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Blood glucose increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood pressure decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure increased	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	5/117 (4.3%)
Blood thyroid stimulating hormone decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood thyroid stimulating hormone increased	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Blood triglycerides increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Coagulation time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Eosinophil count increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Eosinophil percentage increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gamma-glutamyltransferase increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Glucose urine present	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lipids increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Liver function test abnormal	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Low density lipoprotein increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lymphocyte percentage decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neutrophil percentage increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Platelet count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Protein urine present	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Prothrombin time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Smear cervix abnormal	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Sputum test	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urine output decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Weight increased	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
White blood cell count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Anorexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Decreased appetite	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Diabetes mellitus	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypercholesterolaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperlipidaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	18/117 (15.4%)	10/117 (8.5%)	3/117 (2.6%)	31/117 (26.5%)
Arthralgia	4/117 (3.4%)	1/117 (0.9%)	0/117 (0.0%)	5/117 (4.3%)
Arthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Back pain	11/117 (9.4%)	5/117 (4.3%)	2/117 (1.7%)	18/117 (15.4%)
Buttock pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Foot fracture	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Hand fracture	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Joint sprain	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Joint swelling	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Limb discomfort	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Localised osteoarthritis	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Monoarthritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Muscle cramp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle fatigue	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle rigidity	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Muscle twitching	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Musculoskeletal stiffness	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Myalgia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck, shoulder and arm syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nodal osteoarthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pain in extremity	2/117 (1.7%)	2/117 (1.7%)	0/117 (0.0%)	4/117 (3.4%)
Radius fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rib fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sensation of heaviness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Spondylosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tenosynovitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thoracic vertebral fracture	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Traumatic fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Wrist fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	3/117 (2.6%)	0/117 (0.0%)	2/117 (1.7%)	5/117 (4.3%)
Colonic polyp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Fibroadenoma of breast	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fibroma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastric cancer	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)	2/117 (1.7%)
Hepatic cancer metastatic	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Lipoma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Metastases to lymph nodes	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Ovarian neoplasm	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nervous system disorders				
ANY EVENT	10/117 (8.5%)	8/117 (6.8%)	2/117 (1.7%)	20/117 (17.1%)
Autonomic nervous system imbalance	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Depressed level of consciousness	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dizziness	1/117 (0.9%)	3/117 (2.6%)	1/117 (0.9%)	5/117 (4.3%)
Dizziness postural	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysgeusia	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Facial nerve disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Headache	7/117 (6.0%)	2/117 (1.7%)	0/117 (0.0%)	9/117 (7.7%)
Hypoaesthesia	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Intercostal neuralgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neuropathy peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parkinson's disease	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Parosmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sciatica	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tension headache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vertigo	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	10/117 (8.5%)	2/117 (1.7%)	1/117 (0.9%)	13/117 (11.1%)
Amnesia	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Depression	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Depressive symptom	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysphoria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Insomnia	6/117 (5.1%)	2/117 (1.7%)	0/117 (0.0%)	8/117 (6.8%)
Irritability	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neurosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sleep disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Renal and urinary disorders				
ANY EVENT	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Bladder malposition acquired	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysuria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Micturition disorder	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nocturia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pollakiuria	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urge incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urinary incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	51/117 (43.6%)	24/117 (20.5%)	0/117 (0.0%)	75/117 (64.1%)
Breast discomfort	27/117 (23.1%)	1/117 (0.9%)	0/117 (0.0%)	28/117 (23.9%)
Breast disorder	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Breast engorgement	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Breast fibrosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Breast hyperplasia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Breast pain	17/117 (14.5%)	3/117 (2.6%)	0/117 (0.0%)	20/117 (17.1%)
Cervical polyp	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Cervicitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysmenorrhoea	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Endometrial hyperplasia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Fibrocystic breast disease	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	4/117 (3.4%)
Genital discharge	15/117 (12.8%)	1/117 (0.9%)	0/117 (0.0%)	16/117 (13.7%)
Genital haemorrhage	10/117 (8.5%)	11/117 (9.4%)	0/117 (0.0%)	21/117 (17.9%)
Genital pruritus female	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Genital rash	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hot flush	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Menopausal symptoms	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nipple pain	4/117 (3.4%)	4/117 (3.4%)	0/117 (0.0%)	8/117 (6.8%)
Uterine leiomyoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Uterine malposition	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vaginal candidiasis	6/117 (5.1%)	3/117 (2.6%)	0/117 (0.0%)	9/117 (7.7%)
Vaginitis atrophic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulval oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulvitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vulvovaginal discomfort	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	5/117 (4.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	8/117 (6.8%)	4/117 (3.4%)	0/117 (0.0%)	12/117 (10.3%)
Asthma	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Cough	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Dyspnoea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Epistaxis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pharyngolaryngeal pain	5/117 (4.3%)	2/117 (1.7%)	0/117 (0.0%)	7/117 (6.0%)
Pharynx discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Productive cough	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Rhinitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinorrhoea	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	2/117 (1.7%)
Upper respiratory tract inflammation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	20/117 (17.1%)	3/117 (2.6%)	0/117 (0.0%)	23/117 (19.7%)
Acne	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Body tinea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cheilitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermal cyst	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Dermatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis contact	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dry skin	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eczema	6/117 (5.1%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Eczema asteatotic	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Erythema	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Excoriation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Face oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Folliculitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hyperkeratosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Milia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pruritus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Rash	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Rash papular	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rash pustular	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin papilloma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urticaria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Surgical and medical procedures				
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail avulsion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	2/117 (1.7%)	1/117 (0.9%)	1/117 (0.9%)	4/117 (3.4%)
Atherosclerosis obliterans	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Blood pressure fluctuation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chillblains	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Deep vein thrombosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypertension	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypotension	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Peripheral coldness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Peripheral vascular disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
ANY EVENT	124/309 (40.1%)	127/309 (41.1%)	25/309 (8.1%)	276/309 (89.3%)
Blood and lymphatic system disorders				
ANY EVENT	4/309 (1.3%)	1/309 (0.3%)	1/309 (0.3%)	6/309 (1.9%)
Anaemia	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Hypochromic anaemia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Iron deficiency anaemia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Cardiac disorders				
ANY EVENT	3/309 (1.0%)	5/309 (1.6%)	2/309 (0.6%)	10/309 (3.2%)
Angina pectoris	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Arrhythmia	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)	2/309 (0.6%)
Palpitations	3/309 (1.0%)	3/309 (1.0%)	0/309 (0.0%)	6/309 (1.9%)
Supraventricular extrasystoles	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Ear and labyrinth disorders				
ANY EVENT	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	6/309 (1.9%)
Deafness	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Meniere's disease	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Tinnitus	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Endocrine disorders				
ANY EVENT	7/309 (2.3%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Goitre	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Thyroid cyst	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroiditis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Eye disorders				
ANY EVENT	18/309 (5.8%)	4/309 (1.3%)	0/309 (0.0%)	22/309 (7.1%)
Abnormal sensation in eye	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Asthenopia	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Blepharitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cataract	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Conjunctival haemorrhage	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctivitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Corneal dystrophy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis eyelid	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eye pain	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Hordeolum	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Keratoconjunctivitis sicca	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lacrimation increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open angle glaucoma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Periorbital haematoma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Posterior capsule opacification	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pterygium	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinal detachment	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinopathy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vitreous floaters	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Gastrointestinal disorders				
ANY EVENT	74/309 (23.9%)	26/309 (8.4%)	2/309 (0.6%)	102/309 (33.0%)
Abdominal distension	10/309 (3.2%)	1/309 (0.3%)	0/309 (0.0%)	11/309 (3.6%)
Abdominal pain	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal pain lower	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Abdominal pain upper	13/309 (4.2%)	2/309 (0.6%)	0/309 (0.0%)	15/309 (4.9%)
Abdominal rigidity	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Anorectal disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Constipation	15/309 (4.9%)	8/309 (2.6%)	0/309 (0.0%)	23/309 (7.4%)
Diarrhoea	9/309 (2.9%)	1/309 (0.3%)	0/309 (0.0%)	10/309 (3.2%)
Diverticulum intestinal	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Duodenal ulcer	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dyspepsia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epigastric discomfort	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Gastric ulcer	0/309 (0.0%)	3/309 (1.0%)	0/309 (0.0%)	3/309 (1.0%)
Gastritis	12/309 (3.9%)	1/309 (0.3%)	0/309 (0.0%)	13/309 (4.2%)
Gastritis atrophic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastroenteritis	3/309 (1.0%)	2/309 (0.6%)	0/309 (0.0%)	5/309 (1.6%)
Gastrointestinal pain	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Gastrointestinal upset	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Gingivitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Glossitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Haemorrhoids	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Intestinal ischaemia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Intestinal obstruction	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Irritable bowel syndrome	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lip dry	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nausea	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	6/309 (1.9%)
Pancreatitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Parotid gland enlargement	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periodontal disease	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periodontitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Reflux oesophagitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Stomach discomfort	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Stomatitis	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Tongue ulceration	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
(System Organ Class decode continued from previous page)				
Toothache	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vomiting	2/309 (0.6%)	0/309 (0.0%)	1/309 (0.3%)	3/309 (1.0%)
General disorders and administration site conditions				
ANY EVENT	33/309 (10.7%)	7/309 (2.3%)	0/309 (0.0%)	40/309 (12.9%)
Asthenia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Axillary pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Chest discomfort	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Chest pain	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fatigue	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Feeling cold	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Feeling hot	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Malaise	9/309 (2.9%)	1/309 (0.3%)	0/309 (0.0%)	10/309 (3.2%)
Oedema	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Oedema peripheral	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Pyrexia	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Thirst	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Hepatobiliary disorders				
ANY EVENT	3/309 (1.0%)	2/309 (0.6%)	1/309 (0.3%)	6/309 (1.9%)
Cholecystitis	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Hepatic cyst	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatic function abnormal	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Hepatitis B	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatitis C	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Immune system disorders				
ANY EVENT	18/309 (5.8%)	4/309 (1.3%)	0/309 (0.0%)	22/309 (7.1%)
Allergy to plants	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis allergic	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
House dust allergy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinitis allergic	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Seasonal allergy	12/309 (3.9%)	2/309 (0.6%)	0/309 (0.0%)	14/309 (4.5%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Infections and infestations				
ANY EVENT	88/309 (28.5%)	38/309 (12.3%)	2/309 (0.6%)	128/309 (41.4%)
Bronchiolitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Bronchitis	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Bronchitis acute	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Chronic sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cystitis	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Cystitis acute	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Dental caries	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Groin abscess	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Herpes dermatitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Herpes simplex	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Herpes zoster	1/309 (0.3%)	4/309 (1.3%)	0/309 (0.0%)	5/309 (1.6%)
Influenza	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Laryngopharyngitis	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)
Nail tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nasopharyngitis	59/309 (19.1%)	22/309 (7.1%)	1/309 (0.3%)	82/309 (26.5%)
Otitis media	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Otitis media chronic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Paronychia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Pharyngitis	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Pneumonia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tinea pedis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tonsillitis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Upper respiratory tract infection	26/309 (8.4%)	5/309 (1.6%)	0/309 (0.0%)	31/309 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Injury, poisoning and procedural complications				
ANY EVENT	10/309 (3.2%)	7/309 (2.3%)	1/309 (0.3%)	18/309 (5.8%)
Animal bite	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Arthropod sting	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Contusion	2/309 (0.6%)	4/309 (1.3%)	1/309 (0.3%)	7/309 (2.3%)
Haemarthrosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypothermia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Injury	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)
Mouth injury	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open wound	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin injury	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Investigations				
ANY EVENT	56/309 (18.1%)	8/309 (2.6%)	0/309 (0.0%)	64/309 (20.7%)
Activated partial thromboplastin time prolonged	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Antithrombin III decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood bilirubin increased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood creatinine increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood fibrinogen decreased	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Blood glucose increased	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Blood pressure decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood pressure increased	14/309 (4.5%)	2/309 (0.6%)	0/309 (0.0%)	16/309 (5.2%)
Blood thyroid stimulating hormone decreased	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Blood thyroid stimulating hormone increased	9/309 (2.9%)	0/309 (0.0%)	0/309 (0.0%)	9/309 (2.9%)
Blood triglycerides increased	7/309 (2.3%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Coagulation time prolonged	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eosinophil count increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eosinophil percentage increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gamma-glutamyltransferase increased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Glucose urine present	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Lipids increased	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Liver function test abnormal	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Low density lipoprotein increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lymphocyte percentage decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neutrophil percentage increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Platelet count decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Protein urine present	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Prothrombin time prolonged	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Smear cervix abnormal	3/309 (1.0%)	2/309 (0.6%)	0/309 (0.0%)	5/309 (1.6%)
Sputum test	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urine output decreased	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Weight increased	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
White blood cell count decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Metabolism and nutrition disorders				
ANY EVENT	10/309 (3.2%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Anorexia	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Decreased appetite	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Diabetes mellitus	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hypercholesterolaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperlipidaemia	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Musculoskeletal and connective tissue disorders				
ANY EVENT	57/309 (18.4%)	27/309 (8.7%)	8/309 (2.6%)	92/309 (29.8%)
Arthralgia	18/309 (5.8%)	3/309 (1.0%)	0/309 (0.0%)	21/309 (6.8%)
Arthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Back pain	27/309 (8.7%)	13/309 (4.2%)	3/309 (1.0%)	43/309 (13.9%)
Buttock pain	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Foot fracture	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Hand fracture	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Joint sprain	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Joint swelling	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Limb discomfort	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	3/309 (1.0%)
Localised osteoarthritis	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Monoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Muscle cramp	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Muscle fatigue	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Muscle rigidity	10/309 (3.2%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Muscle twitching	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Musculoskeletal stiffness	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Myalgia	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Neck pain	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Neck, shoulder and arm syndrome	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nodal osteoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pain in extremity	8/309 (2.6%)	3/309 (1.0%)	1/309 (0.3%)	12/309 (3.9%)
Radius fracture	0/309 (0.0%)	2/309 (0.6%)	3/309 (1.0%)	5/309 (1.6%)
Rib fracture	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Sensation of heaviness	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Spondylosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tenosynovitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Thoracic vertebral fracture	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Traumatic fracture	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Wrist fracture	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
ANY EVENT	6/309 (1.9%)	1/309 (0.3%)	4/309 (1.3%)	11/309 (3.6%)
Colonic polyp	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Fibroadenoma of breast	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fibroma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastric cancer	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)	3/309 (1.0%)
Hepatic cancer metastatic	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Lipoma	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Metastases to lymph nodes	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Ovarian neoplasm	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Nervous system disorders				
ANY EVENT	40/309 (12.9%)	18/309 (5.8%)	2/309 (0.6%)	60/309 (19.4%)
Autonomic nervous system imbalance	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Depressed level of consciousness	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dizziness	11/309 (3.6%)	5/309 (1.6%)	1/309 (0.3%)	17/309 (5.5%)
Dizziness postural	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysgeusia	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Facial nerve disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Headache	16/309 (5.2%)	6/309 (1.9%)	0/309 (0.0%)	22/309 (7.1%)
Hypoaesthesia	6/309 (1.9%)	1/309 (0.3%)	0/309 (0.0%)	7/309 (2.3%)
Intercostal neuralgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neuropathy peripheral	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Parkinson's disease	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Parosmia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sciatica	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Tension headache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vertigo	5/309 (1.6%)	2/309 (0.6%)	0/309 (0.0%)	7/309 (2.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Psychiatric disorders				
ANY EVENT	21/309 (6.8%)	5/309 (1.6%)	1/309 (0.3%)	27/309 (8.7%)
Amnesia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Depression	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Depressive symptom	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysphoria	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	5/309 (1.6%)
Insomnia	12/309 (3.9%)	4/309 (1.3%)	0/309 (0.0%)	16/309 (5.2%)
Irritability	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neurosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sleep disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Renal and urinary disorders				
ANY EVENT	8/309 (2.6%)	2/309 (0.6%)	0/309 (0.0%)	10/309 (3.2%)
Bladder malposition acquired	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysuria	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Micturition disorder	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nocturia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pollakiuria	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Urge incontinence	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urinary incontinence	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Reproductive system and breast disorders				
ANY EVENT	119/309 (38.5%)	50/309 (16.2%)	0/309 (0.0%)	169/309 (54.7%)
Breast discomfort	64/309 (20.7%)	5/309 (1.6%)	0/309 (0.0%)	69/309 (22.3%)
Breast disorder	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Breast engorgement	8/309 (2.6%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Breast fibrosis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Breast hyperplasia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Breast pain	31/309 (10.0%)	7/309 (2.3%)	0/309 (0.0%)	38/309 (12.3%)
Cervical polyp	6/309 (1.9%)	1/309 (0.3%)	0/309 (0.0%)	7/309 (2.3%)
Cervicitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dysmenorrhoea	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Endometrial hyperplasia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Fibrocystic breast disease	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	6/309 (1.9%)
Genital discharge	36/309 (11.7%)	2/309 (0.6%)	0/309 (0.0%)	38/309 (12.3%)
Genital haemorrhage	14/309 (4.5%)	17/309 (5.5%)	0/309 (0.0%)	31/309 (10.0%)
Genital pruritus female	7/309 (2.3%)	2/309 (0.6%)	0/309 (0.0%)	9/309 (2.9%)
Genital rash	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hot flush	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Menopausal symptoms	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	6/309 (1.9%)
Nipple pain	16/309 (5.2%)	7/309 (2.3%)	0/309 (0.0%)	23/309 (7.4%)
Uterine leiomyoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Uterine malposition	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vaginal candidiasis	11/309 (3.6%)	5/309 (1.6%)	0/309 (0.0%)	16/309 (5.2%)
Vaginitis atrophic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulval oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vulvovaginal discomfort	4/309 (1.3%)	3/309 (1.0%)	0/309 (0.0%)	7/309 (2.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

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Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Respiratory, thoracic and mediastinal disorders				
ANY EVENT	23/309 (7.4%)	6/309 (1.9%)	1/309 (0.3%)	30/309 (9.7%)
Asthma	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	2/309 (0.6%)
Cough	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Dyspnoea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epistaxis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Pharyngolaryngeal pain	9/309 (2.9%)	3/309 (1.0%)	0/309 (0.0%)	12/309 (3.9%)
Pharynx discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Productive cough	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Rhinorrhoea	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	4/309 (1.3%)
Upper respiratory tract inflammation	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Skin and subcutaneous tissue disorders				
ANY EVENT	48/309 (15.5%)	8/309 (2.6%)	1/309 (0.3%)	57/309 (18.4%)
Acne	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Body tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cheilitis	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Dermal cyst	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	4/309 (1.3%)
Dermatitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dermatitis contact	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Dry skin	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eczema	16/309 (5.2%)	1/309 (0.3%)	0/309 (0.0%)	17/309 (5.5%)
Eczema asteatotic	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Erythema	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Excoriation	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Face oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Folliculitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperkeratosis	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Milia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nail disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pruritus	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Rash	7/309 (2.3%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Rash papular	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Rash pustular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin papilloma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Urticaria	5/309 (1.6%)	2/309 (0.6%)	0/309 (0.0%)	7/309 (2.3%)
Surgical and medical procedures				
ANY EVENT	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Nail avulsion	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

(Continued)

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Table 14.3.1.6: Adverse Events - Number (%) of Patients by Maximum Intensity - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	mild	moderate	severe	Total
Vascular disorders				
ANY EVENT	8/309 (2.6%)	1/309 (0.3%)	1/309 (0.3%)	10/309 (3.2%)
Atherosclerosis obliterans	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Blood pressure fluctuation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Chillblains	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Deep vein thrombosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypertension	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hypotension	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Peripheral coldness	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Peripheral vascular disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode
Intensity: the maximum intensity
(Order No. : S0021T)

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表 2.7.6.4- 8　　試験 300103：治験薬との関連性判定別の有害事象発現率（例数，%）

