コセンティクス皮下注 150 mg シリンジ
コセンティクス皮下注 75 mg シリンジ
コセンティクス皮下注 150 mg ペン
に関する資料

ノバルティスファーマ株式会社

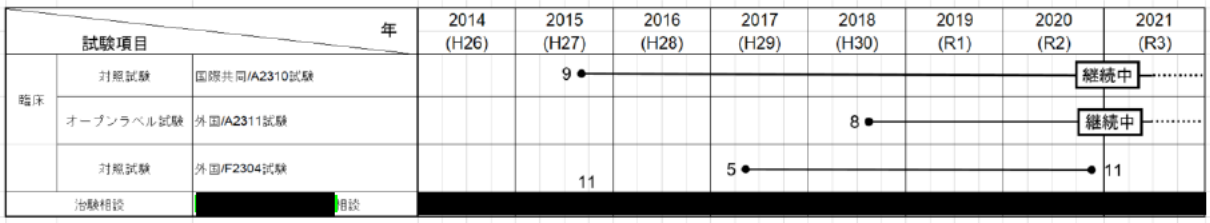
1.5 起源又は発見の経緯及び開発の経緯

1 起原又は発見の経緯

起原又は発見の経緯及び開発の経緯については「2.5 臨床に関する概括評価」を参照。

開発の経緯図を Figure 1-1 に示す。

Figure 1-1 開発の経緯図



1.6 外国における使用状況等に関する資料

目　　次

表 一 覧

1 外国における使用状況等

2021 年 7 月現在，本剤は EU 及び米国をはじめ世界 100 ヶ国以上で承認されている。EU 及び米国での承認状況を，Table 1-1 に示す。

Table 1-1 主要国での承認状況

国名	承認年月日	効能・効果
EU（中央審査方式）	2015 年 1 月 15 日	全身療法の対象となる中等症から重症の成人の局面型皮疹を有する乾癬
	2015 年 11 月 19 日	疾患修飾性抗リウマチ薬で十分な効果が得られない成人の活動性乾癬性関節炎
	2015 年 11 月 19 日	既存治療では十分な効果が得られない成人の活動性強直性脊椎炎
	2020 年 4 月 28 日	NSAIDs では十分な治療効果が得られない成人の客観的な炎症所見を有する X 線基準を満たさない体軸性脊椎関節炎
	2020 年 7 月 31 日	全身療法の対象となる 6 歳以上の小児及び青年における中等症から重症の局面型皮疹を有する乾癬
米国	2015 年 1 月 21 日	全身療法又は光線療法の対象となる中等症から重症の成人の局面型皮疹を有する乾癬
	2016 年 1 月 15 日	成人の活動性乾癬性関節炎
	2016 年 1 月 15 日	成人の活動性強直性脊椎炎
	2020 年 6 月 16 日	成人の客観的な炎症所見を有する活動性の X 線基準を満たさない体軸性脊椎関節炎
	2021 年 5 月 28 日	全身療法又は光線療法の対象となる 6 歳以上の患者における中等症から重症の局面型皮疹を有する乾癬

2 外国の添付文書等の概要

米国の添付文書（2021 年 5 月改訂）及び EU 共通の添付文書（2021 年 3 月改訂）の和訳の概略をそれぞれ Table 2-1，Table 2-2 に示す。

Table 2-1 アメリカの添付文書の概略

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
剤型・含量	注射液：使い捨て Sensoready®ペン*中 150 mg/mL 溶液 注射液：使い捨てプレフィルドシリンジ中 150 mg/mL 溶液 注射液：使い捨てプレフィルドシリンジ中 75 mg/0.5 mL 溶液 注射用：溶解用使い捨てバイアル入り 150 mg 凍結乾燥粉末（医療従事者のみが使用可能） * Sensoready®はプレフィルドペンの商標。原文は Sensoready®と記載されているが，ここではプレフィルドペンと記載する。
効能・効果	全身療法又は光線療法の対象となる 6 歳以上の患者における中等症から重症の局面型皮疹を有する乾癬 成人の活動性乾癬性関節炎 成人の活動性強直性脊椎炎 成人の客観的な炎症所見を有する活動性の X 線基準を満たさない体軸性脊椎関節炎
用法・用量	**局面型皮疹を有する乾癬**

<table>
<tr><td>販売名</td><td>コセンティクス ™（セクキヌマブ）注射液，皮下投与用
注射用コセンティクス ™（セクキヌマブ），皮下投与用</td></tr>
<tr><td></td><td>
<u>成人</u>
300 mg の皮下投与を初期投与として 0 週，1 週，2 週及び 3 週に実施し，4 週以降は毎月 300 mg を維持投与することを推奨する。300 mg を投与する場合，150 mg の用量を 2 回皮下投与する。
一部の患者に対しては 150 mg の投与も可とする。
<u>小児患者</u>
体重に基づいて（表 1）セクキヌマブの皮下投与を初期投与として 0 週，1 週，2 週，3 週に実施し，4 週以降は毎月維持投与することを 6 歳以上の小児患者に推奨する。
表 1　局面型皮疹を有する乾癬の 6 歳以上の小児患者に対する推奨用量
<table>
<tr><td>投与時体重</td><td>推奨用量</td></tr>
<tr><td>50 kg 未満</td><td>75 mg</td></tr>
<tr><td>50 kg 以上</td><td>150 mg</td></tr>
</table>

乾癬性関節炎
中等症から重症の局面型皮疹を有する乾癬を併発する乾癬性関節炎患者に対しては，局面型皮疹を有する乾癬の推奨用量を用いる。
それ以外の乾癬性関節炎患者に対しては，以下の推奨用量でコセンティクスを投与する。
推奨用量：
• 導入投与有りの場合，セクキヌマブ 150 mg を初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降は維持投与としてセクキヌマブ 150 mg を 4 週間隔で皮下投与する。
• 導入投与無しの場合，セクキヌマブ 150 mg を 4 週間隔で皮下投与する。
• 活動性の乾癬性関節炎の症状が継続する患者には，セクキヌマブ 300 mg を 4 週間隔で投与することを検討する
コセンティクスはメトトレキサート使用の有無を問わず投与される。
強直性脊椎炎
以下の推奨用量でコセンティクスを投与する
推奨用量：
• 導入投与有りの場合，セクキヌマブ 150 mg を初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降は維持投与としてセクキヌマブ 150 mg を 4 週間隔で皮下投与する。
• 導入投与無しの場合，セクキヌマブ 150 mg を 4 週間隔で皮下投与する。
• 活動性の強直性脊椎炎の症状が継続する患者には，セクキヌマブ 300 mg を 4 週間隔で投与することを検討する
X 線基準を満たさない体軸性脊椎関節炎
以下の推奨用量でコセンティクスを投与する
推奨用量：
• 導入投与有りの場合，セクキヌマブ 150 mg を初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降は維持投与としてセクキヌマブ 150 mg を 4 週間隔で皮下投与する。
• 導入投与無しの場合，セクキヌマブ 150 mg を 4 週間隔で皮下投与する。
コセンティクス投与開始前の評価
コセンティクスの投与開始前に結核感染について確認すること。
投与に関する重要な指示
</td></tr>
</table>

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	コセンティクスの剤形は 4 種類ある（プレフィルドペン，プレフィルドシリンジ[150 mg/mL, 75 mg/0.5 mL]，溶解用バイアル入り凍結乾燥粉末）。コセンティクス各剤形の「使用に関する指示」には，コセンティクスの調製及び投与に関するより詳細な指示が記載されている。溶解用バイアル入り凍結乾燥粉末は医療従事者のみが使用できる。 コセンティクスは医師の助言及び監督下で使用する。 プレフィルドペン 成人患者或いはその介護者はプレフィルドペンを用いた皮下投与手技に関する適切な訓練を受け，医師が適切と判断した患者或いはその介護者は自己投与してもよい。 小児患者は自己投与を行ってはいけない。その保護者が皮下投与手技に関する適切な訓練を受け，プレフィルドペンを用いて小児患者に投与しても良い。 プレフィルドシリンジ 成人患者或いはその介護者はプレフィルドシリンジを用いた皮下投与手技に関する適切な訓練を受け，医師が適切と判断した患者或いはその介護者は自己投与してもよい。 小児患者は自己投与を行ってはいけない。その保護者が皮下投与手技に関する適切な訓練を受け，プレフィルドシリンジを用いて小児患者に投与しても良い。 投与に関する指示 毎回，前回とは異なる解剖学的部位（上腕，大腿部，又は腹部の 4 つの区分のいずれか）に投与し，圧痛，打撲傷，紅斑，硬化が認められる又は乾癬の影響がある皮膚部位には投与しない。上腕外側への投与は介護者又は医療従事者が行う。 **コセンティクスプレフィルドペン及びプレフィルドシリンジ使用のための準備** 投与前に，コセンティクスプレフィルドペン又はコセンティクスプレフィルドシリンジを冷蔵庫から出し，針キャップを付けたままコセンティクスが室温になるまでおく（15～30 分）。 コセンティクスプレフィルドペン又はコセンティクスプレフィルドシリンジの取り外し可能なキャップには天然ゴムラテックスが含まれるため，ラテックスに感受性の高い者は取り扱ってはならない。 投与前に，粒子や変色がないか目視確認する，コセンティクス注射液は，澄明～わずかに混濁した，無色～微黄色の溶液である。肉眼で見える粒子が含まれているか，変色又は濁りがある場合は使用しない。コセンティクスには防腐剤は含まれていないため，プレフィルドペン又はプレフィルドシリンジは，冷蔵庫から出した後 1 時間以内に投与する。ペン又はシリンジに残った製剤は廃棄する。 **コセンティクス凍結乾燥粉末の溶解及び調製** コセンティクス凍結乾燥粉末は，訓練を受けた医療従事者が，無菌操作で中断せずに注射用滅菌水で調製及び溶解する。栓に穴を開けてから溶解が終わるまでの調製時間は平均 20 分であり，90 分を超えないこと。 a) コセンティクス凍結乾燥粉末のバイアルを冷蔵庫から出し，室温になるまで 15～30 分間おく。注射用滅菌水も室温にすること。 b) 注射用滅菌水 1 mL を，コセンティクス凍結乾燥粉末バイアルにゆっくり注入する。このとき，注射用滅菌水を粉末上に直接滴下する。 c) バイアルを約 45 度傾け，約 1 分間ゆっくりと指先で回転させる。バイアルを振とうしたり反転させたりしてはならない。 d) バイアルを室温に約 10 分間おき，溶解させる。泡が生じる可能性があることに注意する。 e) バイアルを約 45 度傾け，約 1 分間ゆっくりと指先で回転させる。バイアルを振とうしたり反転させたりしてはならない。

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	f) バイアルをそのまま室温に約 5 分間おく。溶解したコセンティクス溶液は，本来肉眼で見える粒子がなく，澄明～わずかに混濁した，無色～微黄色の溶液である。凍結乾燥粉末の溶解が不完全，液体中に眼に見える粒子がある，又は液体に濁りや変色がある場合は使用しない。 g) 必要な数のバイアルを準備する（150 mg 投与の場合 1 本，300 mg 投与の場合 2 本）。 h) コセンティクス溶液 1 mL 中にセクキヌマブは 150 mg 含まれている。溶解後は，直ちに使用するか，2°C～8°C（36°F～46°F）で冷蔵保存する（最長 24 時間）。冷凍はしない。 i) 2°C～8°C（36°F～46°F）で保存した場合，投与前に溶液が室温になるまでおく（15～30 分）。コセンティクスに防腐剤は含まれていないため，2°C～8°C（36°F～46°F）の保存場所から出した後は 1 時間以内に投与する。
使用上の注意	**禁忌** コセンティクスは，セクキヌマブ又は添加物のいずれかに対する重篤な過敏症反応の既往がある患者には禁忌とする。 **警告及び注意** <u>感染症</u> コセンティクスは感染のリスクを増大させる可能性がある。中等症から重症の局面型皮疹を有する乾癬患者を対象とした臨床試験において，プラセボ投与例に比べてコセンティクス投与例の方が感染症の発現率が高かった。プラセボ対照臨床試験において，一般的な感染症の発現率はコセンティクス投与例の方がプラセボ投与例に比べて高く，鼻咽頭炎は 11.4%対 8.6%，上気道感染は 2.5%対 0.7%，皮膚粘膜カンジダ症は 1.2%対 0.3%であった。乾癬性関節炎患者，強直性脊椎炎患者及び X 線基準を満たさない体軸性脊椎関節炎患者を対象としたプラセボ対照試験において，感染症のリスクについて乾癬患者と同様の傾向が見られた。臨床試験において，一部の感染症の発現率は用量依存的であった。また，コセンティクスを投与した患者において市販後で深刻な感染症及び致命的な感染症が報告されている。 慢性感染症を有する患者又は反復感染の既往がある患者にコセンティクスの使用を検討する際は注意すること。 感染を示唆する徴候や症状が生じた場合には医師の診察を受けるよう，患者に指導する。重篤な感染症を発現した患者については十分な観察を行い，感染症が消失するまでコセンティクスを投与しないこと。 <u>結核に関する投与前評価</u> コセンティクスの投与開始前に結核感染について患者を評価すること。活動性結核感染患者にコセンティクスを投与しないこと。コセンティクス投与前に潜在性結核の治療を開始すること。潜在性結核又は活動性結核の既往があり，十分な治療が確認できない患者にコセンティクスの投与を開始する前には，抗結核治療を検討すること。コセンティクスを投与する患者は，投与期間中及び投与後に，活動性結核の徴候及び症状を十分に観察すること。 <u>炎症性腸疾患</u> 炎症性腸疾患患者に対してコセンティクスを処方する際は注意すべきである。局面型皮疹を有する乾癬，乾癬性関節炎，強直性脊椎炎及び X 線基準を満たさない体軸性脊椎関節炎に対する臨床試験においてコセンティクスを投与された患者で，炎症性腸疾患の増悪が認められ，深刻な増悪が起こった事例や，新規の炎症性腸疾患の発現を認めた事例もあった。活動性クローン病の 59 名の患者を対象とした探索的試験において，プラセボ投与群と比較してコセンティクス投与群で，クローン病の疾患活動性増悪と有害事象の増加が見られた。コセンティクスを投与された患者の炎症性腸疾患の症状と徴候を観察すること。 <u>過敏症反応</u>