総括報告書 A23185　表 14-3-1-7（1 年間投与），表 14-3-1-8（2 年間投与）より引用

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	10/20 (50.0%)	2/20 (10.0%)	2/20 (10.0%)	1/20 (5.0%)	1/20 (5.0%)	16/20 (80.0%)
Blood and lymphatic system disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypochromic anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cardiac disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Angina pectoris	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arrhythmia	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Palpitations	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Supraventricular extrasystoles	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deafness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Meniere's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinnitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endocrine disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Goitre	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroid cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroiditis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abnormal sensation in eye	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthenopia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blepharitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Conjunctival haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctivitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Corneal dystrophy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eye pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lacrimation increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open angle glaucoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periorbital haematoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pterygium	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Retinal detachment	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vitreous floaters	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	4/20 (20.0%)	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	6/20 (30.0%)
Abdominal distension	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abdominal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain lower	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Abdominal pain upper	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorectal disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Constipation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diarrhoea	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Dyspepsia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epigastric discomfort	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastritis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastritis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastroenteritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastrointestinal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastrointestinal upset	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glossitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Haemorrhoids	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal ischaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal obstruction	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritable bowel syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lip dry	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nausea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pancreatitis	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Reflux oesophagitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Stomach discomfort	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Stomatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Tongue ulceration	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Toothache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vomiting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	1/20 (5.0%)	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	4/20 (20.0%)
Chest discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Feeling cold	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Feeling hot	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Malaise	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Oedema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Oedema peripheral	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Thirst	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hepatobiliary disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cholecystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic function abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Immune system disorders						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Dermatitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Seasonal allergy	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	8/20 (40.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	9/20 (45.0%)
Bronchiolitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chronic sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Groin abscess	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes simplex	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Herpes zoster	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Laryngopharyngitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nasopharyngitis	6/20 (30.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	6/20 (30.0%)
Otitis media	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Tinea pedis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tonsillitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract infection	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Injury, poisoning and procedural complications						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Arthropod sting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Contusion	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Haemarthrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open wound	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Blood glucose increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Blood thyroid stimulating hormone decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood thyroid stimulating hormone increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood triglycerides increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gamma-glutamyltransferase increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipids increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Liver function test abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Low density lipoprotein increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Protein urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Smear cervix abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sputum test	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urine output decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Weight increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
White blood cell count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Metabolism and nutrition disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorexia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diabetes mellitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypercholesterolaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperlipidaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	1/20 (5.0%)	2/20 (10.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	4/20 (20.0%)
Arthralgia	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Arthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Back pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Buttock pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint swelling	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Limb discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Localised osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle cramp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Musculoskeletal stiffness	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Myalgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck, shoulder and arm syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nodal osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pain in extremity	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Radius fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rib fracture	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Sensation of heaviness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Spondylosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tenosynovitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric cancer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipoma	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Metastases to lymph nodes	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Autonomic nervous system imbalance	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dizziness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysgeusia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Facial nerve disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Headache	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hypoaesthesia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intercostal neuralgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neuropathy peripheral	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parosmia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sciatica	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tension headache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vertigo	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Psychiatric disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depressive symptom	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysphoria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Insomnia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritability	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sleep disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Renal and urinary disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Bladder malposition acquired	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Micturition disorder	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Urge incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urinary incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)	1/20 (5.0%)	3/20 (15.0%)
Breast discomfort	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Breast disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast engorgement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast fibrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast pain	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)	2/20 (10.0%)
Cervical polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cervicitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysmenorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibrocystic breast disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital discharge	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)
Genital haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital pruritus female	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hot flush	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Menopausal symptoms	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Nipple pain	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Uterine malposition	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginal candidiasis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulval oedema	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvovaginal discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngolaryngeal pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharynx discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Productive cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract inflammation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	3/20 (15.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	4/20 (20.0%)
Acne	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Body tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cheilitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermal cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dermatitis contact	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dry skin	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eczema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Eczema asteatotic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Erythema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Excoriation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Face oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hyperkeratosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pruritus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash papular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash pustular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin papilloma	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Urticaria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Surgical and medical procedures						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail avulsion	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vascular disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Atherosclerosis obliterans	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure fluctuation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deep vein thrombosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypertension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypotension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral vascular disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	24/59 (40.7%)	11/59 (18.6%)	2/59 (3.4%)	2/59 (3.4%)	8/59 (13.6%)	47/59 (79.7%)
Blood and lymphatic system disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypochromic anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cardiac disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Angina pectoris	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arrhythmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Palpitations	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Supraventricular extrasystoles	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Deafness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Meniere's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinnitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Endocrine disorders						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Goitre	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Thyroid cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thyroiditis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Abnormal sensation in eye	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Asthenopia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blepharitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctival haemorrhage	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Corneal dystrophy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eye pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lacrimation increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open angle glaucoma	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Periorbital haematoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pterygium	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinal detachment	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vitreous floaters	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	5/59 (8.5%)	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	9/59 (15.3%)
Abdominal distension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain lower	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain upper	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anorectal disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Constipation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Diarrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspepsia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epigastric discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric ulcer	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gastritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastritis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastroenteritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastrointestinal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastrointestinal upset	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Glossitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemorrhoids	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal ischaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal obstruction	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Irritable bowel syndrome	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lip dry	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nausea	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pancreatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Reflux oesophagitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomach discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomatitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tongue ulceration	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Toothache	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vomiting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	5/59 (8.5%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	7/59 (11.9%)
Chest discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest pain	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fatigue	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Feeling cold	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Feeling hot	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Malaise	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Oedema peripheral	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Thirst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Cholecystitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic function abnormal	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Immune system disorders						
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dermatitis allergic	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rhinitis allergic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Seasonal allergy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	15/59 (25.4%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	17/59 (28.8%)
Bronchiolitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bronchitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bronchitis acute	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Chronic sinusitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cystitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Cystitis acute	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Groin abscess	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes simplex	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes zoster	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Laryngopharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nasopharyngitis	11/59 (18.6%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	12/59 (20.3%)
Otitis media	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinea pedis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tonsillitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract infection	2/59 (3.4%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Injury, poisoning and procedural complications						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arthropod sting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Contusion	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemarthrosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open wound	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	1/59 (1.7%)	2/59 (3.4%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Blood glucose increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood thyroid stimulating hormone decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood thyroid stimulating hormone increased	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood triglycerides increased	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gamma-glutamyltransferase increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipids increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Liver function test abnormal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Low density lipoprotein increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Protein urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Smear cervix abnormal	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sputum test	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urine output decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Weight increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
White blood cell count decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metabolism and nutrition disorders						
ANY EVENT	0/59 (0.0%)	2/59 (3.4%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	4/59 (6.8%)
Anorexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Diabetes mellitus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Hypercholesterolaemia	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hyperlipidaemia	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	10/59 (16.9%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	11/59 (18.6%)
Arthralgia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Arthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Back pain	4/59 (6.8%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Buttock pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint swelling	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Limb discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Localised osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle cramp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Musculoskeletal stiffness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Myalgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck, shoulder and arm syndrome	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nodal osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pain in extremity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Radius fracture	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rib fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sensation of heaviness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Spondylosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tenosynovitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric cancer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metastases to lymph nodes	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	3/59 (5.1%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Autonomic nervous system imbalance	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dizziness	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysgeusia	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Facial nerve disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Headache	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Hypoaesthesia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intercostal neuralgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neuropathy peripheral	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Parosmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sciatica	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tension headache	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vertigo	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Psychiatric disorders						
ANY EVENT	4/59 (6.8%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Depressive symptom	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysphoria	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Insomnia	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Irritability	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sleep disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Renal and urinary disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bladder malposition acquired	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysuria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Micturition disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urge incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urinary incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	2/59 (3.4%)	1/59 (1.7%)	1/59 (1.7%)	1/59 (1.7%)	8/59 (13.6%)	13/59 (22.0%)
Breast discomfort	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	4/59 (6.8%)	5/59 (8.5%)
Breast disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast engorgement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast fibrosis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Breast pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)	2/59 (3.4%)	4/59 (6.8%)
Cervical polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cervicitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysmenorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibrocystic breast disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Genital discharge	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Genital haemorrhage	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)	2/59 (3.4%)
Genital pruritus female	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hot flush	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Menopausal symptoms	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nipple pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Uterine malposition	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vaginal candidiasis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulval oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvovaginal discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Asthma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngolaryngeal pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Pharynx discomfort	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Productive cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract inflammation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	4/59 (6.8%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Acne	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Body tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cheilitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dermal cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis contact	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dry skin	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eczema	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Eczema asteatotic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Erythema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Excoriation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Face oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hyperkeratosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pruritus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rash	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash papular	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash pustular	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin papilloma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urticaria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Surgical and medical procedures						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nail avulsion	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vascular disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Atherosclerosis obliterans	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure fluctuation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Deep vein thrombosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypertension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypotension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral vascular disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	5/16 (31.3%)	3/16 (18.8%)	1/16 (6.3%)	3/16 (18.8%)	1/16 (6.3%)	13/16 (81.3%)
Blood and lymphatic system disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypochromic anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cardiac disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Angina pectoris	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arrhythmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Palpitations	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Supraventricular extrasystoles	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deafness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Meniere's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinnitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endocrine disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Goitre	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thyroid cyst	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Thyroiditis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abnormal sensation in eye	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Asthenopia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blepharitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctival haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Corneal dystrophy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eye pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lacrimation increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open angle glaucoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periorbital haematoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pterygium	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinal detachment	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vitreous floaters	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	5/16 (31.3%)	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	7/16 (43.8%)
Abdominal distension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abdominal pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain lower	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain upper	2/16 (12.5%)	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Abdominal rigidity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anorectal disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Constipation	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Diarrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dyspepsia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Epigastric discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastritis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastroenteritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal upset	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glossitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemorrhoids	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal ischaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal obstruction	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Irritable bowel syndrome	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Lip dry	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nausea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pancreatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Reflux oesophagitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Stomach discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Stomatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tongue ulceration	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Toothache	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vomiting	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Chest discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling cold	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling hot	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Malaise	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Oedema	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Oedema peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thirst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cholecystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic function abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Immune system disorders						
ANY EVENT	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Dermatitis allergic	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Rhinitis allergic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Seasonal allergy	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	4/16 (25.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	4/16 (25.0%)
Bronchiolitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chronic sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Groin abscess	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes simplex	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes zoster	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Laryngopharyngitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nasopharyngitis	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Otitis media	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Tinea pedis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tonsillitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Upper respiratory tract infection	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Injury, poisoning and procedural complications						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arthropod sting	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Contusion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemarthrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open wound	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Blood glucose increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood pressure increased	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood thyroid stimulating hormone decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood thyroid stimulating hormone increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood triglycerides increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gamma-glutamyltransferase increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipids increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Liver function test abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Low density lipoprotein increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Protein urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Smear cervix abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sputum test	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urine output decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Weight increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
White blood cell count decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Metabolism and nutrition disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Anorexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Diabetes mellitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypercholesterolaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperlipidaemia	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	4/16 (25.0%)	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	6/16 (37.5%)
Arthralgia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Arthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Back pain	2/16 (12.5%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Buttock pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint swelling	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Limb discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Localised osteoarthritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Muscle cramp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle rigidity	0/16 (0.0%)	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Musculoskeletal stiffness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Myalgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck, shoulder and arm syndrome	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nodal osteoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pain in extremity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Radius fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rib fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sensation of heaviness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Spondylosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tenosynovitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric cancer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Metastases to lymph nodes	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	4/16 (25.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	5/16 (31.3%)
Autonomic nervous system imbalance	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dizziness	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Dysgeusia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Facial nerve disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Hypoaesthesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intercostal neuralgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neuropathy peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parosmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sciatica	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Tension headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vertigo	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Psychiatric disorders						
ANY EVENT	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Depressive symptom	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dysphoria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Insomnia	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Irritability	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sleep disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Renal and urinary disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bladder malposition acquired	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Micturition disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urge incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urinary incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	3/16 (18.8%)	1/16 (6.3%)	5/16 (31.3%)
Breast discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Breast disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast engorgement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast fibrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Cervical polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cervicitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysmenorrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibrocystic breast disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital discharge	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Genital haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital pruritus female	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hot flush	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Menopausal symptoms	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nipple pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)
Uterine malposition	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginal candidiasis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulval oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvovaginal discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Asthma	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Cough	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Pharyngolaryngeal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharynx discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Productive cough	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinorrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Upper respiratory tract inflammation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Acne	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Body tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cheilitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermal cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis contact	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dry skin	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eczema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Eczema asteatotic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Erythema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Excoriation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Face oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperkeratosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pruritus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash papular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash pustular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin papilloma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urticaria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Surgical and medical procedures						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail avulsion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vascular disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Atherosclerosis obliterans	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure fluctuation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deep vein thrombosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypertension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypotension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral vascular disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	15/57 (26.3%)	7/57 (12.3%)	4/57 (7.0%)	7/57 (12.3%)	9/57 (15.8%)	42/57 (73.7%)
Blood and lymphatic system disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypochromic anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cardiac disorders						
ANY EVENT	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Angina pectoris	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Arrhythmia	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Palpitations	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Supraventricular extrasystoles	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Ear and labyrinth disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Deafness	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Meniere's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinnitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endocrine disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Goitre	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thyroid cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thyroiditis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abnormal sensation in eye	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Asthenopia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blepharitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctival haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Corneal dystrophy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eye pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lacrimation increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Open angle glaucoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periorbital haematoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pterygium	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinal detachment	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vitreous floaters	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	6/57 (10.5%)	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	9/57 (15.8%)
Abdominal distension	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abdominal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal pain lower	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal pain upper	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Abdominal rigidity	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anorectal disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Constipation	4/57 (7.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Diarrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dyspepsia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epigastric discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric ulcer	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis atrophic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastroenteritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal upset	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Glossitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Haemorrhoids	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intestinal ischaemia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Intestinal obstruction	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Irritable bowel syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lip dry	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nausea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pancreatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Reflux oesophagitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Stomach discomfort	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Stomatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tongue ulceration	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Toothache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vomiting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Chest discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chest pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fatigue	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Feeling cold	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling hot	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Malaise	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Oedema peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thirst	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hepatobiliary disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cholecystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic function abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Immune system disorders						
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Dermatitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Seasonal allergy	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	14/57 (24.6%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	15/57 (26.3%)
Bronchiolitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis acute	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Chronic sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis acute	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Groin abscess	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes simplex	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes zoster	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Laryngopharyngitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nasopharyngitis	8/57 (14.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	8/57 (14.0%)
Otitis media	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pharyngitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tinea pedis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tonsillitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Upper respiratory tract infection	4/57 (7.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Injury, poisoning and procedural complications						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Arthropod sting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Contusion	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Haemarthrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Open wound	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	5/57 (8.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	7/57 (12.3%)
Blood glucose increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone increased	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood triglycerides increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gamma-glutamyltransferase increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Lipids increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Liver function test abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Low density lipoprotein increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Protein urine present	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Smear cervix abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Sputum test	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Urine output decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Weight increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
White blood cell count decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metabolism and nutrition disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Anorexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Diabetes mellitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypercholesterolaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperlipidaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	10/57 (17.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	11/57 (19.3%)
Arthralgia	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Arthritis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Back pain	6/57 (10.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	6/57 (10.5%)
Buttock pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Joint swelling	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Limb discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Localised osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle cramp	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle rigidity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Musculoskeletal stiffness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Myalgia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck, shoulder and arm syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nodal osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pain in extremity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Radius fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rib fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sensation of heaviness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Spondylosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tenosynovitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric cancer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lipoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metastases to lymph nodes	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	5/57 (8.8%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	7/57 (12.3%)
Autonomic nervous system imbalance	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dizziness	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Dysgeusia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Facial nerve disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Headache	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hypoaesthesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intercostal neuralgia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Neuropathy peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parosmia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sciatica	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tension headache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vertigo	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Psychiatric disorders						
ANY EVENT	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Depressive symptom	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysphoria	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Insomnia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Irritability	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sleep disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Renal and urinary disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bladder malposition acquired	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Micturition disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urge incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urinary incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	3/57 (5.3%)	3/57 (5.3%)	2/57 (3.5%)	7/57 (12.3%)	9/57 (15.8%)	24/57 (42.1%)
Breast discomfort	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	4/57 (7.0%)	3/57 (5.3%)	8/57 (14.0%)
Breast disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast engorgement	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)	1/57 (1.8%)	3/57 (5.3%)
Breast fibrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)	2/57 (3.5%)
Cervical polyp	0/57 (0.0%)	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Cervicitis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dysmenorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibrocystic breast disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Genital discharge	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)	4/57 (7.0%)	6/57 (10.5%)
Genital haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Genital pruritus female	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Hot flush	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Menopausal symptoms	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nipple pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Uterine malposition	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vaginal candidiasis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Vulval oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvovaginal discomfort	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	5/57 (8.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Asthma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cough	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Pharyngolaryngeal pain	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Pharynx discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Productive cough	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Upper respiratory tract inflammation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	7/57 (12.3%)	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	10/57 (17.5%)
Acne	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Body tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cheilitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermal cyst	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis contact	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dry skin	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eczema	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Eczema asteatotic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Erythema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Excoriation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Face oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperkeratosis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nail disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pruritus	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash papular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash pustular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin papilloma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urticaria	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Surgical and medical procedures						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nail avulsion	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vascular disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Atherosclerosis obliterans	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure fluctuation	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Deep vein thrombosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypertension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypotension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Peripheral vascular disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	7/40 (17.5%)	4/40 (10.0%)	7/40 (17.5%)	3/40 (7.5%)	8/40 (20.0%)	29/40 (72.5%)
Blood and lymphatic system disorders						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypochromic anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cardiac disorders						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Angina pectoris	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Arrhythmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Palpitations	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Supraventricular extrasystoles	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Deafness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Meniere's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinnitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endocrine disorders						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Goitre	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroid cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroiditis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	5/40 (12.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Abnormal sensation in eye	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Asthenopia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blepharitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctival haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Corneal dystrophy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eye pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Lacrimation increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open angle glaucoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periorbital haematoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pterygium	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Retinal detachment	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vitreous floaters	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	5/40 (12.5%)	2/40 (5.0%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	9/40 (22.5%)
Abdominal distension	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain lower	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain upper	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Abdominal rigidity	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anorectal disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Constipation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diarrhoea	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Dyspepsia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epigastric discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastritis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastritis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastroenteritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastrointestinal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastrointestinal upset	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glossitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Haemorrhoids	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intestinal ischaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Intestinal obstruction	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Irritable bowel syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lip dry	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nausea	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pancreatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Reflux oesophagitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Stomach discomfort	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Stomatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tongue ulceration	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Toothache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vomiting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	5/40 (12.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Chest discomfort	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chest pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fatigue	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling cold	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling hot	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Malaise	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Oedema peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thirst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatobiliary disorders						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Cholecystitis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatic function abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Immune system disorders						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Dermatitis allergic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis allergic	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Seasonal allergy	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	11/40 (27.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Bronchiolitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chronic sinusitis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Cystitis	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Cystitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Groin abscess	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes simplex	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes zoster	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Laryngopharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nasopharyngitis	5/40 (12.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Otitis media	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinea pedis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tonsillitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Upper respiratory tract infection	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Injury, poisoning and procedural complications						
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Arthropod sting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Contusion	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Haemarthrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open wound	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	3/40 (7.5%)	2/40 (5.0%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	7/40 (17.5%)
Blood glucose increased	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Blood pressure decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure increased	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood thyroid stimulating hormone decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood thyroid stimulating hormone increased	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood triglycerides increased	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gamma-glutamyltransferase increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipids increased	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Liver function test abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Low density lipoprotein increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Protein urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Smear cervix abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sputum test	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urine output decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Weight increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
White blood cell count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metabolism and nutrition disorders						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Anorexia	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diabetes mellitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypercholesterolaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperlipidaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	11/40 (27.5%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	12/40 (30.0%)
Arthralgia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Arthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Back pain	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Buttock pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint swelling	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Limb discomfort	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Localised osteoarthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Muscle cramp	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle rigidity	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Musculoskeletal stiffness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Myalgia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Neck pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neck, shoulder and arm syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nodal osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pain in extremity	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Radius fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rib fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sensation of heaviness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Spondylosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tenosynovitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric cancer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metastases to lymph nodes	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	6/40 (15.0%)	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	9/40 (22.5%)
Autonomic nervous system imbalance	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dizziness	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Dysgeusia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Facial nerve disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Headache	3/40 (7.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Hypoaesthesia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intercostal neuralgia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neuropathy peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parosmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sciatica	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tension headache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vertigo	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Psychiatric disorders						
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Depressive symptom	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysphoria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Insomnia	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Irritability	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sleep disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Renal and urinary disorders						
ANY EVENT	1/40 (2.5%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Bladder malposition acquired	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysuria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Micturition disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urge incontinence	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Urinary incontinence	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	6/40 (15.0%)	3/40 (7.5%)	8/40 (20.0%)	18/40 (45.0%)
Breast discomfort	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)	2/40 (5.0%)	3/40 (7.5%)	9/40 (22.5%)
Breast disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast engorgement	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Breast fibrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast pain	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Cervical polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cervicitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysmenorrhoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibrocystic breast disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Genital discharge	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)	0/40 (0.0%)	1/40 (2.5%)	4/40 (10.0%)
Genital haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Genital pruritus female	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hot flush	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Menopausal symptoms	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nipple pain	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	4/40 (10.0%)	6/40 (15.0%)
Uterine malposition	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vaginal candidiasis	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Vulval oedema	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vulvitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulvovaginal discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Asthma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngolaryngeal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharynx discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Productive cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinorrhoea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Upper respiratory tract inflammation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	3/40 (7.5%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Acne	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Body tinea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cheilitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermal cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis contact	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dry skin	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eczema	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Eczema asteatotic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Erythema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Excoriation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Face oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperkeratosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Nail disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pruritus	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash papular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rash pustular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin papilloma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urticaria	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Surgical and medical procedures						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail avulsion	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vascular disorders						
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Atherosclerosis obliterans	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure fluctuation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Deep vein thrombosis	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypertension	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypotension	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral vascular disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	24/117 (20.5%)	12/117 (10.3%)	10/117 (8.5%)	20/117 (17.1%)	36/117 (30.8%)	102/117 (87.2%)
Blood and lymphatic system disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Anaemia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Hypochromic anaemia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cardiac disorders						
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Angina pectoris	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arrhythmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Palpitations	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Supraventricular extrasystoles	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Deafness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Meniere's disease	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tinnitus	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Endocrine disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Goitre	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thyroid cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thyroiditis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Abnormal sensation in eye	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Asthenopia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blepharitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Conjunctival haemorrhage	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Conjunctivitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Corneal dystrophy	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eye pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lacrimation increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open angle glaucoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Periorbital haematoma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pterygium	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinal detachment	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vitreous floaters	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	13/117 (11.1%)	5/117 (4.3%)	5/117 (4.3%)	3/117 (2.6%)	1/117 (0.9%)	27/117 (23.1%)
Abdominal distension	0/117 (0.0%)	1/117 (0.9%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Abdominal pain	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Abdominal pain lower	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	3/117 (2.6%)	0/117 (0.0%)	5/117 (4.3%)
Abdominal pain upper	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Abdominal rigidity	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Anorectal disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Constipation	4/117 (3.4%)	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	7/117 (6.0%)
Diarrhoea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dyspepsia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Epigastric discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastric ulcer	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastritis	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Gastritis atrophic	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastroenteritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastrointestinal pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastrointestinal upset	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Glossitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Haemorrhoids	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal ischaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal obstruction	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Irritable bowel syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lip dry	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nausea	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pancreatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Reflux oesophagitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomach discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tongue ulceration	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Toothache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vomiting	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	4/117 (3.4%)	3/117 (2.6%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	8/117 (6.8%)
Chest discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Chest pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fatigue	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling cold	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling hot	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Malaise	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Oedema	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Oedema peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thirst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cholecystitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic function abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Immune system disorders						
ANY EVENT	6/117 (5.1%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Dermatitis allergic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinitis allergic	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Seasonal allergy	5/117 (4.3%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	26/117 (22.2%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	28/117 (23.9%)
Bronchiolitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chronic sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cystitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cystitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Groin abscess	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Herpes simplex	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Herpes zoster	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Laryngopharyngitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nasopharyngitis	15/117 (12.8%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	16/117 (13.7%)
Otitis media	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pharyngitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tinea pedis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tonsillitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Upper respiratory tract infection	7/117 (6.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	8/117 (6.8%)
Injury, poisoning and procedural complications						
ANY EVENT	6/117 (5.1%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Arthropod sting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Contusion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Haemarthrosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Injury	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Open wound	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	7/117 (6.0%)	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	13/117 (11.1%)
Blood glucose increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood pressure decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure increased	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Blood thyroid stimulating hormone decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood thyroid stimulating hormone increased	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood triglycerides increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gamma-glutamyltransferase increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lipids increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Liver function test abnormal	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Low density lipoprotein increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Protein urine present	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Smear cervix abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sputum test	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urine output decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Weight increased	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
White blood cell count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Metabolism and nutrition disorders						
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Anorexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Diabetes mellitus	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypercholesterolaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperlipidaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	21/117 (17.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	22/117 (18.8%)
Arthralgia	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Arthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Back pain	12/117 (10.3%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	12/117 (10.3%)
Buttock pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Joint swelling	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Limb discomfort	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Localised osteoarthritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Muscle cramp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle rigidity	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Musculoskeletal stiffness	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Myalgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neck pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck, shoulder and arm syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nodal osteoarthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pain in extremity	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Radius fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rib fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sensation of heaviness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Spondylosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tenosynovitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastric cancer	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lipoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Metastases to lymph nodes	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	5/117 (4.3%)	5/117 (4.3%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	10/117 (8.5%)
Autonomic nervous system imbalance	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dizziness	1/117 (0.9%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Dysgeusia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Facial nerve disorder	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Headache	4/117 (3.4%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Hypoaesthesia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intercostal neuralgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neuropathy peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parosmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sciatica	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tension headache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vertigo	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Psychiatric disorders						
ANY EVENT	7/117 (6.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	8/117 (6.8%)
Depressive symptom	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysphoria	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Insomnia	5/117 (4.3%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Irritability	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Sleep disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Renal and urinary disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Bladder malposition acquired	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysuria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Micturition disorder	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urge incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urinary incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	2/117 (1.7%)	2/117 (1.7%)	10/117 (8.5%)	19/117 (16.2%)	35/117 (29.9%)	68/117 (58.1%)
Breast discomfort	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	5/117 (4.3%)	18/117 (15.4%)	26/117 (22.2%)
Breast disorder	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Breast engorgement	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	1/117 (0.9%)	4/117 (3.4%)
Breast fibrosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Breast pain	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)	7/117 (6.0%)	7/117 (6.0%)	19/117 (16.2%)
Cervical polyp	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Cervicitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysmenorrhoea	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fibrocystic breast disease	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Genital discharge	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	3/117 (2.6%)	8/117 (6.8%)	14/117 (12.0%)
Genital haemorrhage	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	16/117 (13.7%)	19/117 (16.2%)
Genital pruritus female	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)	2/117 (1.7%)
Hot flush	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Menopausal symptoms	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nipple pain	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	6/117 (5.1%)	8/117 (6.8%)
Uterine malposition	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vaginal candidiasis	4/117 (3.4%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Vulval oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulvitis	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vulvovaginal discomfort	0/117 (0.0%)	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	10/117 (8.5%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	10/117 (8.5%)
Asthma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cough	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Pharyngolaryngeal pain	6/117 (5.1%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Pharynx discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Productive cough	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Rhinorrhoea	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Upper respiratory tract inflammation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	17/117 (14.5%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	19/117 (16.2%)
Acne	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Body tinea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cheilitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermal cyst	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis contact	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dry skin	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eczema	3/117 (2.6%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Eczema asteatotic	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Erythema	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Excoriation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Face oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperkeratosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nail disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pruritus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Rash	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Rash papular	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rash pustular	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin papilloma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urticaria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Surgical and medical procedures						
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail avulsion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vascular disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Atherosclerosis obliterans	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure fluctuation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Deep vein thrombosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypertension	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypotension	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Peripheral vascular disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
ANY EVENT	85/309 (27.5%)	39/309 (12.6%)	26/309 (8.4%)	36/309 (11.7%)	63/309 (20.4%)	249/309 (80.6%)
Blood and lymphatic system disorders						
ANY EVENT	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	3/309 (1.0%)
Anaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Hypochromic anaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cardiac disorders						
ANY EVENT	5/309 (1.6%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Angina pectoris	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Arrhythmia	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Palpitations	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Supraventricular extrasystoles	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Ear and labyrinth disorders						
ANY EVENT	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Deafness	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Meniere's disease	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tinnitus	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Endocrine disorders						
ANY EVENT	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Goitre	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroid cyst	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroiditis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	13/309 (4.2%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	13/309 (4.2%)
Abnormal sensation in eye	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Asthenopia	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Blepharitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctival haemorrhage	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctivitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Corneal dystrophy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eye pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lacrimation increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open angle glaucoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periorbital haematoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pterygium	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinal detachment	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vitreous floaters	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	38/309 (12.3%)	14/309 (4.5%)	11/309 (3.6%)	3/309 (1.0%)	1/309 (0.3%)	67/309 (21.7%)
Abdominal distension	0/309 (0.0%)	2/309 (0.6%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Abdominal pain	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Abdominal pain lower	0/309 (0.0%)	2/309 (0.6%)	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal pain upper	4/309 (1.3%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal rigidity	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Anorectal disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Constipation	9/309 (2.9%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	14/309 (4.5%)
Diarrhoea	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Dyspepsia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epigastric discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastric ulcer	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Gastritis	5/309 (1.6%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Gastritis atrophic	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastroenteritis	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Gastrointestinal pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastrointestinal upset	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Glossitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Haemorrhoids	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Intestinal ischaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Intestinal obstruction	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Irritable bowel syndrome	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lip dry	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nausea	1/309 (0.3%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Pancreatitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Reflux oesophagitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Stomach discomfort	1/309 (0.3%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Stomatitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Tongue ulceration	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Toothache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vomiting	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
General disorders and administration site conditions						
ANY EVENT	17/309 (5.5%)	10/309 (3.2%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	28/309 (9.1%)
Chest discomfort	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Chest pain	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fatigue	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Feeling cold	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Feeling hot	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Malaise	5/309 (1.6%)	2/309 (0.6%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	8/309 (2.6%)
Oedema	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Oedema peripheral	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Thirst	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Hepatobiliary disorders						
ANY EVENT	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Cholecystitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatic function abnormal	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Immune system disorders						
ANY EVENT	15/309 (4.9%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	16/309 (5.2%)
Dermatitis allergic	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Rhinitis allergic	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Seasonal allergy	12/309 (3.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	12/309 (3.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	78/309 (25.2%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	84/309 (27.2%)
Bronchiolitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Bronchitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Bronchitis acute	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Chronic sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cystitis	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Cystitis acute	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Groin abscess	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Herpes simplex	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Herpes zoster	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Laryngopharyngitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nasopharyngitis	47/309 (15.2%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	49/309 (15.9%)
Otitis media	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Pharyngitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Tinea pedis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tonsillitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Upper respiratory tract infection	18/309 (5.8%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	21/309 (6.8%)
Injury, poisoning and procedural complications						
ANY EVENT	9/309 (2.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	9/309 (2.9%)
Arthropod sting	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Contusion	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Haemarthrosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Injury	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Open wound	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	20/309 (6.5%)	11/309 (3.6%)	5/309 (1.6%)	0/309 (0.0%)	1/309 (0.3%)	37/309 (12.0%)
Blood glucose increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood pressure decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood pressure increased	6/309 (1.9%)	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Blood thyroid stimulating hormone decreased	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood thyroid stimulating hormone increased	1/309 (0.3%)	2/309 (0.6%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Blood triglycerides increased	1/309 (0.3%)	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Gamma-glutamyltransferase increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lipids increased	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Liver function test abnormal	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Low density lipoprotein increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Protein urine present	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Smear cervix abnormal	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Sputum test	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urine output decreased	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Weight increased	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
White blood cell count decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Metabolism and nutrition disorders						
ANY EVENT	2/309 (0.6%)	5/309 (1.6%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	9/309 (2.9%)
Anorexia	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Diabetes mellitus	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Hypercholesterolaemia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperlipidaemia	0/309 (0.0%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	57/309 (18.4%)	7/309 (2.3%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	66/309 (21.4%)
Arthralgia	13/309 (4.2%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	13/309 (4.2%)
Arthritis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Back pain	26/309 (8.4%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	28/309 (9.1%)
Buttock pain	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Joint swelling	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Limb discomfort	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Localised osteoarthritis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Muscle cramp	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Muscle rigidity	3/309 (1.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Musculoskeletal stiffness	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Myalgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neck pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neck, shoulder and arm syndrome	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nodal osteoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pain in extremity	7/309 (2.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Radius fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rib fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sensation of heaviness	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Spondylosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tenosynovitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Gastric cancer	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lipoma	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Metastases to lymph nodes	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Nervous system disorders						
ANY EVENT	25/309 (8.1%)	13/309 (4.2%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	38/309 (12.3%)
Autonomic nervous system imbalance	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dizziness	5/309 (1.6%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Dysgeusia	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Facial nerve disorder	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Headache	12/309 (3.9%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	15/309 (4.9%)
Hypoaesthesia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Intercostal neuralgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neuropathy peripheral	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Parosmia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sciatica	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tension headache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vertigo	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Psychiatric disorders						
ANY EVENT	16/309 (5.2%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	20/309 (6.5%)
Depressive symptom	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysphoria	3/309 (1.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Insomnia	10/309 (3.2%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	13/309 (4.2%)
Irritability	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sleep disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Renal and urinary disorders						
ANY EVENT	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Bladder malposition acquired	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysuria	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Micturition disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urge incontinence	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urinary incontinence	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	7/309 (2.3%)	7/309 (2.3%)	21/309 (6.8%)	34/309 (11.0%)	62/309 (20.1%)	131/309 (42.4%)
Breast discomfort	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)	13/309 (4.2%)	28/309 (9.1%)	51/309 (16.5%)
Breast disorder	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Breast engorgement	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	4/309 (1.3%)	2/309 (0.6%)	8/309 (2.6%)
Breast fibrosis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Breast pain	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)	10/309 (3.2%)	12/309 (3.9%)	30/309 (9.7%)
Cervical polyp	0/309 (0.0%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Cervicitis	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dysmenorrhoea	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fibrocystic breast disease	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	2/309 (0.6%)
Genital discharge	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)	7/309 (2.3%)	14/309 (4.5%)	28/309 (9.1%)
Genital haemorrhage	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)	19/309 (6.1%)	23/309 (7.4%)
Genital pruritus female	1/309 (0.3%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	4/309 (1.3%)
Hot flush	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Menopausal symptoms	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Nipple pain	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)	3/309 (1.0%)	12/309 (3.9%)	18/309 (5.8%)
Uterine malposition	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vaginal candidiasis	7/309 (2.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	8/309 (2.6%)
Vulval oedema	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvitis	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvovaginal discomfort	1/309 (0.3%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	21/309 (6.8%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	21/309 (6.8%)
Asthma	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Cough	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Pharyngolaryngeal pain	9/309 (2.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	9/309 (2.9%)
Pharynx discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Productive cough	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinorrhoea	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Upper respiratory tract inflammation	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