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	臨床試験において，コセンティクス投与患者でアナフィラキシー及び蕁麻疹が発現した。アナフィラキシー反応又はその他の重篤なアレルギー反応が生じた場合，直ちにコセンティクスの投与を中止し，適切な治療を開始すること。 ラテックスに感受性のある者における過敏症のリスク コセンティクスプレフィルドペン及びコセンティクスプレフィルドシリンジの取り外し可能なキャップには天然ゴムラテックスが含まれる。これはラテックスに感受性のある者においてアレルギー反応をきたす可能性がある。ラテックスに感受性のある者におけるコセンティクスプレフィルドシリンジペン又はプレフィルドシリンジ使用の安全性は検討されていない。 ワクチン接種 コセンティクス投与開始前に，最新の予防接種ガイドラインに従って年齢に応じたすべての予防接種が完了しているかを検討する。コセンティクスを投与された患者に生ワクチンを投与してはならない。 コセンティクス投与期間中に非生ワクチンを接種した場合，疾患予防に十分な免疫反応が惹起されない可能性がある。 **副作用** 次の副作用については添付文書中に詳細に考察されている。 • 感染症 • 炎症性腸疾患 • 過敏症反応 臨床試験の経験 臨床試験は極めて多様な条件下で実施するため，ある薬剤の臨床試験における副作用の発現率を別の薬剤の臨床試験での発現率と直接比較することはできず，実地臨床での発現率を反映するわけでもない。 **局面型皮疹を有する乾癬（成人）** 対照及び非対照臨床試験において，計 3,430 例の局面型乾癬患者にコセンティクスを投与した。このうち 1,641 例が 1 年以上曝露された。 局面型乾癬患者を対象とした 4 件のプラセボ対照第 III 相試験を併合し，試験 1，2，3 及び 4 で投与開始 12 週間後までのコセンティクスの安全性をプラセボと比較評価した。計 2077 例について評価を行った（コセンティクス 300 mg 群に 691 例，コセンティクス 150 mg 群に 692 例，プラセボ群に 694 例）。 プラセボ対照試験の 12 週間プラセボ対照期間中の発現率が 1%以上及びコセンティクス群でプラセボ群よりも発現率が高い副作用を表 1 に要約する。 **表 1　試験 1，2，3 及び 4 の 12 週目までに局面型乾癬患者の 1%以上で報告された副作用**

副作用	**コセンティクス**		**プラセボ (N=694) n (%)**
	300 mg (N=691) n (%)	**150 mg (N=692) n (%)**	
鼻咽頭炎	79 (11.4)	85 (12.3)	60 (8.6)
下痢	28 (4.1)	18 (2.6)	10 (1.4)
上気道感染	17 (2.5)	22 (3.2)	5 (0.7)
鼻炎	10 (1.4)	10 (1.4)	5 (0.7)

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用

口腔ヘルペス	9 (1.3)	1 (0.1)	2 (0.3)
咽頭炎	8 (1.2)	7 (1.0)	0 (0)
蕁麻疹	4 (0.6)	8 (1.2)	1 (0.1)
鼻漏	8 (1.2)	2 (0.3)	1 (0.1)

試験 1，2，3 及び 4 のプラセボ対照期間（12 週目まで）の発現率が 1%未満であった副作用は，副鼻腔炎，足部白癬，結膜炎，扁桃炎，口腔カンジダ症，膿痂疹，中耳炎，外耳炎，炎症性腸疾患，肝トランスアミナーゼ上昇及び好中球減少症であった。

感染症

局面型乾癬を対象とした臨床試験のプラセボ対照期間（コセンティクスを計 1,382 例に，プラセボを 694 例に最長 12 週間投与）において，感染症の発現率はプラセボ投与例では 18.9%であったのに対し，コセンティクス投与例で 28.7%であった。重篤な感染症の発現率は，プラセボ投与患者では 0.3%であったのに対し，コセンティクス投与患者では 0.14%であった。

投与期間全体（コセンティクスを計 3,430 例の局面型乾癬患者に投与，投与期間は患者の大半で最長 52 週間）では，コセンティクス投与患者の 47.5%で感染症が報告された（追跡調査期間の人年あたり 0.9）。重篤な感染症は，コセンティクス投与患者の 1.2%で報告された（追跡調査期間の人年あたり 0.015）。

第 III 相試験のデータによると，セクキヌマブの血清中濃度が増加すると一部の感染症が増加傾向を示した。セクキヌマブの血清中濃度が増加するとカンジダ感染，ヘルペスウイルス感染，ブドウ球菌皮膚感染及び治療を要する感染症が増加した。

局面型乾癬を対象とした PsO1 試験及び PsO2 試験の非盲検投与の継続投与期（追跡調査期間の中央値 3.9 年）の，3582 人年の曝露期間において，74%に感染症が報告された（100 人年あたり 55）。重篤な感染症は，コセンティクス投与患者の 4.5%で報告された（100 人年あたり 1.4）。敗血症が 5 例で報告された（100 人年あたり 0.2）。

臨床試験で好中球減少症が認められた。セクキヌマブに伴う好中球減少症の大部分は一過性かつ可逆的であった。好中球減少症に関連する重篤な感染症はなかった。

PsO1 試験及び PsO2 試験の非盲検投与の継続投与期において，好中球減少症（好中球絶対数＜1 ×10^9/L）がコセンティクス投与患者の 1%に報告された（100 人年あたり 0.3）。重篤な感染症の一部は好中球減少症との関連が見られたが，明らかな因果関係は認められなかった。

炎症性腸疾患

コセンティクスの臨床試験において，重篤な事例も含む炎症性腸疾患の発現が認められた。投与期間全体（コセンティクスを計 3,430 例の局面型皮疹を有する患者に投与，投与期間は最長 52 週間，2, 725 人年）で，クローン病の悪化が 3 例（100 人年あたり 0.11），潰瘍性大腸炎の悪化が 2 例（100 人年あたり 0.08），新たな潰瘍性大腸炎の発生が 2 例（100 人年あたり 0.08）報告された。12 週のプラセボ対照期間中，プラセボ投与例（793 例，176 人年）ではこれらの有害事象は発現しなかった。

クローン病の増悪の 1 例は，局面型皮疹を有する乾癬を対象に実施中の長期臨床試験の非対照期間中に報告された。

過敏症反応

臨床試験において，コセンティクス投与患者でアナフィラキシー及び蕁麻疹が発現した。

局面型皮疹を有する乾癬（小児）

局面型皮疹を有する乾癬の小児患者を対象とした第 3 相試験でコセンティクスの安全性を評価した。

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	最初の試験（PsO6 試験）は無作為化，二重盲検，プラセボ及び実薬対照，236 週間の試験で，全身療法の対象となる重症（PASI スコア≥20， IGA modified 2011 スコアが 4，かつ体表面積が 10%以上と定義）の局面型皮疹を有する 6 歳以上の小児乾癬患者 162 例が組み入れられた。162 例の患者は，プラセボ群，生物学的製剤の実薬対照群，又はコセンティクス投与群に無作為に割り付けられた。コセンティクス投与群では，体重 25 kg 未満の患者には 75 mg を投与し，体重 25 kg 以上 50 kg 未満の患者には 75 mg 又は 150 mg（推奨用量の 2 倍）を投与し，体重 50 kg 以上の患者には 150 mg 又は 300 mg（推奨用量の 2 倍）を投与した。 もう一つの試験（PsO7 試験；NCT03668613）は，208 週間の無作為化非盲検試験であり，中等症から重症（PASI スコアが 12 以上， IGA mod 2011 スコアが 3 以上，かつ無作為割付け時に体表面積が 10%以上と定義）の局面型乾癬を有する 6 歳以上の小児乾癬患者を対象とした。 84 例の患者が，二つのコセンティクス投与群に無作為割り付けされた［第 1 群：50 kg 未満の患者に 75 mg を投与し，50 kg 以上の患者に 150 mg を投与する；第 2 群：25 kg 未満の患者に 75 mg を投与し，25 kg 以上 50 kg 未満の患者に 150 mg を投与し，50 kg 以上の患者に 300 mg を投与する］ これらの試験で報告された安全性プロファイルは，局面型皮疹を有する成人乾癬患者を対象とした試験で報告された安全性プロファイルと一致していた。 *感染症* プラセボ対照期間，コセンティクス投与患者にメチシリン耐性黄色ブドウ球菌（MRSA）による毒素性ショック症候群（TSS）が報告された。 治療期間中にコセンティクスを少なくとも一回投与されたすべての患者で構成される小児の安全性併合集団［198 例（287 人年）］において，22 例（11%）の患者に CTCAE グレード 2 以上の好中球減少症（1,000 cells/mm 3 以上 1,500 cells/mm 3 未満）が報告され，57%の患者が 1 年以上追跡調査され，30%の患者が 2 年以上追跡調査された。 80 例のセクキヌマブ投与患者及び 41 例のプラセボ投与患者を最長 12 週間含むプラセボ対照期間中に，CTCAE グレード 2 以上の好中球減少症がセクキヌマブ投与患者の 3 例（4%）に報告されたが，プラセボ投与患者では報告されなかった。好中球減少症に関連する重篤な感染症は認められなかった。 **乾癬性関節炎** 乾癬性関節炎患者 1,003 例を対象とした 2 つのプラセボ対照試験が実施され，703 例にコセンティクスが，300 例にプラセボが投与された。コセンティクスが投与された 703 例のうち，299 例に対しては皮下投与による導入投与が，404 例に対しては静脈内投与による導入投与が行われ，導入投与後 4 週間ごとに皮下投与でコセンティクスが投与された。乾癬性関節炎患者に対する臨床試験の 16 週のプラセボ対照期間中，有害事象が見られた患者の全体的な割合は投与群間で同様で，コセンティクス投与群で 59%，プラセボ投与群で 58%であった。コセンティクス投与群でプラセボ投与群より 2%以上発現率が高かった有害事象は，鼻咽頭炎，上気道感染，頭痛，吐き気及び高コレステロール血症であった。コセンティクスを投与された乾癬性関節炎患者で見られた安全性プロファイルは，乾癬患者におけるコセンティクスの安全性プロファイルと同等であった。 感染症の患者の割合は，乾癬患者を対象とした臨床試験と同様で，コセンティクス投与群で（29%）でプラセボ投与群（26%）より高かった。 クローン病及び潰瘍性大腸炎の増悪若しくは新規発現が認められた事例もあった。炎症性腸疾患がコセンティクスを投与された 2 例及びプラセボを投与された 1 例の合計 3 例で見られた。 **強直性脊椎炎** 強直性脊椎炎患者590例を対象とした2つのプラセボ対照試験が実施され，394例にコセンティクスが，196例にプラセボが投与された。コセンティクスが投与された394例のうち，145例に対しては皮下投与による導入投与が，249例に対しては静脈内投与による導入投与が行われ，導入投

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	与後4週間ごとに皮下投与でコセンティクスが投与された。強直性脊椎炎患者を対象とした臨床試験の16週のプラセボ対照期間中，有害事象が見られた患者の全体的な割合はプラセボ投与群（59%）と比較してコセンティクス投与群で高かった（66%）。コセンティクス投与群でプラセボ投与群より2%以上発現率が高かった有害事象は，鼻咽頭炎，吐き気及び上気道感染であった。コセンティクスを投与された強直性脊椎炎患者で見られた安全性プロファイルは乾癬患者におけるコセンティクスの安全性プロファイルと同等であった。強直性脊椎炎患者を対象とした3つ目の対照試験において，コセンティクスを300 mg投与した際の安全性プロファイルはコセンティクスを150 mg投与した際と同等であった。 感染症の患者の割合は，乾癬患者を対象とした臨床試験と同様で，コセンティクス投与群で（31%）でプラセボ投与群（18%）より高かった。 強直性脊椎炎を対象とした最初の臨床試験において，コセンティクスを曝露された 571 例中，全投与期間で 8 例の炎症性腸疾患（クローン病が 5 例（100 人年あたり 0.7），潰瘍性大腸炎が 3 例（100 人年あたり 0.4）が見られた。16 週間のプラセボ対照期間中，コセンティクスが投与された患者で重篤な有害事象（クローン病の増悪が 2 例，潰瘍性大腸炎の新規発現が 1 例）が見られたが，プラセボが投与された患者では重篤な有害事象は見られなかった。臨床試験で全患者にコセンティクスが投与された期間中，クローン病の新規発現が 1 例，クローン病の増悪が 2 例，潰瘍性大腸炎の新規発現が 1 例，潰瘍性大腸炎の増悪が 1 例で見られた。 **X線基準を満たさない体軸性脊椎関節炎** X線基準を満たさない体軸性脊椎関節炎患者555例を対象としたプラセボ対照試験が実施され，185例に導入投与ありでコセンティクスが，184例に導入投与なしでコセンティクスが，186例にプラセボが投与された。コセンティクスが投与されたnr-axSpA患者の安全性プロファイルは，強直性脊椎炎患者やその他のコセンティクス投与経験で得られた安全性プロファイル概ね同様であった。Nr-axSpA試験1で導入投与ありの群に割り付けられた患者は導入投与なしの群に割り付けられた患者よりも，鼻咽頭炎，上気道感染，尿路感染を含む感染症及び寄生虫症の発現率が高く（100人年あたり92 vs 100人年あたり72），また胃炎，下腹部痛，大腸炎，下痢，血便を含む胃腸障害の発現率が高かった（100人年あたり27 vs 100人年あたり22）。 **免疫原性** すべての治療用蛋白質と同様，免疫原性の可能性がある。電気化学発光に基づくブリッジング免疫アッセイを用いてコセンティクスの免疫原性を評価した。コセンティクスを最長 52 週間投与された被験者のうち，セクキヌマブに対する抗体が生じた被験者は 1%未満であった。ただし，本アッセイではセクキヌマブ存在下での抗セクキヌマブ抗体の検出に限界があるため，抗体の発現率を正確に測定できなかった可能性がある。抗薬物抗体が発現した被験者のうち約半数では中和抗体に分類される抗体が認められた。中和抗体に伴う有効性の喪失はみられなかった。 抗体形成の検出は，アッセイの感度及び特異性に大きく依存している。さらに，アッセイにおける抗体（中和抗体を含む）陽性の発現率は，アッセイ方法，検体の取扱い，検体採取時期，併用療法及び基礎疾患等いくつかの要因による影響を受ける。以上の理由から，コセンティクスに対する抗体の発現率をほかの薬剤に対する抗体の発現率と比較すると誤解が生じる恐れがある。 **薬物間相互作用** CYP450 基質 慢性炎症では，特定のサイトカイン（例，IL-1，IL-6，IL-10，TNFα，IFN）のレベルが増加すると CYP450 酵素の生成が変動する。 CYP450 基質（特に治療域の狭いもの）を併用している患者にコセンティクスの投与を開始又は中止する際は，治療効果又は薬物濃度のモニタリング及び必要に応じた用量調整を検討する。 **特殊な集団への使用**