(Continued)

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Table 14.3.1.7: Adverse Events - Number (%) of Patients by Relationship to the Drug - 1

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 1 year.	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	35/309 (11.3%)	5/309 (1.6%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	43/309 (13.9%)
Acne	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Body tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cheilitis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dermal cyst	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dermatitis contact	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dry skin	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eczema	10/309 (3.2%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	12/309 (3.9%)
Eczema asteatotic	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Erythema	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Excoriation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Face oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperkeratosis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Nail disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pruritus	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Rash	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Rash papular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rash pustular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin papilloma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urticaria	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Surgical and medical procedures						
ANY EVENT	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nail avulsion	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vascular disorders						
ANY EVENT	3/309 (1.0%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Atherosclerosis obliterans	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood pressure fluctuation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Deep vein thrombosis	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypertension	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypotension	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Peripheral vascular disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0030T)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	8/20 (40.0%)	3/20 (15.0%)	4/20 (20.0%)	1/20 (5.0%)	1/20 (5.0%)	17/20 (85.0%)
Blood and lymphatic system disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypochromic anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Iron deficiency anaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cardiac disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Angina pectoris	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arrhythmia	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Palpitations	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Supraventricular extrasystoles	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deafness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Meniere's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinnitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endocrine disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Goitre	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroid cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thyroiditis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abnormal sensation in eye	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Asthenopia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blepharitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Cataract	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctival haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Conjunctivitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Corneal dystrophy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis eyelid	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eye pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hordeolum	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Keratoconjunctivitis sicca	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lacrimation increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open angle glaucoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periorbital haematoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Posterior capsule opacification	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pterygium	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Retinal detachment	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Retinopathy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vitreous floaters	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	4/20 (20.0%)	2/20 (10.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	7/20 (35.0%)
Abdominal distension	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Abdominal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain lower	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal pain upper	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Abdominal rigidity	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorectal disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Constipation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diarrhoea	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Diverticulum intestinal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Duodenal ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dyspepsia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epigastric discomfort	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastric ulcer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastritis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastritis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastroenteritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastrointestinal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Gastrointestinal upset	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gingivitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glossitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Haemorrhoids	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal ischaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Intestinal obstruction	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritable bowel syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lip dry	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nausea	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pancreatitis	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Parotid gland enlargement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periodontal disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Periodontitis	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Reflux oesophagitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Stomach discomfort	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Stomatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Tongue ulceration	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vomiting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
General disorders and administration site conditions						
ANY EVENT	2/20 (10.0%)	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	5/20 (25.0%)
Asthenia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Axillary pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chest pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Feeling cold	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Feeling hot	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Malaise	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Oedema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Oedema peripheral	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pyrexia	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Thirst	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hepatobiliary disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cholecystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic function abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatitis B	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatitis C	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Immune system disorders						
ANY EVENT	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	3/20 (15.0%)
Allergy to plants	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
House dust allergy	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis allergic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Seasonal allergy	3/20 (15.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	3/20 (15.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	11/20 (55.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	12/20 (60.0%)
Bronchiolitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Bronchitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chronic sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cystitis acute	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dental caries	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Groin abscess	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes dermatitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Herpes simplex	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Herpes zoster	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Influenza	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Laryngopharyngitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nasopharyngitis	8/20 (40.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	8/20 (40.0%)
Otitis media	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Otitis media chronic	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Paronychia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pneumonia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sinusitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tinea pedis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tonsillitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract infection	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Animal bite	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Arthropod sting	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Contusion	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Haemarthrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypothermia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Mouth injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Open wound	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin injury	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	4/20 (20.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	5/20 (25.0%)
Activated partial thromboplastin time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Antithrombin III decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood bilirubin increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood creatinine increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood fibrinogen decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood glucose increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure increased	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Blood thyroid stimulating hormone decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood thyroid stimulating hormone increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood triglycerides increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Coagulation time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eosinophil count increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eosinophil percentage increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gamma-glutamyltransferase increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Glucose urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipids increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Liver function test abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Low density lipoprotein increased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lymphocyte percentage decreased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Neutrophil percentage increased	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Platelet count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Protein urine present	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Prothrombin time prolonged	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Smear cervix abnormal	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sputum test	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urine output decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Weight increased	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
White blood cell count decreased	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Anorexia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Decreased appetite	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Diabetes mellitus	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypercholesterolaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperlipidaemia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	3/20 (15.0%)	2/20 (10.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	6/20 (30.0%)
Arthralgia	2/20 (10.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	3/20 (15.0%)
Arthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Back pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Buttock pain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Foot fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hand fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint sprain	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Joint swelling	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Limb discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Localised osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Monoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle cramp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle fatigue	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Muscle rigidity	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Muscle twitching	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Musculoskeletal stiffness	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Myalgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neck pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Neck, shoulder and arm syndrome	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nodal osteoarthritis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pain in extremity	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Radius fracture	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Rib fracture	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Sensation of heaviness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Spondylosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tenosynovitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Thoracic vertebral fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Traumatic fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Wrist fracture	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Colonic polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibroadenoma of breast	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibroma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Gastric cancer	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hepatic cancer metastatic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Lipoma	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Metastases to lymph nodes	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Ovarian neoplasm	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nervous system disorders						
ANY EVENT	2/20 (10.0%)	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	4/20 (20.0%)
Autonomic nervous system imbalance	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Depressed level of consciousness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dizziness	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Dizziness postural	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysgeusia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Facial nerve disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Headache	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hypoaesthesia	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Intercostal neuralgia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neuropathy peripheral	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parkinson's disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Parosmia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sciatica	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Tension headache	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vertigo	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Amnesia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depression	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Depressive symptom	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysphoria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Insomnia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Irritability	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Neurosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Sleep disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Renal and urinary disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Bladder malposition acquired	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Micturition disorder	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Nocturia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pollakiuria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urge incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Urinary incontinence	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	1/20 (5.0%)	0/20 (0.0%)	3/20 (15.0%)	1/20 (5.0%)	1/20 (5.0%)	6/20 (30.0%)
Breast discomfort	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	1/20 (5.0%)	0/20 (0.0%)	2/20 (10.0%)
Breast disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast engorgement	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast fibrosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast hyperplasia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Breast pain	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)	0/20 (0.0%)	1/20 (5.0%)	3/20 (15.0%)
Cervical polyp	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cervicitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dysmenorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Endometrial hyperplasia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Fibrocystic breast disease	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital discharge	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	1/20 (5.0%)	2/20 (10.0%)
Genital haemorrhage	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital pruritus female	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Genital rash	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Hot flush	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Menopausal symptoms	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Nipple pain	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Uterine leiomyoma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Uterine malposition	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginal candidiasis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vaginitis atrophic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulval oedema	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Vulvovaginal discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	2/20 (10.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	2/20 (10.0%)
Asthma	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dyspnoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Epistaxis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pharyngolaryngeal pain	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Pharynx discomfort	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Productive cough	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rhinitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Rhinorrhoea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Upper respiratory tract inflammation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	3/20 (15.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	4/20 (20.0%)
Acne	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Body tinea	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Cheilitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermal cyst	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dermatitis	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Dermatitis contact	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Dry skin	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Eczema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Eczema asteatotic	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Erythema	0/20 (0.0%)	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Excoriation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Face oedema	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Folliculitis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hyperkeratosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Milia	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Pruritus	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Rash	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash papular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Rash pustular	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Skin papilloma	1/20 (5.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	1/20 (5.0%)
Urticaria	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Surgical and medical procedures						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Nail avulsion	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Atherosclerosis obliterans	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Blood pressure fluctuation	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Chillblains	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Deep vein thrombosis	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypertension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Hypotension	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral coldness	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)
Peripheral vascular disorder	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)	0/20 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	12/59 (20.3%)	7/59 (11.9%)	8/59 (13.6%)	6/59 (10.2%)	20/59 (33.9%)	53/59 (89.8%)
Blood and lymphatic system disorders						
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Anaemia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Hypochromic anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Iron deficiency anaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cardiac disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Angina pectoris	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arrhythmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Palpitations	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Supraventricular extrasystoles	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Deafness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Meniere's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tinnitus	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Endocrine disorders						
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Goitre	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Thyroid cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thyroiditis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Abnormal sensation in eye	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Asthenopia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blepharitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cataract	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Conjunctival haemorrhage	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Conjunctivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Corneal dystrophy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis eyelid	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eye pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hordeolum	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Keratoconjunctivitis sicca	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lacrimation increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Open angle glaucoma	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Periorbital haematoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Posterior capsule opacification	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pterygium	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinal detachment	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Retinopathy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vitreous floaters	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	11/59 (18.6%)	6/59 (10.2%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	17/59 (28.8%)
Abdominal distension	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Abdominal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain lower	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Abdominal pain upper	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Abdominal rigidity	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Anorectal disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Constipation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diarrhoea	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diverticulum intestinal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Duodenal ulcer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspepsia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epigastric discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric ulcer	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gastritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastritis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastroenteritis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Gastrointestinal pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastrointestinal upset	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gingivitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Glossitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Haemorrhoids	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Intestinal ischaemia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Intestinal obstruction	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Irritable bowel syndrome	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lip dry	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nausea	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pancreatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Parotid gland enlargement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Periodontal disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Periodontitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Reflux oesophagitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomach discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Stomatitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tongue ulceration	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vomiting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
General disorders and administration site conditions						
ANY EVENT	6/59 (10.2%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	9/59 (15.3%)
Asthenia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Axillary pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chest pain	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fatigue	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Feeling cold	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Feeling hot	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Malaise	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	4/59 (6.8%)
Oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Oedema peripheral	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pyrexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Thirst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/59 (0.0%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Cholecystitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic function abnormal	0/59 (0.0%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Hepatitis B	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatitis C	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Immune system disorders						
ANY EVENT	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Allergy to plants	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dermatitis allergic	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
House dust allergy	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinitis allergic	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Seasonal allergy	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	24/59 (40.7%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	26/59 (44.1%)
Bronchiolitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Bronchitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bronchitis acute	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Chronic sinusitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cystitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Cystitis acute	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dental caries	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Groin abscess	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes dermatitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Herpes simplex	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Herpes zoster	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Influenza	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Laryngopharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nasopharyngitis	19/59 (32.2%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	20/59 (33.9%)
Otitis media	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Otitis media chronic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Paronychia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pharyngitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pneumonia	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sinusitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tinea pedis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tonsillitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract infection	2/59 (3.4%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Animal bite	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Arthropod sting	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Contusion	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Haemarthrosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypothermia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Mouth injury	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Open wound	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin injury	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	6/59 (10.2%)	4/59 (6.8%)	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	14/59 (23.7%)
Activated partial thromboplastin time prolonged	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Antithrombin III decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood bilirubin increased	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood creatinine increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood fibrinogen decreased	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blood glucose increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure increased	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Blood thyroid stimulating hormone decreased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Blood thyroid stimulating hormone increased	1/59 (1.7%)	1/59 (1.7%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Blood triglycerides increased	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Coagulation time prolonged	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eosinophil count increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Eosinophil percentage increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Gamma-glutamyltransferase increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Glucose urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipids increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Liver function test abnormal	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Low density lipoprotein increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lymphocyte percentage decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neutrophil percentage increased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Platelet count decreased	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Protein urine present	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Prothrombin time prolonged	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Smear cervix abnormal	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Sputum test	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urine output decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Weight increased	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
White blood cell count decreased	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	1/59 (1.7%)	2/59 (3.4%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	5/59 (8.5%)
Anorexia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Decreased appetite	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Diabetes mellitus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)
Hypercholesterolaemia	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Hyperlipidaemia	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	14/59 (23.7%)	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	18/59 (30.5%)
Arthralgia	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Arthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Back pain	7/59 (11.9%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	9/59 (15.3%)
Buttock pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Foot fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hand fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint sprain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Joint swelling	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Limb discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Localised osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Monoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle cramp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle fatigue	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Muscle rigidity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Muscle twitching	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Musculoskeletal stiffness	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Myalgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neck, shoulder and arm syndrome	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nodal osteoarthritis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pain in extremity	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Radius fracture	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Rib fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sensation of heaviness	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Spondylosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Tenosynovitis	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Thoracic vertebral fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Traumatic fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Wrist fracture	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Colonic polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibroadenoma of breast	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibroma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Gastric cancer	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hepatic cancer metastatic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Lipoma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Metastases to lymph nodes	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Ovarian neoplasm	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nervous system disorders						
ANY EVENT	6/59 (10.2%)	4/59 (6.8%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	10/59 (16.9%)
Autonomic nervous system imbalance	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Depressed level of consciousness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dizziness	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dizziness postural	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysgeusia	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Facial nerve disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Headache	2/59 (3.4%)	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	4/59 (6.8%)
Hypoaesthesia	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Intercostal neuralgia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neuropathy peripheral	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Parkinson's disease	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Parosmia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sciatica	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Tension headache	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vertigo	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	4/59 (6.8%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Amnesia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Depression	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Depressive symptom	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysphoria	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Insomnia	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Irritability	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Neurosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Sleep disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Renal and urinary disorders						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Bladder malposition acquired	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dysuria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Micturition disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nocturia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pollakiuria	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Urge incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urinary incontinence	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	2/59 (3.4%)	1/59 (1.7%)	5/59 (8.5%)	6/59 (10.2%)	20/59 (33.9%)	34/59 (57.6%)
Breast discomfort	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)	3/59 (5.1%)	13/59 (22.0%)	19/59 (32.2%)
Breast disorder	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	2/59 (3.4%)
Breast engorgement	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast fibrosis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Breast hyperplasia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Breast pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)	5/59 (8.5%)	7/59 (11.9%)
Cervical polyp	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cervicitis	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Dysmenorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Endometrial hyperplasia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Fibrocystic breast disease	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Genital discharge	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)	3/59 (5.1%)	6/59 (10.2%)
Genital haemorrhage	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	1/59 (1.7%)	6/59 (10.2%)	8/59 (13.6%)
Genital pruritus female	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Genital rash	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hot flush	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Menopausal symptoms	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nipple pain	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	4/59 (6.8%)	5/59 (8.5%)
Uterine leiomyoma	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Uterine malposition	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Vaginal candidiasis	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Vaginitis atrophic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulval oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Vulvovaginal discomfort	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	4/59 (6.8%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	5/59 (8.5%)
Asthma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dyspnoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Epistaxis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Pharyngolaryngeal pain	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Pharynx discomfort	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Productive cough	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rhinorrhoea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Upper respiratory tract inflammation	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	8/59 (13.6%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	9/59 (15.3%)
Acne	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Body tinea	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Cheilitis	1/59 (1.7%)	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dermal cyst	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Dermatitis contact	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Dry skin	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Eczema	3/59 (5.1%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	3/59 (5.1%)
Eczema asteatotic	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Erythema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Excoriation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Face oedema	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Folliculitis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hyperkeratosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Milia	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Nail disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Pruritus	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Rash	2/59 (3.4%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	2/59 (3.4%)
Rash papular	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Rash pustular	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Skin papilloma	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Urticaria	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Surgical and medical procedures						
ANY EVENT	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)
Nail avulsion	1/59 (1.7%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	1/59 (1.7%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Placebo(E2/LNG)