販売名	コセンティクス ™（セクキヌマブ）注射液，皮下投与用 注射用コセンティクス ™（セクキヌマブ），皮下投与用
	妊婦 *リスクの概要* 妊婦でのコセンティクスの使用経験は限られており，薬剤に関連した発達障害のリスクについての情報は十分には得られていない。妊娠サルを用いた胚・胎児発生試験において，最大推奨臨床用量の 30 倍のセクキヌマブを器官形成期に皮下投与した結果，催奇形性及び胚・胎児発生に影響は認められなかった。米国の通常の妊婦における先天性異常のリスクは 2-4%，流産のリスクは 15-20%であるが，コセンティクスを投与した妊婦における先天性異常及び流産のリスクは不明である。 *非臨床試験成績* セクキヌマブのカニクイザルを用いた胚・胎児発生毒性試験を実施した。妊娠サルを用いて，最大推奨臨床用量（体重換算で母動物への投与量は 150 mg/kg）の最大 30 倍のセクキヌマブを器官形成期に週 1 回皮下投与した結果，催奇形性及び胚・胎児発生に影響は認められなかった。 また，セクキヌマブのマウスサロゲート抗体を用いた出生前及び出生後の発生並びに母体機能に関する試験を実施した。マウスに 150 mg/kg/回までの用量で妊娠 6，11 及び 17 日並びに分娩後 4，10 及び 16 日に投与した結果，胎児の機能検査（成熟時の生殖機能，感覚機能及び運動機能），形態学的評価及び免疫原性評価に影響は認められなかった。 授乳 *リスクの概要* セクキヌマブのヒト乳汁中への移行，及び母乳を摂取後の乳児全身循環への授乳や母乳産生へのコセンティクスの影響に関するデータはない。授乳のベネフィットは，母親のコセンティクスの臨床的必要性，コセンティクスまたは授乳婦の状態が子供に与える潜在的な悪影響等をふまえて検討すべきである。 小児への使用 コセンティクスの安全性及び有効性は，中等症から重症の局面型皮疹を有する乾癬の 6 歳以上の小児患者において確認されている。中等症から重症の局面型皮疹を有する乾癬の 6 歳未満の小児患者における安全性及び有効性は確立していない。 他の適応症の小児患者における安全性及び有効性は確立していない。 高齢者への使用 臨床試験でコセンティクスを曝露された局面型乾癬患者 3,430 例中，計 230 例が 65 歳以上であり，32 例が 75 歳以上であった。高齢被験者と若年被験者との間で安全性及び有効性に差は認められなかったが，65 歳以上の被験者の数は，若齢被験者との反応の差を判断するには不十分であった。 **過量投与** 臨床試験では 30 mg/kg（約 2000～3000 mg）までの用量を静脈内投与しても用量制限毒性はみられていない。過量投与の場合は，副作用の徴候及び症状について患者の観察を行い，速やかに適切な対症療法を行うことを推奨する。
承認年月日	2015 年 1 月 21 日

Table 2-2 EU 共通の添付文書の概略

販売名	コセンティクス注射溶液用 150 mg 凍結乾燥製剤 コセンティクスプレフィルドシリンジ入り 150 mg 注射溶液 コセンティクスプレフィルドペン入り 150 mg 注射溶液

<table>
<tr><td>剤型・含量</td><td>各バイアルは，セクキヌマブ*を 150 mg 含有する。溶解後，1 mL の溶液にセクキヌマブは 150 mg 含まれる。
各プレフィルドシリンジは 1 mL の溶液中セクキヌマブ*を 150 mg 含有する。
各プレフィルドペンは 1 mL の溶液中セクキヌマブ*を 150 mg 含有する。
*セクキヌマブはインターロイキン 17A に選択的な組換え完全ヒトモノクローナル抗体である。セクキヌマブはチャイニーズハムスター卵巣（CHO）細胞から産生される IgG1/κ クラス抗体である。</td></tr>
<tr><td>効能・効果</td><td><u>成人における局面型皮疹を有する乾癬</u>
全身療法の対象となる中等症から重症の成人の局面型皮疹を有する乾癬患者
<u>小児における局面型皮疹を有する乾癬</u>
全身療法の対象となる 6 歳以上の小児及び青年における中等症から重症の局面型皮疹を有する乾癬
<u>乾癬性関節炎</u>
疾患修飾性抗リウマチ薬で十分な効果が得られない成人の活動性乾癬性関節炎患者に対し，単剤またはメトトレキサートと併用で使用する
<u>体軸性脊椎関節炎(axSpA)</u>
<u>強直性脊椎炎（AS，X線基準を満たす体軸性脊椎関節炎）</u>
既存治療では十分な効果が得られない成人の活動性強直性脊椎炎患者
<u>X 線基準を満たさない体軸性脊椎関節炎（nr-axSpA）</u>
NSAIDs では十分な治療効果が得られない成人の客観的な炎症所見を有する X 線基準を満たさない体軸性脊椎関節炎</td></tr>
<tr><td>用法・用量</td><td>コセンティクスは乾癬の診断及び治療の経験を有する医師の助言及び監督下で使用する。
<u>用量</u>
<u>成人における局面型皮疹を有する乾癬</u>
セクキヌマブ 300 mg の皮下投与を初期投与として 0 週，1 週，2 週，3 週に実施し，4 週以降は毎月維持投与することを推奨する。300 mg を投与する場合，150 mg の用量を 2 回皮下投与する。
<u>小児における局面型皮疹を有する乾癬（6 歳以上の小児及び青年）</u>
体重に基づいて（表 1）セクキヌマブの皮下投与を初期投与として 0 週，1 週，2 週，3 週に実施し，4 週以降は毎月維持投与することを推奨する。75 mg を投与する場合，75 mg の用量を 1 回皮下投与する。150 mg を投与する場合，150 mg の用量を 1 回皮下投与する。300 mg を投与する場合，150 mg の用量を 2 回皮下投与する。
表 1　小児局面型乾癬に対する推奨用量
<table>
<tr><td>投与時体重</td><td>推奨用量</td></tr>
<tr><td><25 kg</td><td>75 mg</td></tr>
<tr><td>25 to <50 kg</td><td>75 mg</td></tr>
<tr><td>≥50 kg</td><td>150 mg (*300 mg に増量できる)</td></tr>
</table>
*一部の患者では高用量の方が有益である可能性がある。
<u>乾癬性関節炎</u>
中等症から重症の局面型皮疹を有する乾癬を併発する場合，又は抗-TNF で十分な効果が得られない患者に対しては，セクキヌマブ 300 mg の皮下投与を初期投与として 0 週，1 週，2 週， 3 週及び 4 週に実施し，以降は毎月維持投与することを推奨する。300 mg を投与する場合は，150 mg を 2 本皮下投与する。
それ以外の患者に対しては，セクキヌマブ 150 mg の皮下投与を初期投与として 0 週，1 週，2 週，3 週及び 4 週に実施し，以降は毎月維持投与することを推奨する。臨床症状に応じて，300 mg に増量できる。</td></tr>
</table>

	体軸性脊椎関節炎 *強直性脊椎炎（AS, X 線基準を満たす体軸性脊椎関節炎）* セクキヌマブ 150 mg の皮下投与を初期投与として 0 週，1 週，2 週， 3 週及び 4 週に実施し，以降は毎月維持投与することを推奨する。臨床症状に応じて，300 mg に増量できる。300 mg を投与する場合は，150 mg を 2 本皮下投与する。 *X 線基準を満たさない体軸性脊椎関節炎（nr-axSpA）* セクキヌマブ 150 mg の皮下投与を初期投与として 0 週，1 週，2 週， 3 週及び 4 週に実施し，以降は毎月維持投与することを推奨する。 上記のすべての適応症について，臨床データより，治療開始後 16 週以内に奏功が認められている。最長 16 週間投与しても奏効しない患者に対しては投与の中止を検討する。初期に部分奏効がみられた患者では，16 週間を超えて投与を継続すると改善する場合がある。 *高齢患者（65 歳以上）* 用量調整は必要ない。 *腎障害/肝障害* これらの患者集団に関するコセンティクスの試験は実施していない。用量の推奨はできない。 *小児* 6 歳未満の局面型皮疹を有する乾癬の小児におけるコセンティクスの安全性及び有効性は確立されていない。 他の適応症における 18 歳未満の小児におけるコセンティクスの安全性及び有効性は確立されていない。利用可能なデータはない。 用法 コセンティクスは皮下投与する。可能であれば，乾癬を認める皮膚部位への投与は避ける。注射溶液用粉末は使用前に溶解すること。注射用粉末剤の溶解，調製及び投与は医療従事者が行う。 皮下投与手技に関する適切な訓練を受け，医師が適切と判断した場合には，患者自身が自己投与又はその介護者・保護者が投与しても良い。ただし，医師は継続的に患者のフォローアップを行うこと。患者又はその介護者・保護者用のパッケージリーフレットに従い，注射液全量が投与されるよう投与を行うこと。
使用上の注意	**禁忌** 有効成分又は添加物のいずれかに対する過敏症反応をきたす患者 臨床的に重要な活動性感染症（活動性結核等） **使用上の特別な警告・注意** 追跡可能性 医療用生物学的製剤の追跡可能性を改善するため，投与された製品名及びバッチ番号は適切に記録すること。 感染症 セクキヌマブは感染症のリスクを増大させる可能性がある。市販後にセクキヌマブを投与された患者において，重篤な感染症が認められている。慢性感染症を有する患者又は反復性感染の既往がある患者にセクキヌマブの使用を検討する際は注意すること。 感染症を示唆する徴候や症状が生じた場合には医師の診察を受けるよう，患者に指導する。重篤な感染症を発現した患者については十分な観察を行い，感染症が消失するまでセクキヌマブを投与しないこと。

	臨床試験において，セクキヌマブ投与患者で感染症が認められている。これらの大部分は鼻咽頭炎等の軽度から中等度の上気道感染であり，投与を中止する必要はなかった。コセンティクスの作用機序に関連して，乾癬を対象とした臨床試験では，重篤でない粘膜皮膚カンジダ症の報告頻度はプラセボ群に比べてセクキヌマブ群の方が多かった（セクキヌマブ 300 mg 群では 100 人年あたり 3.55 であったのに対し，プラセボ群では 100 人年あたり 1.00）。 臨床試験では，結核に対する感受性の増加は報告されなかった。ただし，活動性結核の患者にセクキヌマブを投与しないこと。潜伏結核患者については，セクキヌマブの投与を開始する前に抗結核治療を検討する。 炎症性腸疾患 クローン病及び潰瘍性大腸炎の新規発症又は悪化の報告がある。クローン病及び潰瘍性大腸炎を含む炎症性腸疾患の患者にセクキヌマブを投与する場合は注意し，投与後十分に経過観察すること。 過敏症反応 臨床試験において，セクキヌマブを投与した患者にアナフィラキシー反応がまれにみられた。アナフィラキシー反応又はその他の重篤なアレルギー反応が生じた場合，直ちにセクキヌマブの投与を中止し，適切な治療を開始すること。 ワクチン接種 生ワクチンをセクキヌマブと同時に接種してはならない。 セクキヌマブを投与する患者に不活化ワクチン又は非生ワクチンを同時に投与してもよい。ある試験において，髄膜炎菌ワクチン及び不活化インフルエンザワクチン接種の後，各ワクチンに対する抗体価が 4 倍以上増加する適切な免疫反応を獲得することができた健康被験者の割合は，セクキヌマブ 150 mg 投与例とプラセボ投与例とで同程度であった。このデータから，セクキヌマブは髄膜炎菌ワクチンやインフルエンザワクチンに対する液性免疫反応を抑制しないことが示唆される。 コセンティクスによる治療を開始する前に，小児患者には最新の予防接種ガイドラインに従った年齢に応じた予防接種をすべて投与することが推奨される。 免疫抑制療法の併用 乾癬の試験において，生物製剤を含む免疫抑制剤又は光療法と併用したときのセクキヌマブの安全性及び有効性は評価していない。関節炎（乾癬性関節炎及び強直性脊椎炎の患者を含む）の試験において，セクキヌマブはメトトレキサート(MTX)，スルファサラジン又はコルチコステロイドと併用投与された。他の免疫抑制剤とセクキヌマブの併用を検討する際は，注意すること。 **相互作用** 生ワクチンをセクキヌマブと同時に接種してはならない。 局面型皮疹を有する乾癬患者を対象とした薬物相互作用試験において，セクキヌマブはミタゾラム（CYP3A4 基質）の PK に影響を及ぼさないことが示された。 乾癬性関節炎患者及び体軸性脊椎関節炎患者の臨床試験において，メトトレキサート又はコルチコステロイドとの併用により，セクキヌマブの安全性に影響はみられなかった。 **受胎能，妊娠及び授乳** 妊娠可能な女性 妊娠可能な女性は，投与中及び投与後少なくとも 20 週間は有効な避妊法を用いること。 妊娠 妊婦へのセクキヌマブ使用に関する十分なデータはない。動物試験では，生殖毒性において直接的又は間接的な毒性変化はみられていない。予防手段として，妊娠中はコセンティクスの使用を避けることが望ましい。 授乳

セクキヌマブのヒト乳汁中への移行は不明である。免疫グロブリンはヒト乳汁中に移行するものの，摂取後のセクキヌマブの全身吸収については不明である。乳児においてセクキヌマブによる副作用の可能性がある。このため，子どもにとっての授乳の有益性と母親にとってのコセンティクス投与の有益性を考慮した上で，投与中及び投与後少なくとも 20 週間は授乳を中止する，又はコセンティクスの投与を中止するとの判断を行う。

受胎能

セクキヌマブがヒト受胎能に及ぼす影響は評価されていない。動物試験では，受胎能に関して直接的又は間接的な毒性変化はみられていない。

運転・機械操作への影響

コセンティクスが運転及び機械操作に及ぼす影響はない又は無視できる程度である。

副作用

安全性プロファイルの要約

報告頻度の最も高い副作用は上気道感染（最も頻度の高い事象は鼻咽頭炎，鼻炎）である。

副作用の一覧表

臨床試験並びに市販後に発現した副作用（表 2）を MedDRA 器官別大分類ごとに一覧で示す。それぞれの器官別大分類内で副作用を頻度の高い順に示している。各頻度グループ内で副作用を重症度の高い順に示す。また，各副作用の頻度カテゴリーは次のとおり慣行に従う：極めて高頻度（1/10 以上），高頻度（1/100 以上 1/10 未満），低頻度（1/1,000 以上 1/100 未満），まれ（1/10,000 以上 1/1,000 未満），極めてまれ（1/10,000 未満），頻度不明（利用可能なデータから推測不能）。