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Atherosclerosis obliterans	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Blood pressure fluctuation	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Chillblains	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Deep vein thrombosis	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypertension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Hypotension	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral coldness	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)
Peripheral vascular disorder	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)	0/59 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	5/16 (31.3%)	3/16 (18.8%)	1/16 (6.3%)	4/16 (25.0%)	1/16 (6.3%)	14/16 (87.5%)
Blood and lymphatic system disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypochromic anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Iron deficiency anaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cardiac disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Angina pectoris	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arrhythmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Palpitations	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Supraventricular extrasystoles	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deafness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Meniere's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinnitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endocrine disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Goitre	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thyroid cyst	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Thyroiditis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Abnormal sensation in eye	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Asthenopia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blepharitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cataract	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctival haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Conjunctivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Corneal dystrophy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis eyelid	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eye pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hordeolum	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Keratoconjunctivitis sicca	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lacrimation increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open angle glaucoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periorbital haematoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Posterior capsule opacification	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pterygium	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinal detachment	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Retinopathy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vitreous floaters	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	7/16 (43.8%)	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	9/16 (56.3%)
Abdominal distension	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain lower	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Abdominal pain upper	2/16 (12.5%)	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Abdominal rigidity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Anorectal disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Constipation	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Diarrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Diverticulum intestinal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Duodenal ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dyspepsia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Epigastric discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric ulcer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastritis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastroenteritis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Gastrointestinal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastrointestinal upset	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gingivitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glossitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Haemorrhoids	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal ischaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intestinal obstruction	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Irritable bowel syndrome	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Lip dry	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nausea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pancreatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parotid gland enlargement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periodontal disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Periodontitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Reflux oesophagitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Stomach discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Stomatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tongue ulceration	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vomiting	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
General disorders and administration site conditions						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Asthenia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Axillary pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chest pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling cold	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Feeling hot	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Malaise	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Oedema	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Oedema peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pyrexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thirst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cholecystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic function abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatitis B	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatitis C	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Immune system disorders						
ANY EVENT	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Allergy to plants	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis allergic	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
House dust allergy	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinitis allergic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Seasonal allergy	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	7/16 (43.8%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	7/16 (43.8%)
Bronchiolitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bronchitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chronic sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cystitis acute	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dental caries	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Groin abscess	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes simplex	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Herpes zoster	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Influenza	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Laryngopharyngitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nasopharyngitis	4/16 (25.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	4/16 (25.0%)
Otitis media	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Otitis media chronic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Paronychia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Pneumonia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sinusitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tinea pedis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tonsillitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Upper respiratory tract infection	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Animal bite	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Arthropod sting	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Contusion	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Haemarthrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypothermia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Mouth injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Open wound	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin injury	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	3/16 (18.8%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	4/16 (25.0%)
Activated partial thromboplastin time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Antithrombin III decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood bilirubin increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood creatinine increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood fibrinogen decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood glucose increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood pressure increased	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Blood thyroid stimulating hormone decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood thyroid stimulating hormone increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood triglycerides increased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Coagulation time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eosinophil count increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eosinophil percentage increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gamma-glutamyltransferase increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Glucose urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipids increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Liver function test abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Low density lipoprotein increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lymphocyte percentage decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neutrophil percentage increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Platelet count decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Protein urine present	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Prothrombin time prolonged	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Smear cervix abnormal	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sputum test	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urine output decreased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Weight increased	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
White blood cell count decreased	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Anorexia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Decreased appetite	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Diabetes mellitus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypercholesterolaemia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperlipidaemia	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	4/16 (25.0%)	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	7/16 (43.8%)
Arthralgia	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Arthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Back pain	2/16 (12.5%)	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	4/16 (25.0%)
Buttock pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Foot fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hand fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint sprain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Joint swelling	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Limb discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Localised osteoarthritis	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Monoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle cramp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle fatigue	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Muscle rigidity	0/16 (0.0%)	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Muscle twitching	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Musculoskeletal stiffness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Myalgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neck, shoulder and arm syndrome	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nodal osteoarthritis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pain in extremity	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Radius fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rib fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sensation of heaviness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Spondylosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Tenosynovitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Thoracic vertebral fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Traumatic fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Wrist fracture	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Colonic polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibroadenoma of breast	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibroma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Gastric cancer	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hepatic cancer metastatic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Lipoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Metastases to lymph nodes	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Ovarian neoplasm	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nervous system disorders						
ANY EVENT	4/16 (25.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	5/16 (31.3%)
Autonomic nervous system imbalance	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depressed level of consciousness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dizziness	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Dizziness postural	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysgeusia	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Facial nerve disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Hypoaesthesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Intercostal neuralgia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neuropathy peripheral	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parkinson's disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Parosmia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sciatica	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Tension headache	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vertigo	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Amnesia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depression	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Depressive symptom	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dysphoria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Insomnia	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Irritability	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Neurosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Sleep disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Renal and urinary disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Bladder malposition acquired	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Micturition disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nocturia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pollakiuria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urge incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urinary incontinence	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)	4/16 (25.0%)	1/16 (6.3%)	7/16 (43.8%)
Breast discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	0/16 (0.0%)	1/16 (6.3%)
Breast disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast engorgement	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast fibrosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast hyperplasia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Breast pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)	0/16 (0.0%)	2/16 (12.5%)
Cervical polyp	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cervicitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dysmenorrhoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Endometrial hyperplasia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Fibrocystic breast disease	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital discharge	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	2/16 (12.5%)
Genital haemorrhage	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital pruritus female	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Genital rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hot flush	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Menopausal symptoms	1/16 (6.3%)	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	2/16 (12.5%)
Nipple pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)	1/16 (6.3%)
Uterine leiomyoma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Uterine malposition	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginal candidiasis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vaginitis atrophic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulval oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Vulvitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Vulvovaginal discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	3/16 (18.8%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	3/16 (18.8%)
Asthma	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Cough	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Dyspnoea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Epistaxis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharyngolaryngeal pain	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pharynx discomfort	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Productive cough	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rhinitis	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Rhinorrhoea	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Upper respiratory tract inflammation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Acne	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Body tinea	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Cheilitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermal cyst	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dermatitis contact	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Dry skin	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Eczema	1/16 (6.3%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	1/16 (6.3%)
Eczema asteatotic	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Erythema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Excoriation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Face oedema	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Folliculitis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hyperkeratosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Milia	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Pruritus	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash papular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Rash pustular	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Skin papilloma	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Urticaria	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Surgical and medical procedures						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Nail avulsion	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Atherosclerosis obliterans	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Blood pressure fluctuation	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Chillblains	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Deep vein thrombosis	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypertension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Hypotension	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral coldness	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)
Peripheral vascular disorder	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)	0/16 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	18/57 (31.6%)	9/57 (15.8%)	5/57 (8.8%)	7/57 (12.3%)	10/57 (17.5%)	49/57 (86.0%)
Blood and lymphatic system disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypochromic anaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Iron deficiency anaemia	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Cardiac disorders						
ANY EVENT	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Angina pectoris	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Arrhythmia	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Palpitations	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Supraventricular extrasystoles	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Ear and labyrinth disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Deafness	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Meniere's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinnitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endocrine disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Goitre	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thyroid cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thyroiditis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abnormal sensation in eye	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Asthenopia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blepharitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cataract	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Conjunctival haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Conjunctivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Corneal dystrophy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis eyelid	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eye pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hordeolum	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Keratoconjunctivitis sicca	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lacrimation increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Open angle glaucoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periorbital haematoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Posterior capsule opacification	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pterygium	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinal detachment	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Retinopathy	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vitreous floaters	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	13/57 (22.8%)	1/57 (1.8%)	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	17/57 (29.8%)
Abdominal distension	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Abdominal pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abdominal pain lower	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Abdominal pain upper	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Abdominal rigidity	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Anorectal disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Constipation	6/57 (10.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	7/57 (12.3%)
Diarrhoea	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Diverticulum intestinal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Duodenal ulcer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dyspepsia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epigastric discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric ulcer	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Gastritis	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Gastritis atrophic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastroenteritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastrointestinal upset	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gingivitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Glossitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Haemorrhoids	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Intestinal ischaemia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Intestinal obstruction	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Irritable bowel syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lip dry	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nausea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pancreatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parotid gland enlargement	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periodontal disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Periodontitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Reflux oesophagitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Stomach discomfort	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Stomatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tongue ulceration	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vomiting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
General disorders and administration site conditions						
ANY EVENT	5/57 (8.8%)	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	7/57 (12.3%)
Asthenia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Axillary pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chest discomfort	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Chest pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fatigue	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling cold	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Feeling hot	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Malaise	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Oedema peripheral	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pyrexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Thirst	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Hepatobiliary disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cholecystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic cyst	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic function abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatitis B	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatitis C	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Immune system disorders						
ANY EVENT	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Allergy to plants	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
House dust allergy	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rhinitis allergic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Seasonal allergy	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	24/57 (42.1%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	25/57 (43.9%)
Bronchiolitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bronchitis acute	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Chronic sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cystitis acute	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dental caries	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Groin abscess	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes simplex	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Herpes zoster	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Influenza	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Laryngopharyngitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nail tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nasopharyngitis	16/57 (28.1%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	16/57 (28.1%)
Otitis media	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Otitis media chronic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Paronychia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pharyngitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Pneumonia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sinusitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tinea pedis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Tonsillitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Upper respiratory tract infection	7/57 (12.3%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	8/57 (14.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Animal bite	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Arthropod sting	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Contusion	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Haemarthrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypothermia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Mouth injury	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Open wound	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin injury	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	6/57 (10.5%)	3/57 (5.3%)	0/57 (0.0%)	2/57 (3.5%)	1/57 (1.8%)	12/57 (21.1%)
Activated partial thromboplastin time prolonged	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Antithrombin III decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood bilirubin increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood creatinine increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood fibrinogen decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood glucose increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood pressure decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure increased	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Blood thyroid stimulating hormone decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood thyroid stimulating hormone increased	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Blood triglycerides increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Coagulation time prolonged	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eosinophil count increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eosinophil percentage increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gamma-glutamyltransferase increased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Glucose urine present	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Lipids increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Liver function test abnormal	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Low density lipoprotein increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lymphocyte percentage decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neutrophil percentage increased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Platelet count decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Protein urine present	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Prothrombin time prolonged	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Smear cervix abnormal	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)	3/57 (5.3%)
Sputum test	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Urine output decreased	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Weight increased	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	2/57 (3.5%)
White blood cell count decreased	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Anorexia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Decreased appetite	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Diabetes mellitus	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypercholesterolaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperlipidaemia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	13/57 (22.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	14/57 (24.6%)
Arthralgia	4/57 (7.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	4/57 (7.0%)
Arthritis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Back pain	6/57 (10.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	6/57 (10.5%)
Buttock pain	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Foot fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hand fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Joint sprain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Joint swelling	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Limb discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Localised osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Monoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle cramp	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle fatigue	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Muscle rigidity	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Muscle twitching	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Musculoskeletal stiffness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Myalgia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neck, shoulder and arm syndrome	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nodal osteoarthritis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pain in extremity	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Radius fracture	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rib fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Sensation of heaviness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Spondylosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tenosynovitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Thoracic vertebral fracture	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Traumatic fracture	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Wrist fracture	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Colonic polyp	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Fibroadenoma of breast	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibroma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Gastric cancer	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hepatic cancer metastatic	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Lipoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Metastases to lymph nodes	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Ovarian neoplasm	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nervous system disorders						
ANY EVENT	8/57 (14.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	10/57 (17.5%)
Autonomic nervous system imbalance	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depressed level of consciousness	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dizziness	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Dizziness postural	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysgeusia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Facial nerve disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Headache	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Hypoaesthesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Intercostal neuralgia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Neuropathy peripheral	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parkinson's disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Parosmia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sciatica	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Tension headache	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vertigo	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	3/57 (5.3%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Amnesia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depression	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Depressive symptom	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysphoria	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Insomnia	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Irritability	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Neurosis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Sleep disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Renal and urinary disorders						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Bladder malposition acquired	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dysuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Micturition disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nocturia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pollakiuria	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urge incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urinary incontinence	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	4/57 (7.0%)	4/57 (7.0%)	3/57 (5.3%)	7/57 (12.3%)	10/57 (17.5%)	28/57 (49.1%)
Breast discomfort	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	4/57 (7.0%)	3/57 (5.3%)	8/57 (14.0%)
Breast disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast engorgement	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)	1/57 (1.8%)	3/57 (5.3%)
Breast fibrosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast hyperplasia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Breast pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	2/57 (3.5%)	3/57 (5.3%)
Cervical polyp	0/57 (0.0%)	4/57 (7.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	4/57 (7.0%)
Cervicitis	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dysmenorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Endometrial hyperplasia	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Fibrocystic breast disease	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Genital discharge	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	2/57 (3.5%)	5/57 (8.8%)	8/57 (14.0%)
Genital haemorrhage	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	0/57 (0.0%)	1/57 (1.8%)
Genital pruritus female	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Genital rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hot flush	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Menopausal symptoms	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Nipple pain	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)	1/57 (1.8%)
Uterine leiomyoma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Uterine malposition	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vaginal candidiasis	2/57 (3.5%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Vaginitis atrophic	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Vulval oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Vulvovaginal discomfort	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	6/57 (10.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	6/57 (10.5%)
Asthma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cough	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Dyspnoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Epistaxis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pharyngolaryngeal pain	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Pharynx discomfort	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Productive cough	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rhinitis	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rhinorrhoea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Upper respiratory tract inflammation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	11/57 (19.3%)	1/57 (1.8%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	14/57 (24.6%)
Acne	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Body tinea	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Cheilitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermal cyst	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Dermatitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dermatitis contact	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Dry skin	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Eczema	3/57 (5.3%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	3/57 (5.3%)
Eczema asteatotic	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Erythema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Excoriation	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Face oedema	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Folliculitis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hyperkeratosis	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Milia	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Nail disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Pruritus	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Rash	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Rash papular	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	1/57 (1.8%)
Rash pustular	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Skin papilloma	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Urticaria	3/57 (5.3%)	0/57 (0.0%)	2/57 (3.5%)	0/57 (0.0%)	0/57 (0.0%)	5/57 (8.8%)
Surgical and medical procedures						
ANY EVENT	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Nail avulsion	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 0.5mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Atherosclerosis obliterans	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Blood pressure fluctuation	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Chillblains	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Deep vein thrombosis	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypertension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Hypotension	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)
Peripheral coldness	1/57 (1.8%)	1/57 (1.8%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	2/57 (3.5%)
Peripheral vascular disorder	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)	0/57 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	7/40 (17.5%)	7/40 (17.5%)	9/40 (22.5%)	4/40 (10.0%)	8/40 (20.0%)	35/40 (87.5%)
Blood and lymphatic system disorders						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypochromic anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Iron deficiency anaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cardiac disorders						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Angina pectoris	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Arrhythmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Palpitations	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Supraventricular extrasystoles	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Deafness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Meniere's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinnitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endocrine disorders						
ANY EVENT	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Goitre	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroid cyst	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thyroiditis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	5/40 (12.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Abnormal sensation in eye	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Asthenopia	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blepharitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cataract	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctival haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Conjunctivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Corneal dystrophy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis eyelid	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eye pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hordeolum	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Keratoconjunctivitis sicca	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lacrimation increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open angle glaucoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periorbital haematoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Posterior capsule opacification	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pterygium	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Retinal detachment	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Retinopathy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vitreous floaters	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	6/40 (15.0%)	3/40 (7.5%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Abdominal distension	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Abdominal pain lower	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Abdominal pain upper	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Abdominal rigidity	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Anorectal disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Constipation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diarrhoea	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Diverticulum intestinal	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Duodenal ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dyspepsia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epigastric discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric ulcer	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastritis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastritis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastroenteritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Gastrointestinal pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastrointestinal upset	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gingivitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glossitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Haemorrhoids	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intestinal ischaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Intestinal obstruction	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Irritable bowel syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lip dry	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nausea	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Pancreatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parotid gland enlargement	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periodontal disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Periodontitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Reflux oesophagitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Stomach discomfort	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Stomatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tongue ulceration	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vomiting	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
General disorders and administration site conditions						
ANY EVENT	6/40 (15.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	6/40 (15.0%)
Asthenia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Axillary pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chest discomfort	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chest pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fatigue	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling cold	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Feeling hot	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Malaise	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Oedema peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pyrexia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Thirst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatobiliary disorders						
ANY EVENT	0/40 (0.0%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Cholecystitis	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatic cyst	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatic function abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hepatitis B	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hepatitis C	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Immune system disorders						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Allergy to plants	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis allergic	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
House dust allergy	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis allergic	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Seasonal allergy	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	16/40 (40.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	16/40 (40.0%)
Bronchiolitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Bronchitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Chronic sinusitis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Cystitis	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Cystitis acute	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dental caries	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Groin abscess	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes simplex	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Herpes zoster	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Influenza	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Laryngopharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail tinea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Nasopharyngitis	9/40 (22.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	9/40 (22.5%)
Otitis media	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Otitis media chronic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Paronychia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pneumonia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sinusitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tinea pedis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tonsillitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Upper respiratory tract infection	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Animal bite	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Arthropod sting	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Contusion	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Haemarthrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypothermia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Mouth injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Open wound	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin injury	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	4/40 (10.0%)	4/40 (10.0%)	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Activated partial thromboplastin time prolonged	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Antithrombin III decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood bilirubin increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood creatinine increased	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Blood fibrinogen decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood glucose increased	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood pressure decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure increased	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Blood thyroid stimulating hormone decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood thyroid stimulating hormone increased	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Blood triglycerides increased	0/40 (0.0%)	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Coagulation time prolonged	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Eosinophil count increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eosinophil percentage increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gamma-glutamyltransferase increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Glucose urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipids increased	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Liver function test abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Low density lipoprotein increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lymphocyte percentage decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neutrophil percentage increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Platelet count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Protein urine present	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Prothrombin time prolonged	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Smear cervix abnormal	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sputum test	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urine output decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Weight increased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
White blood cell count decreased	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Anorexia	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Decreased appetite	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Diabetes mellitus	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hypercholesterolaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperlipidaemia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	13/40 (32.5%)	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	16/40 (40.0%)
Arthralgia	4/40 (10.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Arthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Back pain	5/40 (12.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	6/40 (15.0%)
Buttock pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Foot fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hand fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint sprain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Joint swelling	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Limb discomfort	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Localised osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Monoarthritis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Muscle cramp	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle fatigue	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Muscle rigidity	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Muscle twitching	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Musculoskeletal stiffness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Myalgia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Neck pain	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neck, shoulder and arm syndrome	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nodal osteoarthritis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pain in extremity	4/40 (10.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Radius fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rib fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sensation of heaviness	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Spondylosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tenosynovitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Thoracic vertebral fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Traumatic fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Wrist fracture	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Colonic polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibroadenoma of breast	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Fibroma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Gastric cancer	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hepatic cancer metastatic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Lipoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Metastases to lymph nodes	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Ovarian neoplasm	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Nervous system disorders						
ANY EVENT	8/40 (20.0%)	3/40 (7.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	11/40 (27.5%)
Autonomic nervous system imbalance	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Depressed level of consciousness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dizziness	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Dizziness postural	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysgeusia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Facial nerve disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Headache	3/40 (7.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Hypoaesthesia	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Intercostal neuralgia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neuropathy peripheral	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parkinson's disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Parosmia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sciatica	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Tension headache	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vertigo	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Amnesia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Depression	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Depressive symptom	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysphoria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Insomnia	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Irritability	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Neurosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Sleep disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Renal and urinary disorders						
ANY EVENT	3/40 (7.5%)	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	5/40 (12.5%)
Bladder malposition acquired	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysuria	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Micturition disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nocturia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pollakiuria	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Urge incontinence	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Urinary incontinence	1/40 (2.5%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	0/40 (0.0%)	1/40 (2.5%)	6/40 (15.0%)	4/40 (10.0%)	8/40 (20.0%)	19/40 (47.5%)
Breast discomfort	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)	3/40 (7.5%)	4/40 (10.0%)	11/40 (27.5%)
Breast disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast engorgement	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Breast fibrosis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast hyperplasia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Breast pain	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)	1/40 (2.5%)	0/40 (0.0%)	3/40 (7.5%)
Cervical polyp	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cervicitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dysmenorrhoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Endometrial hyperplasia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	1/40 (2.5%)
Fibrocystic breast disease	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Genital discharge	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)	0/40 (0.0%)	1/40 (2.5%)	4/40 (10.0%)
Genital haemorrhage	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)
Genital pruritus female	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Genital rash	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hot flush	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Menopausal symptoms	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nipple pain	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	1/40 (2.5%)	4/40 (10.0%)	6/40 (15.0%)
Uterine leiomyoma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Uterine malposition	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vaginal candidiasis	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Vaginitis atrophic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulval oedema	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Vulvitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Vulvovaginal discomfort	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Asthma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dyspnoea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Epistaxis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pharyngolaryngeal pain	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Pharynx discomfort	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Productive cough	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rhinorrhoea	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Upper respiratory tract inflammation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	5/40 (12.5%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	6/40 (15.0%)
Acne	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Body tinea	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Cheilitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermal cyst	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Dermatitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dermatitis contact	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Dry skin	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Eczema	2/40 (5.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	3/40 (7.5%)
Eczema asteatotic	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Erythema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Excoriation	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Face oedema	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Folliculitis	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Hyperkeratosis	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Milia	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Pruritus	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Rash papular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Rash pustular	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Skin papilloma	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Urticaria	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Surgical and medical procedures						
ANY EVENT	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Nail avulsion	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	3/40 (7.5%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	4/40 (10.0%)
Atherosclerosis obliterans	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Blood pressure fluctuation	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Chillblains	2/40 (5.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	2/40 (5.0%)
Deep vein thrombosis	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypertension	1/40 (2.5%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	1/40 (2.5%)
Hypotension	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral coldness	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)
Peripheral vascular disorder	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	23/117 (19.7%)	13/117 (11.1%)	13/117 (11.1%)	22/117 (18.8%)	37/117 (31.6%)	108/117 (92.3%)
Blood and lymphatic system disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Anaemia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Hypochromic anaemia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Iron deficiency anaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cardiac disorders						
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Angina pectoris	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arrhythmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Palpitations	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Supraventricular extrasystoles	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Ear and labyrinth disorders						
ANY EVENT	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Deafness	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Meniere's disease	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tinnitus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Endocrine disorders						
ANY EVENT	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Goitre	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thyroid cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thyroiditis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	8/117 (6.8%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	9/117 (7.7%)
Abnormal sensation in eye	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Asthenopia	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Blepharitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cataract	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Conjunctival haemorrhage	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Conjunctivitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Corneal dystrophy	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis eyelid	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eye pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hordeolum	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Keratoconjunctivitis sicca	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lacrimation increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open angle glaucoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Periorbital haematoma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Posterior capsule opacification	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pterygium	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinal detachment	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Retinopathy	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vitreous floaters	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	26/117 (22.2%)	5/117 (4.3%)	6/117 (5.1%)	3/117 (2.6%)	1/117 (0.9%)	41/117 (35.0%)
Abdominal distension	0/117 (0.0%)	1/117 (0.9%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Abdominal pain	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Abdominal pain lower	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	3/117 (2.6%)	0/117 (0.0%)	5/117 (4.3%)
Abdominal pain upper	3/117 (2.6%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Abdominal rigidity	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)
Anorectal disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Constipation	8/117 (6.8%)	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	12/117 (10.3%)
Diarrhoea	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Diverticulum intestinal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Duodenal ulcer	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dyspepsia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Epigastric discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastric ulcer	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastritis	2/117 (1.7%)	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Gastritis atrophic	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastroenteritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastrointestinal pain	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gastrointestinal upset	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gingivitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Glossitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Haemorrhoids	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Intestinal ischaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Intestinal obstruction	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Irritable bowel syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lip dry	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nausea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pancreatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parotid gland enlargement	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Periodontal disease	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Periodontitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Reflux oesophagitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomach discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Stomatitis	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Tongue ulceration	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vomiting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
General disorders and administration site conditions						
ANY EVENT	8/117 (6.8%)	3/117 (2.6%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	12/117 (10.3%)
Asthenia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Axillary pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Chest discomfort	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Chest pain	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Discomfort	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fatigue	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Feeling cold	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Feeling hot	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Malaise	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Oedema	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Oedema peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pyrexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Thirst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatobiliary disorders						
ANY EVENT	0/117 (0.0%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Cholecystitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic cyst	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatic function abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hepatitis B	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hepatitis C	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Immune system disorders						
ANY EVENT	9/117 (7.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	9/117 (7.7%)
Allergy to plants	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dermatitis allergic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
House dust allergy	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinitis allergic	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Seasonal allergy	6/117 (5.1%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	40/117 (34.2%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	42/117 (35.9%)
Bronchiolitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Bronchitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chronic sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Cystitis	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Cystitis acute	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dental caries	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Groin abscess	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Herpes dermatitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Herpes simplex	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Herpes zoster	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Influenza	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Laryngopharyngitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Nail tinea	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nasopharyngitis	24/117 (20.5%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	25/117 (21.4%)
Otitis media	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Otitis media chronic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Paronychia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pharyngitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pneumonia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sinusitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tinea pedis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tonsillitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Upper respiratory tract infection	11/117 (9.4%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	12/117 (10.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	7/117 (6.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	7/117 (6.0%)
Animal bite	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Arthropod sting	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Contusion	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Haemarthrosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypothermia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Injury	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Mouth injury	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Open wound	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin injury	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	9/117 (7.7%)	6/117 (5.1%)	1/117 (0.9%)	2/117 (1.7%)	0/117 (0.0%)	18/117 (15.4%)
Activated partial thromboplastin time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Antithrombin III decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood bilirubin increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood creatinine increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood fibrinogen decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood glucose increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Blood pressure decreased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure increased	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Blood thyroid stimulating hormone decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood thyroid stimulating hormone increased	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Blood triglycerides increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Coagulation time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Eosinophil count increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Eosinophil percentage increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Gamma-glutamyltransferase increased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Glucose urine present	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Lipids increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Liver function test abnormal	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Low density lipoprotein increased	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lymphocyte percentage decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neutrophil percentage increased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Platelet count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Protein urine present	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Prothrombin time prolonged	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Smear cervix abnormal	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)
Sputum test	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urine output decreased	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Weight increased	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
White blood cell count decreased	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Anorexia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Decreased appetite	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Diabetes mellitus	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypercholesterolaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hyperlipidaemia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	29/117 (24.8%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	31/117 (26.5%)
Arthralgia	5/117 (4.3%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Arthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Back pain	18/117 (15.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	18/117 (15.4%)
Buttock pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Foot fracture	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hand fracture	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Joint sprain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Joint swelling	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Limb discomfort	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Localised osteoarthritis	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Monoarthritis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Muscle cramp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle fatigue	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Muscle rigidity	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Muscle twitching	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Musculoskeletal stiffness	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Myalgia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck pain	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neck, shoulder and arm syndrome	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nodal osteoarthritis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pain in extremity	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Radius fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rib fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sensation of heaviness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Spondylosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Tenosynovitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Thoracic vertebral fracture	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Traumatic fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Wrist fracture	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Colonic polyp	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Fibroadenoma of breast	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Fibroma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Gastric cancer	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Hepatic cancer metastatic	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Lipoma	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Metastases to lymph nodes	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Ovarian neoplasm	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nervous system disorders						
ANY EVENT	11/117 (9.4%)	9/117 (7.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	20/117 (17.1%)
Autonomic nervous system imbalance	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Depressed level of consciousness	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dizziness	3/117 (2.6%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)
Dizziness postural	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysgeusia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Facial nerve disorder	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Headache	6/117 (5.1%)	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	9/117 (7.7%)
Hypoaesthesia	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Intercostal neuralgia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Neuropathy peripheral	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Parkinson's disease	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Parosmia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sciatica	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Tension headache	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vertigo	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	11/117 (9.4%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	13/117 (11.1%)
Amnesia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Depression	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Depressive symptom	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysphoria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Insomnia	7/117 (6.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	8/117 (6.8%)
Irritability	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Neurosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Sleep disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Renal and urinary disorders						
ANY EVENT	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Bladder malposition acquired	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dysuria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Micturition disorder	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nocturia	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pollakiuria	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urge incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urinary incontinence	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	2/117 (1.7%)	5/117 (4.3%)	11/117 (9.4%)	21/117 (17.9%)	36/117 (30.8%)	75/117 (64.1%)
Breast discomfort	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)	5/117 (4.3%)	19/117 (16.2%)	28/117 (23.9%)
Breast disorder	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	3/117 (2.6%)
Breast engorgement	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	1/117 (0.9%)	4/117 (3.4%)
Breast fibrosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Breast hyperplasia	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Breast pain	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)	8/117 (6.8%)	7/117 (6.0%)	20/117 (17.1%)
Cervical polyp	0/117 (0.0%)	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Cervicitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Dysmenorrhoea	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	0/117 (0.0%)	2/117 (1.7%)
Endometrial hyperplasia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Fibrocystic breast disease	0/117 (0.0%)	1/117 (0.9%)	2/117 (1.7%)	0/117 (0.0%)	1/117 (0.9%)	4/117 (3.4%)
Genital discharge	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)	3/117 (2.6%)	8/117 (6.8%)	16/117 (13.7%)
Genital haemorrhage	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)	18/117 (15.4%)	21/117 (17.9%)
Genital pruritus female	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	1/117 (0.9%)	3/117 (2.6%)
Genital rash	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hot flush	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Menopausal symptoms	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nipple pain	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	1/117 (0.9%)	6/117 (5.1%)	8/117 (6.8%)
Uterine leiomyoma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Uterine malposition	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vaginal candidiasis	6/117 (5.1%)	2/117 (1.7%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	9/117 (7.7%)
Vaginitis atrophic	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulval oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Vulvitis	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Vulvovaginal discomfort	0/117 (0.0%)	4/117 (3.4%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	5/117 (4.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	11/117 (9.4%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	12/117 (10.3%)
Asthma	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cough	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	3/117 (2.6%)
Dyspnoea	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Epistaxis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Pharyngolaryngeal pain	6/117 (5.1%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	7/117 (6.0%)
Pharynx discomfort	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Productive cough	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Rhinitis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rhinorrhoea	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Upper respiratory tract inflammation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	20/117 (17.1%)	3/117 (2.6%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	23/117 (19.7%)
Acne	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Body tinea	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Cheilitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermal cyst	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Dermatitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dermatitis contact	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Dry skin	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Eczema	4/117 (3.4%)	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	6/117 (5.1%)
Eczema asteatotic	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Erythema	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Excoriation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Face oedema	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Folliculitis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hyperkeratosis	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Milia	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Pruritus	2/117 (1.7%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	2/117 (1.7%)
Rash	4/117 (3.4%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Rash papular	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Rash pustular	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Skin papilloma	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Urticaria	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Surgical and medical procedures						
ANY EVENT	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Nail avulsion	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: E2, 1.0mg/LNG, 40ug

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	3/117 (2.6%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	4/117 (3.4%)
Atherosclerosis obliterans	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Blood pressure fluctuation	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Chillblains	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Deep vein thrombosis	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Hypertension	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Hypotension	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)
Peripheral coldness	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)
Peripheral vascular disorder	1/117 (0.9%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	0/117 (0.0%)	1/117 (0.9%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
ANY EVENT	73/309 (23.6%)	42/309 (13.6%)	40/309 (12.9%)	44/309 (14.2%)	77/309 (24.9%)	276/309 (89.3%)
Blood and lymphatic system disorders						
ANY EVENT	4/309 (1.3%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
Anaemia	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	4/309 (1.3%)
Hypochromic anaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Iron deficiency anaemia	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cardiac disorders						
ANY EVENT	6/309 (1.9%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Angina pectoris	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Arrhythmia	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Palpitations	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Supraventricular extrasystoles	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Ear and labyrinth disorders						
ANY EVENT	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Deafness	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Meniere's disease	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tinnitus	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Endocrine disorders						
ANY EVENT	6/309 (1.9%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Goitre	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Thyroid cyst	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Thyroiditis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Eye disorders						
ANY EVENT	21/309 (6.8%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	22/309 (7.1%)
Abnormal sensation in eye	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Asthenopia	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Blepharitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cataract	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Conjunctival haemorrhage	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Conjunctivitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Corneal dystrophy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis eyelid	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eye pain	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hordeolum	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Keratoconjunctivitis sicca	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lacrimation increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open angle glaucoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periorbital haematoma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Posterior capsule opacification	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pterygium	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinal detachment	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Retinopathy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vitreous floaters	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Gastrointestinal disorders						
ANY EVENT	67/309 (21.7%)	18/309 (5.8%)	13/309 (4.2%)	3/309 (1.0%)	1/309 (0.3%)	102/309 (33.0%)
Abdominal distension	1/309 (0.3%)	4/309 (1.3%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	11/309 (3.6%)
Abdominal pain	4/309 (1.3%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Abdominal pain lower	1/309 (0.3%)	2/309 (0.6%)	2/309 (0.6%)	3/309 (1.0%)	0/309 (0.0%)	8/309 (2.6%)
Abdominal pain upper	11/309 (3.6%)	2/309 (0.6%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	15/309 (4.9%)
Abdominal rigidity	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)
Anorectal disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Constipation	17/309 (5.5%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	23/309 (7.4%)
Diarrhoea	8/309 (2.6%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Diverticulum intestinal	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Duodenal ulcer	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dyspepsia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epigastric discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastric ulcer	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Gastritis	8/309 (2.6%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	13/309 (4.2%)
Gastritis atrophic	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastroenteritis	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Gastrointestinal pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastrointestinal upset	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Gingivitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Glossitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Haemorrhoids	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Intestinal ischaemia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Intestinal obstruction	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Irritable bowel syndrome	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lip dry	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nausea	2/309 (0.6%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Pancreatitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Parotid gland enlargement	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periodontal disease	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Periodontitis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Reflux oesophagitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Stomach discomfort	1/309 (0.3%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Stomatitis	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Tongue ulceration	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
(System Organ Class decode continued from previous page)						
Toothache	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vomiting	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
General disorders and administration site conditions						
ANY EVENT	27/309 (8.7%)	10/309 (3.2%)	1/309 (0.3%)	1/309 (0.3%)	1/309 (0.3%)	40/309 (12.9%)
Asthenia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Axillary pain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Chest discomfort	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Chest pain	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fatigue	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Feeling cold	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Feeling hot	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Malaise	6/309 (1.9%)	2/309 (0.6%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	10/309 (3.2%)
Oedema	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Oedema peripheral	1/309 (0.3%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Pyrexia	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Thirst	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Hepatobiliary disorders						
ANY EVENT	0/309 (0.0%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Cholecystitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatic cyst	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatic function abnormal	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hepatitis B	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hepatitis C	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Immune system disorders						
ANY EVENT	21/309 (6.8%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	22/309 (7.1%)
Allergy to plants	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dermatitis allergic	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
House dust allergy	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinitis allergic	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Seasonal allergy	14/309 (4.5%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	14/309 (4.5%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Infections and infestations						
ANY EVENT	122/309 (39.5%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	128/309 (41.4%)
Bronchiolitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Bronchitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Bronchitis acute	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Chronic sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cystitis	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Cystitis acute	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dental caries	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Groin abscess	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Herpes dermatitis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Herpes simplex	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Herpes zoster	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Influenza	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Laryngopharyngitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Nail tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nasopharyngitis	80/309 (25.9%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	82/309 (26.5%)
Otitis media	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Otitis media chronic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Paronychia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pharyngitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Pneumonia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sinusitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tinea pedis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Tonsillitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Upper respiratory tract infection	28/309 (9.1%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	31/309 (10.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Injury, poisoning and procedural complications						
ANY EVENT	18/309 (5.8%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	18/309 (5.8%)
Animal bite	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Arthropod sting	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Contusion	7/309 (2.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Haemarthrosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypothermia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Injury	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Mouth injury	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Open wound	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin injury	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Investigations						
ANY EVENT	32/309 (10.4%)	19/309 (6.1%)	8/309 (2.6%)	4/309 (1.3%)	1/309 (0.3%)	64/309 (20.7%)
Activated partial thromboplastin time prolonged	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Antithrombin III decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood bilirubin increased	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood creatinine increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood fibrinogen decreased	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood glucose increased	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Blood pressure decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Blood pressure increased	11/309 (3.6%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	16/309 (5.2%)
Blood thyroid stimulating hormone decreased	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Blood thyroid stimulating hormone increased	1/309 (0.3%)	3/309 (1.0%)	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	9/309 (2.9%)
Blood triglycerides increased	2/309 (0.6%)	3/309 (1.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Coagulation time prolonged	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eosinophil count increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eosinophil percentage increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gamma-glutamyltransferase increased	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Glucose urine present	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lipids increased	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Liver function test abnormal	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Low density lipoprotein increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lymphocyte percentage decreased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neutrophil percentage increased	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Platelet count decreased	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Protein urine present	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Prothrombin time prolonged	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Smear cervix abnormal	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	2/309 (0.6%)	1/309 (0.3%)	5/309 (1.6%)
Sputum test	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urine output decreased	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Weight increased	2/309 (0.6%)	3/309 (1.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	6/309 (1.9%)
White blood cell count decreased	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Metabolism and nutrition disorders						
ANY EVENT	3/309 (1.0%)	5/309 (1.6%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	10/309 (3.2%)
Anorexia	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Decreased appetite	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Diabetes mellitus	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Hypercholesterolaemia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperlipidaemia	0/309 (0.0%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Musculoskeletal and connective tissue disorders						
ANY EVENT	76/309 (24.6%)	14/309 (4.5%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	92/309 (29.8%)
Arthralgia	20/309 (6.5%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	21/309 (6.8%)
Arthritis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Back pain	38/309 (12.3%)	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	43/309 (13.9%)
Buttock pain	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Foot fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hand fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Joint sprain	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Joint swelling	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Limb discomfort	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Localised osteoarthritis	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Monoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Muscle cramp	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Muscle fatigue	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Muscle rigidity	7/309 (2.3%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Muscle twitching	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Musculoskeletal stiffness	4/309 (1.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Myalgia	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Neck pain	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Neck, shoulder and arm syndrome	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nodal osteoarthritis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pain in extremity	10/309 (3.2%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	12/309 (3.9%)
Radius fracture	5/309 (1.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Rib fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sensation of heaviness	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Spondylosis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Tenosynovitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Thoracic vertebral fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Traumatic fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Wrist fracture	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
ANY EVENT	5/309 (1.6%)	4/309 (1.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	11/309 (3.6%)
Colonic polyp	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Fibroadenoma of breast	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Fibroma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Gastric cancer	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Hepatic cancer metastatic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Lipoma	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Metastases to lymph nodes	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Ovarian neoplasm	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Nervous system disorders						
ANY EVENT	39/309 (12.6%)	21/309 (6.8%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	60/309 (19.4%)
Autonomic nervous system imbalance	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Depressed level of consciousness	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dizziness	11/309 (3.6%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	17/309 (5.5%)
Dizziness postural	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysgeusia	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Facial nerve disorder	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Headache	16/309 (5.2%)	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	22/309 (7.1%)
Hypoaesthesia	4/309 (1.3%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Intercostal neuralgia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neuropathy peripheral	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Parkinson's disease	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Parosmia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sciatica	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Tension headache	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vertigo	3/309 (1.0%)	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Psychiatric disorders						
ANY EVENT	20/309 (6.5%)	6/309 (1.9%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	27/309 (8.7%)
Amnesia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Depression	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Depressive symptom	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysphoria	4/309 (1.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	5/309 (1.6%)
Insomnia	12/309 (3.9%)	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	16/309 (5.2%)
Irritability	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Neurosis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Sleep disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Renal and urinary disorders						
ANY EVENT	8/309 (2.6%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Bladder malposition acquired	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Dysuria	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Micturition disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nocturia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pollakiuria	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Urge incontinence	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urinary incontinence	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Reproductive system and breast disorders						
ANY EVENT	10/309 (3.2%)	11/309 (3.6%)	29/309 (9.4%)	43/309 (13.9%)	76/309 (24.6%)	169/309 (54.7%)
Breast discomfort	0/309 (0.0%)	0/309 (0.0%)	13/309 (4.2%)	17/309 (5.5%)	39/309 (12.6%)	69/309 (22.3%)
Breast disorder	1/309 (0.3%)	1/309 (0.3%)	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	5/309 (1.6%)
Breast engorgement	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	4/309 (1.3%)	2/309 (0.6%)	8/309 (2.6%)
Breast fibrosis	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Breast hyperplasia	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Breast pain	0/309 (0.0%)	0/309 (0.0%)	9/309 (2.9%)	14/309 (4.5%)	15/309 (4.9%)	38/309 (12.3%)
Cervical polyp	0/309 (0.0%)	6/309 (1.9%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Cervicitis	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dysmenorrhoea	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	2/309 (0.6%)
Endometrial hyperplasia	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)
Fibrocystic breast disease	0/309 (0.0%)	1/309 (0.3%)	3/309 (1.0%)	0/309 (0.0%)	2/309 (0.6%)	6/309 (1.9%)
Genital discharge	0/309 (0.0%)	0/309 (0.0%)	11/309 (3.6%)	9/309 (2.9%)	18/309 (5.8%)	38/309 (12.3%)
Genital haemorrhage	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	5/309 (1.6%)	25/309 (8.1%)	31/309 (10.0%)
Genital pruritus female	4/309 (1.3%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	9/309 (2.9%)
Genital rash	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hot flush	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Menopausal symptoms	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Nipple pain	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)	3/309 (1.0%)	16/309 (5.2%)	23/309 (7.4%)
Uterine leiomyoma	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Uterine malposition	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vaginal candidiasis	12/309 (3.9%)	3/309 (1.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	16/309 (5.2%)
Vaginitis atrophic	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulval oedema	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Vulvitis	1/309 (0.3%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Vulvovaginal discomfort	1/309 (0.3%)	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Respiratory, thoracic and mediastinal disorders						
ANY EVENT	28/309 (9.1%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	30/309 (9.7%)
Asthma	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Cough	6/309 (1.9%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Dyspnoea	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Epistaxis	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Pharyngolaryngeal pain	11/309 (3.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	12/309 (3.9%)
Pharynx discomfort	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Productive cough	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Rhinitis	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Rhinorrhoea	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Upper respiratory tract inflammation	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2
by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Skin and subcutaneous tissue disorders						
ANY EVENT	48/309 (15.5%)	6/309 (1.9%)	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	57/309 (18.4%)
Acne	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Body tinea	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Cheilitis	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Dermal cyst	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Dermatitis	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Dermatitis contact	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Dry skin	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Eczema	14/309 (4.5%)	2/309 (0.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	17/309 (5.5%)
Eczema asteatotic	3/309 (1.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	3/309 (1.0%)
Erythema	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Excoriation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Face oedema	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Folliculitis	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hyperkeratosis	4/309 (1.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	4/309 (1.3%)
Milia	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nail disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Pruritus	5/309 (1.6%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	6/309 (1.9%)
Rash	7/309 (2.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Rash papular	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Rash pustular	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Skin papilloma	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Urticaria	5/309 (1.6%)	0/309 (0.0%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	7/309 (2.3%)
Surgical and medical procedures						
ANY EVENT	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Nail avulsion	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

(Continued)

Nihon Schering K.K.