さまざまな適応症（局面型皮疹を有する乾癬，乾癬性関節炎，体軸性脊椎関節炎及びその他の自己免疫疾患）における盲検及び非盲検臨床試験で 18,000 例を超える患者にセクキヌマブが投与され，曝露は 30,565 人年であった。このうち 11,700 例以上の患者は 1 年以上セクキヌマブに曝露された。全適応症でセクキヌマブの安全性プロファイルは同様であった。

表 2　　臨床試験 [1)] 及び市販後における副作用の一覧表

SOC 分類	**頻度**	**副作用**
感染症および寄生虫症	極めて高頻度	上気道感染
	高頻度	口腔ヘルペス
		足部白癬
	低頻度	口腔カンジダ症
		外耳炎
		下気道感染
	頻度不明	粘膜および皮膚カンジダ症（食道カンジダ症を含む）
血液およびリンパ系障害	低頻度	好中球減少症
免疫系障害	まれ	アナフィラキシー反応
神経系障害	高頻度	頭痛
眼障害	低頻度	結膜炎
呼吸器，胸郭および縦隔障害	高頻度	鼻漏
胃腸障害	高頻度	下痢
	高頻度	悪心
	低頻度	炎症性腸疾患

皮膚および皮下組織障害	低頻度	蕁麻疹
	まれ	剥脱性皮膚炎 2)
一般的障害および投与部位の状態	高頻度	倦怠感

1) 局面型皮疹を有する乾癬，乾癬性関節炎，強直性脊椎炎若しくは X 線基準を満たさない体軸性脊椎炎患者を対象としたそれぞれのプラセボ対照第 III 相臨床試験で 300 mg，150 mg，75 mg 又はプラセボを 12 週間（局面型皮疹を有する乾癬）又は 16 週間（乾癬性関節炎，強直性脊椎炎若しくは X 線基準を満たさない体軸性脊椎炎）まで曝露した。

2) 乾癬症の患者において事象が報告されている

特定の副作用に関する記述

感染症

局面型乾癬を対象とした臨床試験のプラセボ対照期間（セクキヌマブを計 1,382 例，プラセボを 694 例の患者に最長 12 週間投与）において，感染症の発現率は，プラセボ投与患者では 18.9%であったのに対し，セクキヌマブ投与患者では 28.7%であった。感染症の大部分は，重篤ではない鼻咽頭炎等の軽度又は中等度の上気道感染で，投与を中止する必要がなかった。作用機序に一致して粘膜又は皮膚のカンジダ症が増加したが，これらは軽度又は中等度であり，重篤ではなく，標準治療に反応し，投与を中止する必要がなかった。重篤な感染症の発現率は，プラセボ投与患者では 0.3%であったのに対し，セクキヌマブ投与患者では 0.14%であった。

投与期間全体（セクキヌマブを計 3,430 例に投与，投与期間は患者の大半で最長 52 週間）では，セクキヌマブ投与患者の 47.5%で感染症が報告された（追跡調査期間の人年あたり 0.9）。重篤な感染症は，セクキヌマブ投与患者の 1.2%で報告された（追跡調査期間の人年あたり 0.015）。

乾癬性関節炎患者及び体軸性脊椎関節炎（強直性脊椎炎及び X 線基準を満たさない体軸性脊椎関節炎）患者をそれぞれ対象とした臨床試験での感染症の発現率は，局面型皮疹を有する乾癬患者を対象とした臨床試験での発現率と同様であった。

好中球減少症

好中球減少症の頻度はプラセボに比べてセクキヌマブの方が高かったが，大部分は軽度で，一過性及び可逆的であった。1.0～0.5×10^9/L 未満（CTCAE グレード 3）の好中球減少症がセクキヌマブ投与患者 3,430 例中 18 例（0.5%）で報告され，18 例中 15 例は用量に依存せず感染症との時間的関連がなかった。より重度な好中球減少症の報告はなかった。残りの 3 例では，標準治療に通常の反応を示し，セクキヌマブの投与を中止する必要がない，重篤でない感染症が報告された。

乾癬性関節炎患者及び体軸性脊椎関節炎（強直性脊椎炎及び X 線基準を満たさない体軸性脊椎関節炎）患者における好中球減少症の発現頻度は，局面型皮疹を有する乾癬患者と同様であった。0.5×10^9/L 未満（CTCAE グレード 4）の好中球減少症がまれに報告された。

過敏症反応

臨床試験において，蕁麻疹，及びまれにセクキヌマブに対するアナフィラキシー反応が認められた。

免疫原性

セクキヌマブを最長 52 週間投与された患者のうち，セクキヌマブに対する抗体が発現した患者は 1%未満であった。試験治療下で発現した抗薬物抗体の約半数が中和抗体であったが，有効性の喪失又は薬物動態の異常は伴わなかった。

小児集団

6 歳以上の局面型乾癬小児患者における好ましくない作用

	セクキヌマブの安全性は，局面型皮疹を有する乾癬の小児患者を対象とした 2 つの第 III 相試験で評価された。最初の試験（小児試験 1）は二重盲検，プラセボ対照試験であり，6 歳以上 18 歳未満の重症局面型皮疹を有する乾癬患者 162 例が組み入れられた。2 回目の試験（小児試験 2）は 6 歳以上 18 歳未満の中等症から重症の局面型皮疹を有する乾癬患者 84 例を対象とした非盲検試験である。これら 2 試験で得られた安全性プロファイルは報告されていた成人局面型乾癬患者の安全性プロファイルと一致していた。 副作用の疑いの報告 医薬品の認可後に，副作用の疑いを報告することは重要である。これにより，医薬品の有益性/危険性のバランスを継続的にモニタリングすることが可能となる。副作用の疑いがあれば，国の報告システムを介して報告するよう，医療従事者に依頼する。 **過量投与** 臨床試験において過量投与の事例は報告されていない。 臨床試験では 30 mg/kg（約 2,000～3,000 mg）までの用量を静脈内投与しても用量制限毒性はみられていない。過量投与の場合は，副作用の徴候及び症状について患者の観察を行い，速やかに適切な対症療法を行うことを推奨する。
承認年月日	2015 年 1 月 15 日

NOVARTIS

[redacted]

COSENTYX®/™ (secukinumab)

150 mg Powder for solution for injection
300 mg/2 mL Solution for injection in a pre-filled syringe or pre-filled pen
150 mg/1 mL Solution for injection in a pre-filled syringe or pre-filled pen
75 mg/0.5 mL Solution for injection in a pre-filled syringe

Core Data Sheet (CDS)

[redacted]

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use COSENTYX safely and effectively. See full prescribing information for COSENTYX.