Table 14.3.1.8: Adverse Events - Number (%) of Patients by Relationship to the Drug - 2

by Treatment Group
Analysis set: Safety

Treatment: Overall

EVENT(MedDRA) for 2 years	no	unlikely	possible	probable	definite	Total
Vascular disorders						
ANY EVENT	7/309 (2.3%)	1/309 (0.3%)	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	10/309 (3.2%)
Atherosclerosis obliterans	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Blood pressure fluctuation	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Chillblains	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Deep vein thrombosis	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Hypertension	2/309 (0.6%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Hypotension	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)
Peripheral coldness	1/309 (0.3%)	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	2/309 (0.6%)
Peripheral vascular disorder	1/309 (0.3%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	0/309 (0.0%)	1/309 (0.3%)

Note: events are given as System Organ Class decode / Preferred Term decode

(Order No. : S0031T)

表 2.7.6.4- 9　試験 300103：AE コード用語の対比表（MedDRA ver 7.1 基本語 vs MedDRA ver 6.1 基本語）

CTD 統合解析の AE コード語（MedDRA 日本語, Ver7.1）		総括報告書中の AE コード語（MedDRA 英語, Ver6.1）		CRF 中の医師報告用語
SOC 分類名	PT 用語	SOC 分類名	PT 用語	
胃腸障害	悪心	Gastrointestinal disorders	Nausea	悪心，吐き気，嘔気
	胃炎	Gastrointestinal disorders	Gastritis	胃がムカムカする（胃炎の悪化），胃炎，胃炎の悪化，急性胃炎
	胃潰瘍	Gastrointestinal disorders	Gastric ulcer	胃潰瘍
	胃不快感	Gastrointestinal disorders	Gastrointestinal upset	胃のもたれ，胃もたれ感
	胃不快感	Gastrointestinal disorders	Stomach discomfort	胃部不快感
	萎縮性胃炎	Gastrointestinal disorders	Gastritis atrophic	慢性萎縮性胃炎
	下腹部痛	Gastrointestinal disorders	Abdominal pain lower	下腹痛，下腹部痛
	下痢	Gastrointestinal disorders	Diarrhoea	下痢，下痢（軟便），下痢症
	過敏性腸症候群	Gastrointestinal disorders	Irritable bowel syndrome	過敏性腸症候群
	逆流性食道炎	Gastrointestinal disorders	Reflux oesophagitis	逆流性食道炎
	結腸ポリープ	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Colonic polyp	大腸ポリープ
	結腸良性ポリープ	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Colonic polyp	消化管良性腫瘍（結腸ポリープ）
	口腔内不快感	Nervous system disorders	Facial nerve disorder	右口角下垂感
	口唇炎	Skin and subcutaneous tissue disorders	Cheilitis	口角炎，口唇炎の悪化
	口唇乾燥	Gastrointestinal disorders	Lip dry	口唇乾燥
	口内炎	Gastrointestinal disorders	Stomatitis	口内炎
	歯周炎	Gastrointestinal disorders	Periodontitis	急性歯周炎，歯槽膿漏
	歯周病	Gastrointestinal disorders	Periodontal disease	歯周病
	歯痛	Gastrointestinal disorders	Toothache	歯痛
	歯肉炎	Gastrointestinal disorders	Gingivitis	化膿性歯肉炎
	痔核	Gastrointestinal disorders	Haemorrhoids	痔，痔核
	耳下腺腫大	Gastrointestinal disorders	Parotid gland enlargement	耳下腺腫脹
	十二指腸潰瘍	Gastrointestinal disorders	Duodenal ulcer	十二指腸潰瘍の悪化
	消化器痛	Gastrointestinal disorders	Gastrointestinal pain	胃腸部の痛み
	消化不良	Gastrointestinal disorders	Dyspepsia	胸やけ
	上腹部痛	Gastrointestinal disorders	Abdominal pain upper	胃痛，上腹部痛，心窩部痛
	心窩部不快感	Gastrointestinal disorders	Epigastric discomfort	心窩部不快感
	舌炎	Gastrointestinal disorders	Glossitis	舌炎
	舌潰瘍	Gastrointestinal disorders	Tongue ulceration	舌潰瘍
	腸管虚血	Gastrointestinal disorders	Intestinal ischaemia	虚血性腸炎
	腸管閉塞	Gastrointestinal disorders	Intestinal obstruction	腸閉塞
	腸憩室	Gastrointestinal disorders	Diverticulum intestinal	大腸憩室
	直腸脱	Gastrointestinal disorders	Anorectal disorder	直腸下垂
	腹痛	Gastrointestinal disorders	Abdominal pain	腹痛，腹部膨満感を伴った腹痛
	腹部硬直	Gastrointestinal disorders	Abdominal rigidity	腹部硬直感
	腹部膨満	Gastrointestinal disorders	Abdominal distension	下腹部緊満感，下腹部膨満，下腹部膨満感，腹部の張り，腹部膨満感，腹満感
	便秘	Gastrointestinal disorders	Abdominal distension	便秘による腹部膨満感
	便秘	Gastrointestinal disorders	Constipation	便秘，便秘症
	嘔吐	Gastrointestinal disorders	Vomiting	嘔吐，嘔吐脱水症
	膵炎	Gastrointestinal disorders	Pancreatitis	膵炎疑い（背部痛）
感染症および寄生虫症	Ｂ型肝炎	Hepatobiliary disorders	Hepatitis B	Ｂ型肝炎の悪化
	Ｃ型肝炎	Hepatobiliary disorders	Hepatitis C	慢性Ｃ型肝炎の悪化
	インフルエンザ	Infections and infestations	Influenza	インフルエンザ
	ヘルペスウイルス感染	Infections and infestations	Herpes dermatitis	ヘルペス　左前腕～左肩
	胃腸炎	Gastrointestinal disorders	Gastroenteritis	胃腸炎，急性胃腸炎，慢性胃腸炎
	咽喉頭炎	Infections and infestations	Laryngopharyngitis	咽喉頭炎，慢性咽喉頭炎
	咽頭炎	Infections and infestations	Pharyngitis	咽頭炎

CTD 統合解析の AE コード語 (MedDRA 日本語, Ver7.1)		総括報告書中の AE コード語 (MedDRA 英語, Ver6.1)		CRF 中の医師報告用語
SOC 分類名	PT 用語	SOC 分類名	PT 用語	
	外陰部炎	Reproductive system and breast disorders	Vulvitis	外陰炎
	気管支炎	Infections and infestations	Bronchitis	気管支炎
	急性気管支炎	Infections and infestations	Bronchitis acute	急性気管支炎
	細気管支炎	Infections and infestations	Bronchiolitis	急性細気管支炎
	子宮頚管炎	Reproductive system and breast disorders	Cervicitis	慢性子宮頚管炎
	足部白癬	Infections and infestations	Tinea pedis	足白癬
	帯状疱疹	Infections and infestations	Herpes zoster	帯状疱疹，帯状疱疹（左腹～腰部）
	単純ヘルペス	Infections and infestations	Herpes simplex	外陰部ヘルペスの悪化，口唇ヘルペス
	中耳炎	Infections and infestations	Otitis media	中耳炎
	爪囲炎	Infections and infestations	Paronychia	爪囲炎
	爪白癬	Infections and infestations	Nail tinea	爪白癬（足）
	膿疱性皮疹	Skin and subcutaneous tissue disorders	Rash pustular	顔面化膿疹
	肺炎	Infections and infestations	Pneumonia	肺炎
	白癬感染	Skin and subcutaneous tissue disorders	Body tinea	白癬症（胸部湿疹）
	麦粒腫	Eye disorders	Hordeolum	左麦粒腫
	鼻咽頭炎	Infections and infestations	Nasopharyngitis	かぜ，感冒，感冒（くしゃみ，鼻水），感冒（咳），感冒（上気道炎），感冒（発熱３７．８℃鼻水），感冒（鼻汁，咽頭痛），感冒（鼻汁，咳嗽），感冒（鼻汁・咳嗽），感冒（鼻汁），感冒（腹痛・下痢），感冒症状，風邪，風邪（悪寒），風邪（鼻炎），腹痛，嘔吐，下痢を伴う感冒
	鼻炎	Respiratory, thoracic and mediastinal disorders	Rhinitis	鼻炎
	副鼻腔炎	Infections and infestations	Sinusitis	副鼻腔炎
	慢性中耳炎	Infections and infestations	Otitis media chronic	右慢性中耳炎
	慢性副鼻腔炎	Infections and infestations	Chronic sinusitis	慢性副鼻腔炎
	毛包炎	Skin and subcutaneous tissue disorders	Folliculitis	毛嚢炎（右小陰唇）
	扁桃炎	Infections and infestations	Tonsillitis	扁桃炎
	膀胱炎	Infections and infestations	Cystitis	膀胱炎，膀胱炎（頻尿）
	膀胱炎	Infections and infestations	Cystitis acute	急性細菌性膀胱炎
	腟カンジダ症	Reproductive system and breast disorders	Vaginal candidiasis	カンジタ腟外陰炎，カンジダ症（膣部），カンジダ腟炎，カンジダ腟外陰炎，外陰部腟カンジダ症，外陰膣カンジダ症，外陰腟カンジタ症，膣カンジダ症，腟カンジタ症
	腟真菌症	Reproductive system and breast disorders	Vaginal candidiasis	真菌性腟炎（外陰部そう痒感）
	鼠径部膿瘍	Infections and infestations	Groin abscess	左ソ頚膿瘍
	齲歯	Infections and infestations	Dental caries	う歯
肝胆道系障害	肝機能異常	Hepatobiliary disorders	Hepatic function abnormal	肝機能障害
	肝嚢胞	Hepatobiliary disorders	Hepatic cyst	肝嚢胞
	胆嚢炎	Hepatobiliary disorders	Cholecystitis	胆石症による胆嚢炎
眼障害	開放隅角緑内障	Eye disorders	Open angle glaucoma	開放隅角緑内障（視神経萎縮）の悪化
	眼の異常感	Eye disorders	Abnormal sensation in eye	眼内異物感
	眼乾燥	Eye disorders	Keratoconjunctivitis sicca	ドライアイ
	眼精疲労	Eye disorders	Asthenopia	つかれ眼，眼精疲労
	眼痛	Eye disorders	Eye pain	右眼の痛み，眼痛
	眼瞼炎	Eye disorders	Blepharitis	眼瞼炎
	眼瞼炎	Eye disorders	Dermatitis eyelid	眼瞼周囲湿疹
	結膜炎	Eye disorders	Conjunctivitis	結膜炎

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	結膜出血	Eye disorders	Conjunctival haemorrhage	左眼球結膜出血
	後嚢部混濁	Eye disorders	Posterior capsule opacification	左後発白内障
	硝子体浮遊物	Eye disorders	Vitreous floaters	飛蚊症
	白内障	Eye disorders	Cataract	白内障の悪化
	網膜症	Eye disorders	Retinopathy	右中心性網膜症
	網膜剥離	Eye disorders	Retinal detachment	網膜剥離（右眼）
	翼状片	Eye disorders	Pterygium	翼状片
	流涙増加	Eye disorders	Lacrimation increased	涙目
筋骨格系および結合組織障害	関節炎	Musculoskeletal and connective tissue disorders	Arthritis	顎関節炎
	関節腫脹	Musculoskeletal and connective tissue disorders	Joint swelling	膝関節腫脹
	関節痛	Musculoskeletal and connective tissue disorders	Arthralgia	右肩の疼痛，右肩関節痛，右手関節痛，右膝関節痛，右膝痛，右肘痛，下肢関節痛，顎関節痛，肩関節痛，肩痛，五十肩，五十肩（右肩）の悪化，左肩痛，左手関節痛，左手指関節痛，膝が痛い，膝の痛み，膝関節痛，変形性関節痛（指），両膝関節痛
	筋緊張	Nervous system disorders	Tension headache	筋緊張性疼痛（首，肩，頭）の悪化
	筋骨格硬直	Musculoskeletal and connective tissue disorders	Muscle fatigue	右腰～大腿部のつっぱり感
	筋骨格硬直	Musculoskeletal and connective tissue disorders	Muscle rigidity	肩こり，肩こりの悪化，肩凝り，両肩の張り（肩こり）
	筋骨格硬直	Musculoskeletal and connective tissue disorders	Musculoskeletal stiffness	手のこわばり，手指のこわばり，手足のむくみ，こわばり，首のこり，首筋が張る，足の裏のしこり感
	筋痛	Musculoskeletal and connective tissue disorders	Back pain	背筋痛
	筋痛	Musculoskeletal and connective tissue disorders	Myalgia	筋肉痛
	筋痛	Musculoskeletal and connective tissue disorders	Neck pain	頚部痛（筋肉痛）
	筋肉疲労	Musculoskeletal and connective tissue disorders	Myalgia	筋肉疲労による痛み（左肋骨痛，左腋の痛み，左背部痛）
	筋攣縮	Musculoskeletal and connective tissue disorders	Muscle twitching	右眼周囲のれん縮
	筋痙攣	Musculoskeletal and connective tissue disorders	Muscle cramp	下肢痙攣，左腋窩のつり感
	頚部痛	Musculoskeletal and connective tissue disorders	Neck pain	後頚部痛
	結節性変形性関節炎	Musculoskeletal and connective tissue disorders	Localised osteoarthritis	右中指ＰＩＰ変形性関節炎
	結節性変形性関節炎	Musculoskeletal and connective tissue disorders	Nodal osteoarthritis	ヘバーデン結節
	限局性骨関節炎	Musculoskeletal and connective tissue disorders	Localised osteoarthritis	左第４指変形性関節症，足関節炎，膝痛（変形性膝関節症），変形性膝関節症
	四肢痛	Musculoskeletal and connective tissue disorders	Pain in extremity	右下肢痛，右肩～上腕痛，右腰～大腿痛，右中指のむくみを伴った痛み，右踵痛，右踵部の痛み，左の踵が少し痛い，左下腿痛，左下腿部痛，左手掌痛，両足中趾の痛み，腕・肩の痛み
	四肢不快感	Musculoskeletal and connective tissue disorders	Limb discomfort	左手小指の違和感，手指違和感，大腿部違和感
	重感	Musculoskeletal and connective tissue disorders	Sensation of heaviness	左半身の重い感じ，背中が重苦しい

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	出血性関節症	Injury, poisoning and procedural complications	Haemarthrosis	右手第５中手指節間関節内出血
	脊椎症	Musculoskeletal and connective tissue disorders	Spondylosis	（頭部不快感，背部痛）頚椎症の悪化
	単関節炎	Musculoskeletal and connective tissue disorders	Monoarthritis	左股関節炎
	殿部痛	Musculoskeletal and connective tissue disorders	Buttock pain	臀部痛
	背部痛	Musculoskeletal and connective tissue disorders	Back pain	右腰部痛，腰痛，腰痛の悪化，腰痛症，腰痛症の悪化，腰部打撲による腰痛
	腱鞘炎	Musculoskeletal and connective tissue disorders	Tenosynovitis	左膝腱鞘炎
血液およびリンパ系障害	低色素性貧血	Blood and lymphatic system disorders	Hypochromic anaemia	小球性低色素性貧血の悪化
	鉄欠乏性貧血	Blood and lymphatic system disorders	Iron deficiency anaemia	鉄欠乏性貧血（RBC，Hb，Ht 減少）
	貧血	Blood and lymphatic system disorders	Anaemia	貧血，貧血症
血管障害	ほてり	Reproductive system and breast disorders	Hot flush	Hot flash，hot flush
	血圧変動	Vascular disorders	Blood pressure fluctuation	血圧の変動
	高血圧	Vascular disorders	Hypertension	高血圧症の悪化
	深部静脈血栓症	Vascular disorders	Deep vein thrombosis	深部静脈血栓の疑い。（左足のむくみ，下肢つっぱり感）
	低血圧	General disorders and administration site conditions	Feeling cold	血圧低下による冷感
	低血圧	Vascular disorders	Hypotension	低血圧
	閉塞性動脈硬化症	Vascular disorders	Atherosclerosis obliterans	閉塞性動脈硬化症の悪化
	末梢血管障害	Vascular disorders	Peripheral vascular disorder	末梢循環障害（両手指）
	末梢冷感	Vascular disorders	Peripheral coldness	手指冷感，両足冷感
呼吸器，胸郭および縦隔障害	アレルギー性鼻炎	Immune system disorders	Rhinitis allergic	アレルギー性鼻炎，アレルギー性鼻炎の悪化
	咽喉頭疼痛	Respiratory, thoracic and mediastinal disorders	Pharyngolaryngeal pain	咽頭痛
	咽頭不快感	Respiratory, thoracic and mediastinal disorders	Pharyngolaryngeal pain	のどの違和感，咽頭違和感
	咽頭不快感	Respiratory, thoracic and mediastinal disorders	Pharynx discomfort	咽頭不快感
	咳嗽	Respiratory, thoracic and mediastinal disorders	Cough	咳，咳嗽
	湿性咳嗽	Investigations	Sputum test	痰
	湿性咳嗽	Respiratory, thoracic and mediastinal disorders	Productive cough	痰のからむ咳
	上気道の炎症	Infections and infestations	Upper respiratory tract infection	上気道炎，上気道炎（胸がつまっている感じ），上気道炎（鼻汁），鼻水（上気道炎）
	上気道の炎症	Respiratory, thoracic and mediastinal disorders	Upper respiratory tract inflammation	急性上気道炎
	息詰まり感	Respiratory, thoracic and mediastinal disorders	Dyspnoea	息苦しい感じがする
	鼻出血	Respiratory, thoracic and mediastinal disorders	Epistaxis	鼻血，鼻出血
	鼻漏	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	鼻汁
	喘息	Respiratory, thoracic and mediastinal disorders	Asthma	気管支喘息の悪化，気管支喘息の発作，気管支喘息発作
耳および迷路障害	ろう	Ear and labyrinth disorders	Deafness	耳鳴を伴う難聴
	メニエール病	Ear and labyrinth disorders	Meniere's disease	右メニエール病の疑い
	一過性難聴	Ear and labyrinth disorders	Deafness	難聴
	回転性眩暈	Nervous system disorders	Vertigo	めまい，眩暈
	耳鳴	Ear and labyrinth disorders	Tinnitus	耳なり，耳鳴，耳鳴り

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傷害，中毒および処置合併症	開放創	Injury, poisoning and procedural complications	Open wound	右口唇創傷
	外傷性骨折	Musculoskeletal and connective tissue disorders	Foot fracture	左母趾末節骨骨折（外傷性）
	外傷性骨折	Musculoskeletal and connective tissue disorders	Rib fracture	転倒による肋骨骨折
	外傷性骨折	Musculoskeletal and connective tissue disorders	Traumatic fracture	右第４趾骨折（外傷性）
	関節損傷	Injury, poisoning and procedural complications	Contusion	左膝外傷
	関節捻挫	Musculoskeletal and connective tissue disorders	Joint sprain	ねんざ（足の甲のしびれ）
	眼窩周囲血腫	Eye disorders	Periorbital haematoma	左眼部挫傷
	胸椎骨折	Musculoskeletal and connective tissue disorders	Thoracic vertebral fracture	胸椎骨折（Th12）
	挫傷	General disorders and administration site conditions	Chest pain	打撲による胸部痛
	挫傷	Injury, poisoning and procedural complications	Contusion	右臀部打撲（自転車で転倒），左手関節打撲，左前腕打撲，全身打撲，打撲痛，臀部打撲
	挫傷	Injury, poisoning and procedural complications	Mouth injury	口内打撲
	擦過傷	Skin and subcutaneous tissue disorders	Excoriation	左親指表皮剥離
	四肢損傷	Injury, poisoning and procedural complications	Injury	左拇指切傷
	手骨折	Musculoskeletal and connective tissue disorders	Hand fracture	右第５指骨折
	手首関節骨折	Musculoskeletal and connective tissue disorders	Wrist fracture	右手首ヒビ
	節足動物刺傷	Injury, poisoning and procedural complications	Arthropod sting	刺傷（ハチ刺され，左足）
	損傷	Injury, poisoning and procedural complications	Skin injury	切創
	爪裂離	Surgical and medical procedures	Nail avulsion	右手指（２指）のつめ，剥離及同部の化膿症
	凍瘡	Vascular disorders	Chillblains	凍瘡（右耳），凍瘡（指の関節と背面）
	頭部損傷	Injury, poisoning and procedural complications	Injury	頭部切傷
	咬刺傷	Injury, poisoning and procedural complications	Animal bite	咬創（左手指，右前腕）
	橈骨骨折	Musculoskeletal and connective tissue disorders	Radius fracture	右橈骨遠位端骨折，右橈骨骨折，左橈骨遠位端骨折，左橈骨骨折
心臓障害	狭心症	Cardiac disorders	Angina pectoris	胸～背部の疼痛（狭心症の疑い）
	上室性期外収縮	Cardiac disorders	Supraventricular extrasystoles	心房性期外収縮
	動悸	Cardiac disorders	Palpitations	動悸
	肥大型心筋症	Cardiac disorders	Arrhythmia	肥大型心筋症による不整脈
	不整脈	Cardiac disorders	Arrhythmia	不整脈
神経系障害	パーキンソン病	Nervous system disorders	Parkinson's disease	パーキンソン症候群
	意識レベルの低下	Nervous system disorders	Depressed level of consciousness	意識レベルの低下
	外傷後頭痛	Nervous system disorders	Headache	頭部打撲による頭痛
	感覚減退	Nervous system disorders	Hypoaesthesia	右下肢のしびれ，下肢しびれ，左半身のしびれ，手のしびれ，朝のみ右手・足にしびれ，頭皮のしびれ，両手のしびれ，両足底しびれ
	感覚障害	Reproductive system and breast disorders	Menopausal symptoms	体がザーザーした感じ
	頚腕症候群	Musculoskeletal and connective tissue disorders	Neck, shoulder and arm syndrome	頚肩腕症，肩頚腕症

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	健忘	Psychiatric disorders	Amnesia	老人性痴呆に伴う健忘症の悪化
	坐骨神経痛	Nervous system disorders	Sciatica	坐骨神経痛
	自律神経失調	Nervous system disorders	Autonomic nervous system imbalance	自律神経失調症（ほてり，のどの違和感），自律神経失調症の悪化，自律神経失調症の悪化（体調が悪い　疲れやすい　手のふるえ　不眠）
	体位性めまい	Nervous system disorders	Dizziness postural	立ちくらみ
	頭痛	Nervous system disorders	Headache	肩～頭痛，頭重感，頭痛
	浮動性めまい	Nervous system disorders	Dizziness	ふらつき，めまい
	浮動性めまい	Nervous system disorders	Vertigo	頭重感を伴うめまい
	末梢性ニューロパシー	Nervous system disorders	Neuropathy peripheral	左下肢末梢神経炎，末梢神経障害（右手掌のしびれ感）
	味覚異常	Nervous system disorders	Dysgeusia	味覚の異常（塩味が感じない），味覚異常，味覚障害の悪化
	肋間神経痛	Nervous system disorders	Intercostal neuralgia	左肋間神経痛
	嗅覚錯誤	Nervous system disorders	Parosmia	嗅覚異常
腎および尿路障害	切迫性尿失禁	Renal and urinary disorders	Urge incontinence	切迫性尿失禁
	尿失禁	Renal and urinary disorders	Urinary incontinence	尿もれ，尿失禁
	排尿困難	Renal and urinary disorders	Dysuria	排尿痛
	排尿困難	Renal and urinary disorders	Micturition disorder	排尿不快感
	頻尿	Renal and urinary disorders	Pollakiuria	頻尿
	夜間頻尿	Renal and urinary disorders	Nocturia	夜間頻尿
	膀胱脱	Renal and urinary disorders	Bladder malposition acquired	膀胱下垂
生殖系および乳房障害	萎縮性腟炎	Reproductive system and breast disorders	Vaginitis atrophic	老人性腟炎
	陰部そう痒症	Reproductive system and breast disorders	Genital pruritus female	陰部の痒み，陰部掻痒
	外陰浮腫	Reproductive system and breast disorders	Vulval oedema	外陰部の膨れ
	外陰浮腫	Reproductive system and breast disorders	Vulvovaginal discomfort	外陰部腫脹感
	外陰腟不快感	Reproductive system and breast disorders	Vulvovaginal discomfort	外陰部に異和感，外陰部違和感，外陰部痛，外陰部不快感，排尿時　外陰部痛
	月経困難症	Reproductive system and breast disorders	Dysmenorrhoea	月経痛，腹痛（生理痛）
	子宮頚管ポリープ	Reproductive system and breast disorders	Cervical polyp	子宮頚管ポリープ，子宮頸管ポリープ，子宮頸管粘膜ポリープ
	子宮出血	Reproductive system and breast disorders	Genital haemorrhage	子宮出血
	子宮脱	Reproductive system and breast disorders	Uterine malposition	子宮下垂
	子宮内膜増殖症	Reproductive system and breast disorders	Endometrial hyperplasia	単純型子宮内膜増殖症
	女性陰部そう痒症	Reproductive system and breast disorders	Genital pruritus female	外陰～そ径部の痒み，外陰部かゆみ，外陰部そう痒（痒み），外陰部そう痒感，外陰部の掻痒感，外陰部掻痒感，外陰部痒み
	性器出血	Reproductive system and breast disorders	Genital haemorrhage	出血（性器出血），性器出血
	性器発疹	Reproductive system and breast disorders	Genital rash	小陰唇発疹
	性器分泌物	Reproductive system and breast disorders	Genital discharge	黄色帯下，帯下，帯下感，白帯下
	乳頭腫脹	Reproductive system and breast disorders	Breast engorgement	乳輪部のはれた感じ
	乳頭痛	Reproductive system and breast disorders	Nipple pain	乳首が敏感になる，乳首の痛，乳頭過敏，乳頭痛，両乳頭痛

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	乳房過形成	Reproductive system and breast disorders	Breast hyperplasia	右乳房低分化過形成，左乳房低分化型過形成
	乳房腫脹	Reproductive system and breast disorders	Breast engorgement	胸の腫れ，痛み，乳房腫張
	乳房障害	Reproductive system and breast disorders	Breast disorder	乳腺症，乳腺症（両側），両側乳腺症
	乳房線維化	Reproductive system and breast disorders	Breast fibrosis	右乳房間質性線維症
	乳房痛	Reproductive system and breast disorders	Breast pain	右乳房痛，左乳房痛，乳房痛，両側乳房痛，両乳房痛
	乳房嚢胞	Reproductive system and breast disorders	Fibrocystic breast disease	左乳腺のう胞，乳腺のう胞，乳腺のう胞（左側），乳房のう胞症
	乳房不快感	Reproductive system and breast disorders	Breast discomfort	右乳房緊満感，胸のはり，胸のはり（乳のはり），胸の張り，左側乳房緊満感，左乳房緊満感，乳房の緊満感，乳房の張り，乳房緊満，乳房緊満感，乳房緊満感（乳房痛），乳房膨張感，両側乳房緊満感，両乳房緊満感
	不正子宮出血	Reproductive system and breast disorders	Genital haemorrhage	不正出血
	閉経期症状	Reproductive system and breast disorders	Menopausal symptoms	更年期障害（頭痛）の悪化
	閉経期障害	Reproductive system and breast disorders	Menopausal symptoms	更年期障害の悪化
	腟分泌物	Reproductive system and breast disorders	Genital discharge	褐色帯下
精神障害	うつ病	Psychiatric disorders	Depression	うつ状態
	易刺激性	Psychiatric disorders	Irritability	イライラ感
	神経症	Psychiatric disorders	Neurosis	神経症の悪化
	睡眠障害	Psychiatric disorders	Sleep disorder	睡眠障害
	不快気分	Psychiatric disorders	Dysphoria	気分不快，気分不良
	不眠症	Psychiatric disorders	Insomnia	不眠，不眠症，不眠症の悪化
	抑うつ症状	Psychiatric disorders	Depressive symptom	うつ症状
先天性，家族性および遺伝性障害	角膜ジストロフィー	Eye disorders	Corneal dystrophy	角膜ジストロフィーの悪化
全身障害および投与局所様態	胸痛	General disorders and administration site conditions	Chest pain	狭心症様の疼痛，胸痛，胸痛の悪化，左胸部痛，左側胸部痛，前胸部痛
	胸部不快感	General disorders and administration site conditions	Chest discomfort	胸がしめつけられる感じ，胸部圧迫感，胸部違和感，心圧迫感
	倦怠感	General disorders and administration site conditions	Malaise	だるさ，倦怠感，全身倦怠感，足の倦怠感，体のだるさ
	口渇	General disorders and administration site conditions	Thirst	口渇
	低体温	Injury, poisoning and procedural complications	Hypothermia	低体温
	熱感	General disorders and administration site conditions	Feeling hot	口周囲の違和感（ほてり），体があたたかくなる（特に下肢），体があつくなる様な感じ
	発熱	General disorders and administration site conditions	Pyrexia	倦怠感を伴う発熱，発熱
	疲労	General disorders and administration site conditions	Fatigue	疲労，疲労感，疲労感（気分が悪い，頭が重い，眼がしみる）
	不快感	General disorders and administration site conditions	Discomfort	少し早くあるくと気分悪い
	浮腫	General disorders and administration site conditions	Oedema	むくみ，浮腫

CTD 統合解析の AE コード語 (MedDRA 日本語, Ver7.1)		総括報告書中の AE コード語 (MedDRA 英語, Ver6.1)		CRF 中の医師報告用語
SOC 分類名	PT 用語	SOC 分類名	PT 用語	
	末梢性浮腫	General disorders and administration site conditions	Oedema peripheral	右手中指腫脹感，右足先発赤腫脹，左足のはれ，浮腫（下肢），両下腿の脹れ，両母指腫脹
	無力症	General disorders and administration site conditions	Asthenia	体調悪化
	冷感	General disorders and administration site conditions	Feeling cold	寒気
	腋窩痛	General disorders and administration site conditions	Axillary pain	腋窩部痛
代謝および栄養障害	高コレステロール血症	Metabolism and nutrition disorders	Hypercholesterolaemia	高コレステロール血症
	高脂血症	Metabolism and nutrition disorders	Hyperlipidaemia	高脂血症，高脂血症の悪化
	食欲減退	Metabolism and nutrition disorders	Decreased appetite	食欲減退
	食欲不振	Metabolism and nutrition disorders	Anorexia	食欲不振
	糖尿病	Metabolism and nutrition disorders	Diabetes mellitus	糖尿病，糖尿病（疑い）
内分泌障害	甲状腺炎	Endocrine disorders	Thyroiditis	萎縮性甲状腺炎，無痛性甲状腺炎
	甲状腺腫	Endocrine disorders	Goitre	右甲状腺腫瘍，甲状腺腫
	甲状腺嚢腫	Endocrine disorders	Thyroid cyst	甲状腺のう胞
皮膚および皮下組織障害	ざ瘡	Skin and subcutaneous tissue disorders	Acne	尋常性ざ瘡
	そう痒症	Skin and subcutaneous tissue disorders	Pruritus	右肩前胸部にかゆみ，掻痒感（躯幹・上肢），掻痒感（背中），背中のかゆみ，皮膚そう痒症，皮膚掻痒（肩周囲），皮膚掻痒感
	アレルギー性皮膚炎	Immune system disorders	Dermatitis allergic	アレルギー性皮膚炎，アレルギー性皮膚炎（両四肢，体幹）
	過角化	Skin and subcutaneous tissue disorders	Hyperkeratosis	鶏眼，胼胝腫
	顔面浮腫	Skin and subcutaneous tissue disorders	Face oedema	顔の浮腫
	丘疹	Skin and subcutaneous tissue disorders	Rash papular	右外眼角の丘疹，手指紅色丘疹
	紅斑	Skin and subcutaneous tissue disorders	Erythema	紅斑（躯幹・四肢），発赤（顔面）
	湿疹	Skin and subcutaneous tissue disorders	Eczema	外陰部湿疹，湿疹，湿疹（右手甲），湿疹（右前腕），湿疹（肩・前腕），湿疹（腰部）の悪化，湿疹（左ふくらはぎ内側），湿疹（耳後，前胸部），湿疹（首），湿疹（背中），湿疹の悪化，足湿疹
	接触性皮膚炎	Skin and subcutaneous tissue disorders	Dermatitis contact	接触性皮膚炎（顔面），接触皮フ炎（上肢）
	全身性皮疹	Skin and subcutaneous tissue disorders	Rash	発疹（全身）
	多汗症	Reproductive system and breast disorders	Menopausal symptoms	発汗
	爪の障害	Skin and subcutaneous tissue disorders	Nail disorder	両足母趾の爪の変形
	発疹	Skin and subcutaneous tissue disorders	Dermatitis contact	かぶれ（ナプキンによる）
	発疹	Skin and subcutaneous tissue disorders	Rash	頚部発疹，発疹，発疹（右上腹部・背部），両前腕発疹
	皮脂欠乏性湿疹	Skin and subcutaneous tissue disorders	Eczema asteatotic	皮脂欠乏性湿疹，乏脂性湿疹（臀部・両下肢）
	皮膚炎	Skin and subcutaneous tissue disorders	Dermatitis	慢性皮膚炎の悪化，目，口周囲のかぶれ
	皮膚乾燥	Skin and subcutaneous tissue disorders	Dry skin	皮膚乾燥感
	皮膚嚢腫	Skin and subcutaneous tissue disorders	Dermal cyst	アテローム（右乳房），左頚部粉瘤の悪化，粘液のう胞（指爪），粉瘤
	稗粒腫	Skin and subcutaneous tissue disorders	Milia	稗粒腫（顔）
	蕁麻疹	Skin and subcutaneous tissue disorders	Urticaria	じん麻疹，顔面膨疹，蕁麻疹，蕁麻疹，湿疹
免疫系障害	家塵アレルギー	Immune system disorders	House dust allergy	ダニアレルギー

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SOC 分類名	PT 用語	SOC 分類名	PT 用語	
	季節性アレルギー	Immune system disorders	Seasonal allergy	スギ花粉症，花粉症，花粉症（アレルギー性鼻炎，アレルギー性結膜炎）
	植物アレルギー	Immune system disorders	Allergy to plants	ぶた草アレルギー
	節足動物刺傷アレルギー	Injury, poisoning and procedural complications	Arthropod sting	虫刺症，虫刺症（右上肢）
良性，悪性および詳細不明の新生物（嚢胞およびポリープを含む）	リンパ節転移	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to lymph nodes	胃癌によるリンパ節転移
	胃癌	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Gastric cancer	胃癌
	肝転移	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Hepatic cancer metastatic	胃癌による肝転移
	子宮平滑筋腫	Reproductive system and breast disorders	Uterine leiomyoma	子宮筋腫
	脂肪腫	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Lipoma	脂肪腫（右肩），脂肪腫（良性）（右膝部側面内側）
	乳腺線維腫	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Fibroma	左乳頭良性線維腫の悪化
	乳腺線維腺腫	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Fibroadenoma of breast	乳腺線維腺腫
	皮膚乳頭腫	Skin and subcutaneous tissue disorders	Skin papilloma	いぼ（首）
	卵巣新生物	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Ovarian neoplasm	左卵巣嚢腫，卵巣のう腫
臨床検査	アンチトロンビンＩＩＩ減少	Investigations	Antithrombin III decreased	ATⅢ抗原量減少
	プロトロンビン時間延長	Investigations	Prothrombin time prolonged	PT 時間延長，PT 増加
	リンパ球百分率減少	Investigations	Lymphocyte percentage decreased	Lympho 低下
	γ－グルタミルトランスフェラーゼ増加	Investigations	Gamma-glutamyltransferase increased	γ－GTP 上昇
	活性化部分トロンボプラスチン時間延長	Investigations	Activated partial thromboplastin time prolonged	APTT 延長，APTT 増加
	肝機能検査値異常	Investigations	Liver function test abnormal	肝機能検査値上昇
	凝固時間延長	Investigations	Coagulation time prolonged	血液凝固時間延長（APTT，PT）
	血圧上昇	Investigations	Blood pressure increased	一過性の血圧上昇，血圧上昇
	血圧低下	Investigations	Blood pressure decreased	血圧低下
	血小板数減少	Investigations	Platelet count decreased	血小板減少
	血中クレアチニン増加	Investigations	Blood creatinine increased	クレアチニン上昇
	血中トリグリセリド増加	Investigations	Blood triglycerides increased	TG の上昇，TG 高値上昇，中性脂肪高値，中性脂肪上昇，中性脂肪値の上昇，中性脂肪値上昇
	血中ビリルビン増加	Investigations	Blood bilirubin increased	T－Bill 上昇，総ビリルビンの上昇
	血中フィブリノゲン減少	Investigations	Blood fibrinogen decreased	フィブリノーゲン減少，フィブリノーゲン低下
	血中ブドウ糖増加	Investigations	Blood glucose increased	血糖（空腹時）上昇，血糖値の高値異常，血糖値上昇
	血中甲状腺刺激ホルモン減少	Investigations	Blood thyroid stimulating hormone decreased	TSH の低下，TSH 減少，TSH 低下
	血中甲状腺刺激ホルモン増加	Investigations	Blood thyroid stimulating hormone increased	TSH の上昇，TSH 高値，TSH 上昇，TSH 値上昇

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SOC 分類名	PT 用語	SOC 分類名	PT 用語	
	好酸球数増加	Investigations	Eosinophil count increased	好酸球の増加
	好酸球百分率増加	Investigations	Eosinophil percentage increased	白血球像（Eosino）増加
	好中球百分率増加	Investigations	Neutrophil percentage increased	Neutr 上昇
	子宮頚部スミア異常	Investigations	Smear cervix abnormal	子宮頚部細胞診 classⅢ，子宮頚部細胞診 classⅢa，子宮頸部細胞診 classⅢa，子宮頸部細胞診Ⅲa，子宮頸部細胞診 classⅢa
	脂質増加	Investigations	Lipids increased	血清脂質値上昇（T－cho，LDL－cho，アポ蛋白 B），血清脂質値上昇（T－cho，LDL－cho，アポ蛋白 B），血清脂質値上昇（総コレステロール，LDL－コレステロール，TG），脂質系検査値（T－cho，LDL－cho，アポ蛋白 B）の異常変動
	体重増加	Investigations	Weight increased	体重増加
	低比重リポ蛋白増加	Investigations	Low density lipoprotein increased	LDL－コレステロール値の上昇
	尿中ブドウ糖陽性	Investigations	Glucose urine present	尿糖（陽性）
	尿中蛋白陽性	Investigations	Protein urine present	尿蛋白（２＋）
	尿量減少	Investigations	Urine output decreased	尿量減少
	白血球数減少	Investigations	White blood cell count decreased	白血球数の低下，白血球数減少

表 2.7.6.4- 10 試験 010646：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%）

総括報告書 B123，表 14-3-1-1 より引用

14-3-1-1 随伴症状要約表 1/2

随伴症状種類別発現例数

	薬剤群			合計
	2.0mg 群	0.5mg 群	1.0mg 群	
乳房緊満（感）	3		1	4
湿疹	1	1	1	3
そう痒感	2			2
帯下	2			2
乳房痛	1	1		2
胃不快感		1	1	2
腹部膨満感	2			2
浮腫	1			1
下腹部緊迫感	1			1
むかつき		1		1
頭痛		1		1
ふらつき（感）		1		1
肩こり	1			1
下腹部痛	1			1
子宮内膜炎	1			1
かゆみ		1		1
下痢	1			1
咽頭痛		1		1
アレルギー性結膜炎	1			1
便秘	1			1

副作用種類別発現例数

	薬剤群			合計
	2.0mg 群	0.5mg 群	1.0mg 群	
乳房緊満（感）	3		1	4
乳房痛	1	1		2
湿疹	1		1	2
腹部膨満感	2			2
浮腫	1			1
下腹部緊迫感	1			1
むかつき		1		1
頭痛		1		1
ふらつき（感）		1		1
肩こり	1			1
下腹部痛	1			1
帯下	1			1
胃不快感		1		1
アレルギー性結膜炎	1			1
そう痒感	1			1
便秘	1			1

14-3-1-1 随伴症状要約表 2/2

重症度・因果関係別随伴症状

	0.5mg群						1.0mg群						2.0mg群						合計
	軽度		中等度		高度		軽度		中等度		高度		軽度		中等度		高度		
	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	関連なし	関連あり	
乳房緊満（感）												1		3					4
湿疹	1									1						1			3
乳房痛		1														1			2
そう痒感														1	1				2
帯下														1	1				2
胃不快感				1			1												2
腹部膨満感														1		1			2
咽頭痛			1																1
むかつき				1															1
肩こり																1			1
アレルギー性結膜炎																		1	1
下痢													1						1
頭痛				1															1
かゆみ	1																		1
下腹部痛														1					1
下腹部緊迫感														1					1
浮腫														1					1
便秘																1			1
ふらつき（感）				1															1
子宮内膜炎																	1		1

関連なし：関連なし／ないらしい

表 2.7.6.4- 11　　試験 010730：重症度別の有害事象発現率（例数，%）

総括報告書 A02614，表 14.3.1 より引用
（但し，治験薬との関連性判定別の有害事象の発現率は，報告書中に該当資料なし）

14.3.1　有害事象の表示

器官分類別有害事象一覧

	10μg					20μg					40μg				
症状	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)
皮膚・皮膚付属器障害															
ざ瘡	0	0	0	0	0	1	0	0	1	1.2	2	0	0	2	2.3
そう痒（症）	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
そう痒感	1	0	0	1	1.2	1	0	0	1	1.2	0	0	0	0	0
陰部そう痒症	3	0	0	3	3.6	0	1	0	1	1.2	0	0	0	0	0
湿疹	1	0	0	1	1.2	1	1	0	2	2.4	3	0	0	3	3.4
肌荒れ	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
発疹	0	1	0	1	1.2	1	0	0	1	1.2	1	0	0	1	1.1
皮膚疾患	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
腟そう痒	2	0	0	2	2.4	0	0	0	0	0	0	0	0	0	0
蕁麻疹	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
泌尿器系障害															
眼瞼浮腫	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
顔面浮腫	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
排尿困難	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
膀胱炎	1	0	0	1	1.2	1	1	0	2	2.4	0	1	0	1	1.1
抵抗機構障害															
帯状疱疹	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1.1
腟カンジダ症	0	1	0	1	1.2	0	0	0	0	0	0	0	0	0	0
聴覚・前庭障害															
耳の障害	0	0	0	0	0	2	0	0	2	2.4	1	0	0	1	1.1
耳鳴	1	0	0	1	1.2	1	0	0	1	1.2	0	0	0	0	0
難聴	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
中枢・末梢神経系障害															
ふらつき（感）	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
めまい	2	1	0	3	3.6	2	0	0	2	2.4	1	2	1	4	4.5
肩こり	0	0	0	0	0	1	0	0	1	1.2	2	1	0	3	3.4
頭重（感）	1	1	0	2	2.4	0	0	0	0	0	2	0	0	2	2.3
頭痛	4	1	0	5	6	6	1	1	8	9.6	5	0	0	5	5.7
頭部不快感	0	0	1	1	1.2	0	0	0	0	0	0	0	0	0	0
粘膜乾燥	1	0	0	1	1.2	0	0	0	0	0	1	0	0	1	1.1
代謝・栄養障害															
下肢浮腫	0	0	0	0	0	1	0	0	1	1.2	1	0	0	1	1.1
四肢浮腫	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
全身浮腫	1	0	0	1	1.2	1	0	0	1	1.2	1	0	0	1	1.1
体重増加	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
浮腫	0	1	0	1	1.2	0	0	0	0	0	1	0	0	1	1.1

症状	10μg					20μg					40μg				
	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)
赤血球障害															
貧血	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
精神障害															
いらいら感	1	1	0	2	2.4	2	0	0	2	2.4	0	0	0	0	0
自殺企図	0	0	1	1	1.2	0	0	0	0	0	0	0	0	0	0
不眠（症）	0	0	0	0	0	1	0	0	1	1.2	1	0	0	1	1.1
消化管障害															
胃ポリープ	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
胃痛	0	0	0	0	0	0	2	0	2	2.4	0	1	0	1	1.1
胃不快感	2	0	0	2	2.4	2	0	0	2	2.4	1	0	0	1	1.1
下腹部痛	4	2	0	6	7.2	3	2	0	5	6	2	1	0	3	3.4
消化管良性腫瘍	0	0	0	0	0	0	0	1	1	1.2	0	0	0	0	0
心窩部痛(心窩部の疼痛)	0	0	0	0	0	0	1	0	1	1.2	0	0	0	0	0
腹痛	2	0	0	2	2.4	2	0	0	2	2.4	2	4	0	6	6.8
むかつき	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
悪心	1	0	0	1	1.2	2	0	0	2	2.4	2	3	0	5	5.7
胃もたれ感	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
胃不調	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
胸やけ	1	0	0	1	1.2	1	0	0	1	1.2	0	0	0	0	0
口内炎	2	0	0	2	2.4	2	0	0	2	2.4	0	0	0	0	0
歯周炎	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
歯痛	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1.1
歯肉出血	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
十二指腸潰瘍	0	0	0	0	0	0	0	1	1	1.2	0	0	0	0	0
舌荒れ	0	1	0	1	1.2	0	0	0	0	0	0	0	0	0	0
潰瘍性大腸炎	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
吐き気	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
腹部膨満感	6	1	0	7	8.4	2	1	0	3	3.6	6	0	0	6	6.8
嘔気	0	0	0	0	0	1	0	0	1	1.2	1	1	0	2	2.3
女性生殖（器）障害															
外陰炎	0	1	0	1	1.2	1	0	0	1	1.2	0	0	0	0	0
外陰部不快感	1	0	0	1	1.2	0	0	0	0	0	2	0	0	2	2.3
月経痛	1	0	0	1	1.2	0	0	0	0	0	1	0	0	1	1.1
子宮の障害	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
子宮頸部ポリープ	2	0	0	2	2.4	0	0	0	0	0	1	0	0	1	1.1
帯下	8	3	0	11	13.3	6	1	0	7	8.4	3	1	0	4	4.5
乳房緊満（感）	8	1	0	9	10.8	10	2	0	12	14.5	13	2	0	15	17
乳房痛	5	0	0	5	6	6	0	0	6	7.2	2	1	0	3	3.4
非産褥性乳汁分泌	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
卵巣腫大	0	0	0	0	0	0	1	0	1	1.2	0	0	0	0	0
腟部不快感	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
自律神経系障害															
下痢	1	1	0	2	2.4	2	0	0	2	2.4	0	1	0	1	1.1
乾燥症	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
動悸	1	0	0	1	1.2	1	0	0	1	1.2	1	0	0	1	1.1
便秘	1	0	0	1	1.2	1	1	0	2	2.4	1	0	0	1	1.1

症状	10μg					20μg					40μg				
	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)	軽度	中等度	高度	計	発現率(%)
視覚障害															
眼の充血	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
眼痛	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
眼瞼痙攣	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
白内障	0	0	1	1	1.2	0	0	0	0	0	0	0	0	0	0
霧視（感）	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
呼吸器系障害															
かぜ症候群	9	0	0	9	10.8	6	1	0	7	8.4	6	3	0	9	10.2
咽頭痛	0	0	1	1	1.2	1	0	0	1	1.2	0	0	0	0	0
過呼吸	0	1	0	1	1.2	0	0	0	0	0	0	0	0	0	0
咳	1	0	1	2	2.4	1	0	0	1	1.2	0	0	0	0	0
咳嗽	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
上気道感染	1	0	0	1	1.2	2	0	0	2	2.4	0	0	0	0	0
鼻炎	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1.1
鼻汁	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
鼻出血	1	0	0	1	1.2	1	0	0	1	1.2	0	0	0	0	0
扁桃炎	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
痰	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
血管（心臓外）障害															
静脈炎	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1.1
筋・骨格系障害															
関節痛	0	0	0	0	0	2	0	0	2	2.4	2	0	0	2	2.3
頸部痛	1	1	0	2	2.4	0	0	0	0	0	0	0	0	0	0
腰痛	4	1	0	5	6	2	2	1	5	6	4	0	0	4	4.5
骨痛	0	0	0	0	0	1	0	0	1	1.2	0	0	0	0	0
一般的全身障害															
胸痛	0	0	0	0	0	1	0	0	1	1.2	1	0	0	1	1.1
倦怠（感）	0	0	0	0	0	1	0	0	1	1.2	1	1	0	2	2.3
脱力（感）	1	0	0	1	1.2	0	0	0	0	0	0	0	0	0	0
発熱	2	2	0	4	4.8	4	1	0	5	6	1	0	0	1	1.1
疲労	0	1	0	1	1.2	0	0	0	0	0	1	0	0	1	1.1
微熱	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1
その他の特殊感覚障害															
にがみ	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1.1

表 2.7.6.4- 12　　試験 010731：重症度別の有害事象発現率（例数，%）

総括報告書 A02103 14 項，表 19（投与群別発現率），表 20（投与群別発現率）より引用

14-表19 薬剤群別の有害事象

有害事象の症状	Ⅰ群			Ⅱ群			Ⅲ群			全体		
	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間
GOT上昇*	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
GPT上昇*	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
いらいら感	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
かぜ症候群	5	10.0	3.0 ～ 21.8	5	9.8	3.3 ～ 21.4	0	-	-	10	6.6	3.2 ～ 11.8
かゆみ	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
くしゃみ発作	0	-	-	0	-	-	1	2.0	0.1 ～ 10.6	1	0.7	0.0 ～ 3.6
そう痒感	0	-	-	1	2.0	0.0 ～ 10.4	1	2.0	0.1 ～ 10.6	2	1.3	0.2 ～ 4.7
めまい	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
胃腸障害	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
胃痛	0	-	-	2	3.9	0.5 ～ 13.5	1	2.0	0.1 ～ 10.6	3	2.0	0.4 ～ 5.7
咽頭痛	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
下肢痛	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
下肢浮腫	0	-	-	0	-	-	1	2.0	0.1 ～ 10.6	1	0.7	0.0 ～ 3.6
下肢冷感	0	-	-	0	-	-	1	2.0	0.1 ～ 10.6	1	0.7	0.0 ～ 3.6
下腹部痛	1	2.0	0.1 ～ 10.6	5	9.8	3.3 ～ 21.4	4	8.0	2.2 ～ 19.2	10	6.6	3.2 ～ 11.8
下痢	0	-	-	2	3.9	0.5 ～ 13.5	2	4.0	0.5 ～ 13.7	4	2.6	0.7 ～ 6.6
外陰部不快感	0	-	-	0	-	-	1	2.0	0.1 ～ 10.6	1	0.7	0.0 ～ 3.6
肝(細胞)癌	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
関節痛	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
眼の炎症	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
眼瞼浮腫	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
顔面湿疹	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
気管支炎	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
頚部痛	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
血圧上昇	1	2.0	0.1 ～ 10.6	1	2.0	0.0 ～ 10.4	0	-	-	2	1.3	0.2 ～ 4.7
月経痛	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
肩こり	2	4.0	0.5 ～ 13.7	0	-	-	0	-	-	2	1.3	0.2 ～ 4.7
口渇	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
口唇炎	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
口唇痛	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
喉頭炎	1	2.0	0.1 ～ 10.6	0	-	-	0	-	-	1	0.7	0.0 ～ 3.6
喉頭痛	0	-	-	1	2.0	0.0 ～ 10.4	0	-	-	1	0.7	0.0 ～ 3.6
腰痛	2	4.0	0.5 ～ 13.7	4	7.8	2.2 ～ 18.9	1	2.0	0.1 ～ 10.6	7	4.6	1.9 ～ 9.3

*：院内検査の結果にて有害事象と判定

14-表19 薬剤群別の有害事象（続き）

有害事象の症状	Ⅰ群			Ⅱ群			Ⅲ群			全体		
	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間	症例数	発現率(%)	95%信頼区間
坐骨神経痛	0	-	-	1	2.0	0.0～10.4	0	-	-	1	0.7	0.0～3.6
痔出血	1	2.0	0.1～10.6	0	-	-	1	2.0	0.1～10.6	2	1.3	0.2～4.7
耳鳴	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
湿疹	2	4.0	0.5～13.7	5	9.8	3.3～21.4	1	2.0	0.1～10.6	8	5.3	2.3～10.2
手指しびれ(感)	0	-	-	1	2.0	0.0～10.4	0	-	-	1	0.7	0.0～3.6
腫瘤	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
上気道感染	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
食欲減退	0	-	-	0	-	-	1	2.0	0.1～10.6	1	0.7	0.0～3.6
食欲不振	0	-	-	1	2.0	0.0～10.4	0	-	-	1	0.7	0.0～3.6
舌疼痛	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
全身浮腫	0	-	-	1	2.0	0.0～10.4	1	2.0	0.1～10.6	2	1.3	0.2～4.7
息苦しい	0	-	-	1	-	-	0	-	-	1	0.7	0.0～3.6
息切れ	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
体重増加	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
帯下	11	22.0	11.5～36.0	12	23.5	2.8～37.5	9	18.0	8.6～31.4	32	21.2	5.0 28.6
中耳炎	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
腸管閉塞	0	-	-	0	-	-	1	2.0	0.1～10.6	1	0.7	0.0～3.6
吐き気	0	-	-	3	5.9	1.2～16.2	0	-	-	3	2.0	0.4～5.7
頭痛	2	4.0	0.5～13.7	7	13.7	5.7～26.3	1	2.0	0.1～10.6	10	6.6	3.2～11.8
動悸	1	2.0	0.1～10.6	1	2.0	0.0～10.4	0	-	-	2	1.3	0.2～4.7
乳房緊満(感)	5	10.0	3.3～21.8	7	13.7	5.7～26.3	10	20.0	10.0～33.7	22	14.6	9.4～21.2
乳房痛	1	2.0	0.1～10.6	4	7.8	2.2～18.9	2	4.0	0.5～13.7	7	4.6	1.9～9.3
背(部)痛	0	-	-	0	-	-	1	2.0	0.1～10.6	1	0.7	0.0～3.6
発疹	1	2.0	0.1～10.6	0	-	-	1	2.0	0.1～10.6	2	1.3	0.2～4.7
発熱	0	-	-	2	3.9	0.5～13.5	0	-	-	2	1.3	0.2～4.7
疲労	2	4.0	0.5～13.7	0	-	-	0	-		2	1.3	0.2～4.7
鼻汁	0	-	-	0	-	-	1	2.0	0.1～10.6	1	0.7	0.0～3.6
鼻出血	2	4.0	0.5～13.7	1	2.0	0.0～10.4	0	-	-	3	2.0	0.4～5.7
頻尿	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
腹痛	2	4.0	0.5～13.7	1	2.0	0.0～10.4	2	4.0	0.5～13.7	5	3.3	1.1～7.6
腹部膨満感	3	6.0	1.3～16.5	5	9.8	3.3～21.4	5	10.0	3.3～21.8	13	8.6	4.7～14.3
便秘	0	-	-	0	-	-	2	4.0	0.5～13.7	2	1.3	0.2～4.7
味覚異常	0	-	-	1	2.0	0.0～10.4	0	-	-	1	0.7	0.0～3.6
喘息発作	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
嘔吐	0	-	-	0	-	-	1	2.0	0.1～10.6	1	0.7	0.0～3.6
膀胱炎	1	2.0	0.1～10.6	0	-	-	0	-	-	1	0.7	0.0～3.6
腟そう痒	0	-	-	1	2.0	0.0～10.4	1	2.0	0.1～10.6	2	1.3	0.2～4.7
蕁麻疹	0	-	-	1	2.0	0.0～10.4	0	-	-	1	0.7	0.0～3.6

14-表20 症状の程度別の有害症状

症状	程度			合計
	軽度	中等度	高度	
GOT上昇*	0	1	0	1
GPT上昇*	0	1	0	1
いらいら感	1	0	0	1
かぜ症候群	10	0	0	10
かゆみ	1	0	0	1
くしゃみ発作	0	1	0	1
そう痒感	2	0	0	2
めまい	1	0	0	1
胃腸障害	1	0	0	1
胃痛	2	1	0	3
咽頭痛	1	0	0	1
下肢痛	0	1	0	1
下肢浮腫	0	1	0	1
下肢冷感	0	1	0	1
下腹部痛	8	2	0	10
下痢	3	1	0	4
外陰部不快感	1	0	0	1
肝(細胞)癌	0	0	1	1
関節痛	1	0	0	1
眼の炎症	1	0	0	1
眼瞼浮腫	1	0	0	1
顔面湿疹	1	0	0	1
気管支炎	1	0	0	1
頚部痛	1	0	0	1
血圧上昇	1	1	0	2
月経痛	1	0	0	1
肩こり	2	0	0	2
口渇	1	0	0	1
口唇炎	1	0	0	1
口唇痛	0	1	0	1
喉頭炎	1	0	0	1
喉頭痛	1	0	0	1
腰痛	6	1	0	7
坐骨神経痛	0	1	0	1
痔出血	1	1	0	2
耳鳴	0	1	0	1

症状	程度			合計
	軽度	中等度	高度	
湿疹	8	0	0	8
手指しびれ(感)	1	0	0	1
腫瘤	0	1	0	1
上気道感染	1	0	0	1
食欲減退	1	0	0	1
食欲不振	1	0	0	1
舌疼痛	0	1	0	1
全身浮腫	2	0	0	2
息苦しい	1	0	0	1
息切れ	0	1	0	1
体重増加	0	1	0	1
帯下	32	0	0	32
中耳炎	0	1	0	1
腸管閉塞	0	1	0	1
吐き気	3	0	0	3
頭痛	7	2	1	10
動悸	2	0	0	2
乳房緊満(感)	22	0	0	22
乳房痛	6	1	0	7
背(部)痛	1	0	0	1
発疹	2	0	0	2
発熱	1	1	0	2
疲労	2	0	0	2
鼻汁	0	1	0	1
鼻出血	3	0	0	3
頻尿	1	0	0	1
腹痛	5	0	0	5
腹部膨満感	12	1	0	13
便秘	2	0	0	2
味覚異常	1	0	0	1
喘息発作	1	0	0	1
嘔吐	1	0	0	1
膀胱炎	0	1	0	1
腟そう痒	2	0	0	2
蕁麻疹	1	0	0	1

*：院内検査の結果にて有害事象と判定

表 2.7.6.4- 13　　試験 010568：重症度別，治験薬との関連性判定別の有害事象発現率（例数，%）

総括報告書 B006　表 14-3-1 より引用

症状単位集計			重症度					関連性							
器官分類	症状	投与群	症状なし	軽度	中等度	高度	対象例数	症状なし	関連なし	不明	可能性あり	おそらくあり	明らかにあり	随伴症状(%)	関連性ありの随伴症状(%)
皮膚・皮膚付属器障害	湿疹	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	1	0	0	0	0	4.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	白斑	ﾌﾟﾗｾﾎﾞ	21	1	0	0	22	21	1	0	0	0	0	4.5	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
筋・骨格系障害	腰痛	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	1	0	0	0	0	4.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	骨折	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	26	0	0	1	27	26	1	0	0	0	0	3.7	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	変形性脊椎症	ﾌﾟﾗｾﾎﾞ	21	0	1	0	22	21	1	0	0	0	0	4.5	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
中枢・末梢神経系障害	頭痛	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	0	1	0	25	24	0	0	1	0	0	4.0	4.0
		1.0 mg	26	0	0	1	27	26	0	0	0	0	1	3.7	3.7
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	下肢しびれ（感）	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	1	0	0	0	0	4.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
自律神経系障害	嘔吐	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	0	0	0	0	1	3.8	3.8

症状単位集計			重症度					関連性							
器官分類	症状	投与群	症状なし	軽度	中等度	高度	対象例数	症状なし	関連なし	不明	可能性あり	おそらくあり	明らかにあり	随伴症状(%)	関連性ありの随伴症状(%)
自律神経系障害	下痢	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	0	1	0	0	0	4.0	4.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	血圧上昇	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	1	0	0	0	0	4.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
聴覚・前庭障害	難聴	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	1	0	0	0	0	3.8	0.0
消化管障害	嘔気	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	0	1	0	25	24	1	0	0	0	0	4.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	0	0	0	0	1	3.8	3.8
	悪心	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	0	1	0	25	24	0	0	0	1	0	4.0	4.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	吐き気	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	25	1	0	1	27	25	0	0	0	0	2	7.4	7.4
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	胃痛	ﾌﾟﾗｾﾎﾞ	21	1	0	0	22	21	1	0	0	0	0	4.5	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	26	1	0	0	27	26	1	0	0	0	0	3.7	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	上腹部痛	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	26	1	0	0	27	26	1	0	0	0	0	3.7	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0

症状単位集計			重症度				対象例数	関連性						随伴症状(%)	関連性ありの随伴症状(%)
器官分類	症状	投与群	症状なし	軽度	中等度	高度		症状なし	関連なし	不明	可能性あり	おそらくあり	明らかにあり		
消化管障害	腹部膨満感	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	1	0	0	26	25	0	0	0	0	1	3.8	3.8
代謝・栄養障害	体重増加	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	1	0	0	26	25	0	0	0	1	0	3.8	3.8
血管（心臓外）障害	静脈血栓（症）	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	0	0	1	0	0	3.8	3.8
呼吸器系障害	はなかぜ	ﾌﾟﾗｾﾎﾞ	21	1	0	0	22	21	1	0	0	0	0	4.5	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	喉頭良性腫瘍	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	1	0	0	0	0	3.8	0.0
女性生殖（器）障害	陰門腫脹感	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	1	0	0	26	25	0	1	0	0	0	3.8	3.8
	子宮内膜増殖(症)	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	26	0	0	0	1	0	3.7	3.7
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	乳房痛	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	26	1	0	0	27	26	0	0	0	1	0	3.7	3.7
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	乳房緊満（感）	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	1	0	0	25	24	0	0	1	0	0	4.0	4.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	23	2	1	0	26	23	0	0	1	1	1	11.5	11.5

症状単位集計			重症度				対象例数	関連性						随伴症状(%)	関連性ありの随伴症状(%)
器官分類	症状	投与群	症状なし	軽度	中等度	高度		症状なし	関連なし	不明	可能性あり	おそらくあり	明らかにあり		
女性生殖（器）障害	帯下	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	0	0	0	0	1	3.8	3.8
一般的全身障害	疼痛	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	24	0	1	0	25	24	0	1	0	0	0	4.0	4.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	26	0	0	0	26	26	0	0	0	0	0	0.0	0.0
	発熱	ﾌﾟﾗｾﾎﾞ	22	0	0	0	22	22	0	0	0	0	0	0.0	0.0
		0.5 mg	25	0	0	0	25	25	0	0	0	0	0	0.0	0.0
		1.0 mg	27	0	0	0	27	27	0	0	0	0	0	0.0	0.0
		2.0 mg	25	0	1	0	26	25	1	0	0	0	0	3.8	0.0

表 2.7.6.4- 14　　試験 ■216：有害事象例数

総括報告書 A00403 14 項, T135 より引用

T 135:　　AEs during treatment period: Frequency of adverse events (safety population + center no. 6)

	cohort	
	safety population	center no.6
	N	N
Preferred Term		
Vaginal hemorrhage	32	0
Hypertension	7	0
Breast pain	6	0
Uterine fibroids enlarged	4	0
Rash	3	0
Abdominal pain	3	0
Cyst	3	0
Allergic reaction	2	0
Infection	2	0
Peripheral edema	2	0
Dizziness	2	0
Pain	2	0
Angina pectoris	2	0
Arrhythmia	2	0
Anxiety	2	0
Chills	2	0
Bronchitis	2	0
Pain in extremity	2	0
Herpes simplex	1	0
Hyperthyroidism	1	0

(Continued)

T 135: Frequency of adverse events during treatment period (safety population + center no. 6) (ctd.)

	cohort	
	safety population	center no.6
	N	N
Preferred Term		
Stomach ulcer	1	0
Urticaria	1	0
Endometrial disorder	1	0
Endometrial neoplasm	1	0
Depression	1	0
Muscle cramps	1	0
Urinary incontinence	1	0
Superficial thrombophlebitis	1	0
Spontaneous bone fracture	1	0
Headache	1	0
Gamma-GT increased	1	0
Hyperglycemia	1	0
Palpitation	1	0
Leukocytosis	1	0
Hot flashes	0	1
Uterine disorder	1	0
Tachycardia	1	0
Weight gain	1	0
Pharyngitis	1	0
Fibrocystic breast	1	0
Vaginitis	1	0
Agitation	1	0
Bilirubinemia	1	0
All	104	1

表 2.7.6.4- 15 試験 ■216 の 1 年延長試験：有害事象発現例数

総括報告書 A06276, TT54, TT53（重症度別の SOC 分類集計）, T39（関連性別の SOC 分類集計）より引用

TT 54: AEs by preferred term (HARTS): Visit 7 – Visit 11 (safety)

Preferred Term	cohort
	safety population
	N
Back pain	3
Uterine fibroids enlarged	2
Vaginal hemorrhage	2
Bronchitis	2
Cerebral ischemia	1
Hyperglycemia	1
Peptic ulcer	1
Pharyngitis	1
Abdominal pain	1
All	14

TT 53: Intensity of AEs by body system: Visit 7 – Visit 11 (safety)

HARTS-Code	cohort			
	safety popul.			
	Maximum intensity			
	mild	moderate	severe	N
Body as a Whole	1	3	0	4
Cardiovascular System	0	0	1	1
Digestive System	0	1	0	1
Metabolic and Nutritional Disorders	0	1	0	1
Respiratory System	2	1	0	3
Urogenital System	4	0	0	4
All	7	6	1	14

T 39: Causal relationship of AEs to SH T 594 B

Body-System	Related to study drug		
	no	unlikely	possible
	n	n	n
Body as a Whole	4	0	0
Cardiovascular System	0	0	1
Digestive System	0	0	1
Metabolic and Nutritional Disorders	0	1	0
Respiratory System	3	0	0
Urogenital System	0	0	4
All	7	1	6

表 2.7.6.4- 16　　試験 ■065：有害事象発現率（例数，%）

総括報告書 A00404，T62，TT72（関連性別の SOC 分類集計）TT77（関連性別の SOC 分類集計）より引用

T 62:　　Adverse events (preferred term) during treatment period

Events during Treatment (Preferred Term)	SH T 594 B	CEE/MPA＊
	N	N
Preferred Term		
Vaginal hemorrhage	41	10
Hypertension	9	4
Urinary tract infection	9	1
Bronchitis	6	2
Infection	5	3
Uterine fibroids enlarged	5	3
WBC abnormal	6	2
Vaginitis	4	3
Papanicolaou smear suspicious	3	2
Pharyngitis	2	2
Headache	2	2
Surgery	3	1
Breast pain	1	3
Gamma-GT increased	3	1
Liver function test abnormal	2	2
Cervix disorder	3	0
Gingivitis	1	2
Hyperglycemia	2	1
Hematuria	2	1
Endometrial disorder	1	1
Abdominal pain	2	0
Arthrosis	2	0

(Continued)

＊新薬承認情報提供時に置き換え

T 62: Adverse events (preferred term) during treatment period (ctd.)

Events during Treatment (Preferred Term)	SH T 594 B	CEE/MPA＊
	N	N
Preferred Term		
Back pain	2	0
Endometrial hyperplasia	1	1*
Pain	1	1
Peripheral edema	2	0
Diabetes mellitus	2	0
Dyspepsia	0	2
Cyst	2	0
Gastritis	1	0
Weight gain	1	0
Endometrial neoplasm	1	0
Vertigo	0	1
Hemorrhage	1	0
Hypotension	1	0
Insomnia	1	0
Rash	1	0
Suicide attempt other than overdose	1	0
Muscle cramps	0	1
Depression	1	0
Urogenital disorder	0	1
Herpes zoster	1	0
Gastrointestinal carcinoma	1	0
Cholelithiasis	0	1
Spontaneous bone fracture	1	0
Hyperlipemia	1	0

* This was the finding of the local pathologist, the final classification of the central pathologists was 'strips of benign surface'

(Continued)

T 62: Adverse events (preferred term) during treatment period (ctd.)

Events during Treatment (Preferred Term)	SH T 594 B	CEE/MPA＊
	N	N
Preferred Term		
Otitis externa	1	0
Tachycardia	1	0
Menorrhagia	1	0
Asthma	1	0
Pleural disorder	1	0
Cholecystitis	1	0
Bilirubinemia	1	0
Urinary urgency	0	1
BUN increased	0	1
Anemia	1	0
Joint disorder	1	0
Diarrhea	1	0
Libido decreased	1	0
Varicose vein	0	1
Superficial thrombophlebitis	0	1
Creatinine increased	1	0
Metrorrhagia	0	1
Vulvovaginitis	0	1
Asthenia	1	0
Laryngitis	1	0
Hemorrhagic gastritis	0	1
Gastrointestinal disorder	0	1
Rhinitis	0	1
Alkaline phosphatase increased	0	1
All	151	64

＊新薬承認情報提供時に置き換え

TT 72: AEs during treatment period

Body-System by group	SH T 594 B			CEE/MPA＊			
	Intensity			Intensity			
	mild	moderate	severe	mild	moderate	severe	
	n	n	n	n	n	n	n
Body as a Whole	4	10	3	1	1	3	22
Cardiovascular System	8	3	1	3	2	1	18
Digestive System	1	5	1	4	5	0	16
Endocrine System	2	0	0	0	0	0	2
Hemic and Lymphatic System	6	1	0	2	0	0	9
Metabolic & Nutritional System	5	6	0	3	1	0	15
Musculoskeletal System	3	1	0	0	1	0	5
Nervous System	1	3	1	1	1	1	8
Respiratory System	1	10	0	2	2	1	16
Skin and Appendages	2	1	0	1	2	0	6
Special Senses	0	1	0	0	0	0	1
Urogenital System	25	12	34	10	10	6	97
All	58	53	40	27	25	12	215

＊新薬承認情報提供時に置き換え

Nihon Schering K.K.

TT 77: Adverse events – relation to study drug

HARTS Body System	SH T 594 B Total = 151 AEs Relation to study drug					CEE/MPA＊ Total = 64 AEs Relation to study drug				
	none	un-likely	pos-sible	pro-bable	defi-nite	none	un-likely	pos-sible	pro-bable	defi-nite
Body as a whole	12	1	2	1	1	4	0	1	0	0
Cardiovascular system	7	1	3	1	0	2	0	2	2	0
Digestive system	4	1	2	0	0	6	2	1	0	0
Endocrine System	2	0	0	0	0	0	0	0	0	0
Hemic & Lymphatic System	6	1	0	0	0	2	0	0	0	0
Metabolic & Nutritional Disorders	3	2	5	1	0	2	1	1	0	0
Musculoskeletal System	3	1	0	0	0	0	0	1	0	0
Nervous System	0	1	3	0	1	0	1	2	0	0
Respiratory System	10	1	0	0	0	4	1	0	0	0
Skin & appendages	1	0	1	1	0	0	0	3	0	0
Special Senses	1	0	0	0	0	0	0	0	0	0
Urogenital System	21	4	21	21	4	10	1	11	4	0
All	70	13	37	25	6	30	6	22	6	0

＊新薬承認情報提供時に置き換え