COSENTYX® (secukinumab) injection, for subcutaneous use
COSENTYX® (secukinumab) for injection, for subcutaneous use
Initial U.S. Approval: 2015

----------RECENT MAJOR CHANGES----------

Indications and Usage (1.1)	05/2021
Dosage and Administration (2.1, 2.2, 2.6)	05/2021
Warnings and Precautions (5.1)	05/2021

----------INDICATIONS AND USAGE----------

COSENTYX is a human interleukin-17A antagonist indicated for the treatment of:

- moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy (1.1)
- adults with active psoriatic arthritis (PsA) (1.2)
- adults with active ankylosing spondylitis (AS) (1.3)
- adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation (1.4)

----------DOSAGE AND ADMINISTRATION----------

- Prior to COSENTYX initiation, complete all age appropriate vaccinations, evaluate patients for tuberculosis (TB) (2.1)See Full Prescribing Information for instructions on preparation and administration of COSENTYX (2.6, 2.7, 2.8)
- **Plaque Psoriasis:**
  - *Adults:* Recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. For some patients, a dose of 150 mg may be acceptable. (2.2)
  - *Pediatric Patients 6 Years and Older:* Recommended dosage based on body weight and administered by subcutaneous injection at Weeks 0,1,2,3, and 4 and every 4 weeks thereafter (2.2):

Body Weight at Time of Dosing	Recommended Dose
Less than 50 kg	75 mg
Greater than or equal to 50 kg	150 mg

- **Psoriatic Arthritis:** Recommended dosages are:
  - For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosage and administration for plaque psoriasis. (2.2)
  - For other psoriatic arthritis patients, administer with or without a loading dosage.
    - With a loading dosage: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
    - Without a loading dosage: 150 mg every 4 weeks
    - If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg every 4 weeks. (2.3)
- **Ankylosing Spondylitis:** Administer with or without a loading dosage. The recommended dosages are:
  - With a loading dosage: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
  - Without a loading dosage: 150 mg every 4 weeks
  - If a patient continues to have active ankylosing spondylitis, consider a dosage of 300 mg every 4 weeks. (2.4)
- **Non-Radiographic Axial Spondyloarthritis:** Administer with or without a loading dosage. The recommended dosage is:
  - With a loading dosage: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. (2.5)
  - Without a loading dosage: 150 mg every 4 weeks. (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

- Injection: 150 mg/mL solution in a single-dose Sensoready® pen and in a single-dose prefilled syringe. (3)
- Injection: 75 mg/0.5 mL solution in a single-dose prefilled syringe (for pediatric patients). (3)
- For Injection: 150 mg, lyophilized powder in a single-dose vial for reconstitution (for healthcare professional use only). (3)

----------CONTRAINDICATIONS----------

Serious hypersensitivity to secukinumab or any excipients in COSENTYX. (4)

----------WARNINGS AND PRECAUTIONS----------

- Infections: Serious infections have occurred. Caution should be exercised when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection. If a serious infection develops, discontinue COSENTYX until the infection resolves. (5.1)
- Tuberculosis (TB): Prior to initiating treatment with COSENTYX, evaluate for TB. (5.2)
- Inflammatory Bowel Disease: Cases of inflammatory bowel disease were observed in clinical trials. Caution should be exercised when prescribing COSENTYX to patients with inflammatory bowel disease. (5.3)
- Hypersensitivity Reactions: If an anaphylactic reaction or other serious allergic reaction occurs, discontinue COSENTYX immediately and initiate appropriate therapy. (5.4)
- Immunizations: Avoid use of live vaccines in patients treated with COSENTYX. (5.6)

----------ADVERSE REACTIONS----------

Most common adverse reactions (> 1%) are nasopharyngitis, diarrhea, and upper respiratory tract infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 5/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Plaque Psoriasis

COSENTYX® is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy.

1.2 Psoriatic Arthritis

COSENTYX is indicated for the treatment of adult patients with active psoriatic arthritis.

1.3 Ankylosing Spondylitis

COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis.

1.4 Non-Radiographic Axial Spondyloarthritis

COSENTYX is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

2 DOSAGE AND ADMINISTRATION

2.1 Testing and Procedures Prior to Treatment Initiation

- Perform the following evaluations prior to COSENTYX initiation:
  - Evaluate patients for tuberculosis (TB) infection. COSENTYX initiation is not recommended in patients with active TB infection. Initiate treatment of latent TB prior to initiation of COSENTYX *[see Warnings and Precautions (5.2)]*.
  - Complete all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with COSENTYX *[see Warnings and Precautions (5.6)]*.

2.2 Plaque Psoriasis

Adults

The recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. Each 300 mg dosage is given as 2 subcutaneous injections of 150 mg.

For some patients, a dose of 150 mg may be acceptable.

Pediatric Patients

The recommended dosage for pediatric patients 6 years of age and older is based on body weight (Table 1) and administered by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks.

Table 1: Recommended Dose of COSENTYX for Pediatric Patients 6 Years of Age and Older with Plaque Psoriasis

Body Weight at Time of Dosing	**Recommended Dose**
Less than 50 kg	75 mg
Greater than or equal to 50 kg	150 mg

2.3 Psoriatic Arthritis

For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis *[see Dosage and Administration (2.1)]*.

For other psoriatic arthritis patients, administer COSENTYX with or without a loading dosage by subcutaneous injection. The recommended dosage:

- With a loading dosage is 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks
- If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg every 4 weeks.

COSENTYX may be administered with or without methotrexate.

2.4 Ankylosing Spondylitis

Administer COSENTYX with or without a loading dosage by subcutaneous injection. The recommended dosage:

- With a loading dosage is 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks
- If a patient continues to have active ankylosing spondylitis, consider a dosage of 300 mg every 4 weeks.

2.5 Non-Radiographic Axial Spondyloarthritis

Administer COSENTYX with or without a loading dosage by subcutaneous injection. The recommended dosage:

- With a loading dosage is 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks.

2.6 Important Administration Instructions

There are four presentations for COSENTYX (i.e., Sensoready pen, prefilled syringes [150 mg/mL, 75 mg/0.5 mL], and lyophilized powder in vial for reconstitution). The COSENTYX "Instructions for Use" for each presentation contains more detailed instructions on the preparation and administration of COSENTYX *[see Instructions for Use]*. The lyophilized powder in vial for reconstitution is for healthcare provider use only.

COSENTYX is intended for use under the guidance and supervision of a physician.

Sensoready Pen

Adult patients may self-administer COSENTYX or be injected by a caregiver after proper training in subcutaneous injection technique using the Sensoready pen.

Pediatric patients should not self-administer COSENTYX using the Sensoready pen. An adult caregiver should prepare and inject COSENTYX after proper training in subcutaneous injection technique using the Sensoready pen.

Prefilled Syringe

Adult patients may self-administer COSENTYX or be injected by a caregiver after proper training in subcutaneous injection technique using the prefilled syringe.

Pediatric patients should not self-administer COSENTYX using the prefilled syringe. An adult caregiver should prepare and inject COSENTYX after proper training in subcutaneous injection technique using the prefilled syringe.

Administration Instructions

Administer each injection at a different anatomic location (such as upper arms, thighs, or any quadrant of abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, indurated, or affected by psoriasis. Administration of COSENTYX in the upper, outer arm may be performed by a caregiver or healthcare provider.

2.7 Preparation for Use of COSENTYX Sensoready® Pen and Prefilled Syringe

Before injection, remove COSENTYX Sensoready pen or COSENTYX prefilled syringe from the refrigerator and allow COSENTYX to reach room temperature (15 to 30 minutes) without removing the needle cap.

The removable cap of the COSENTYX Sensoready pen and the COSENTYX prefilled syringe contain natural rubber latex and should not be handled by latex-sensitive individuals *[see Warnings and Precautions (5.5)]*.

Inspect COSENTYX visually for particulate matter and discoloration prior to administration. COSENTYX injection is a clear to slightly opalescent, colorless to slightly yellow solution. Do not use if the liquid contains visible particles, is discolored or cloudy. COSENTYX does not contain preservatives; therefore, administer the Sensoready pen or prefilled syringe within 1 hour after removal from the refrigerator. Discard any unused product remaining in the Sensoready pen or prefilled syringe.

2.8 Reconstitution and Preparation of COSENTYX Lyophilized Powder

COSENTYX lyophilized powder should be prepared and reconstituted with Sterile Water for Injection by a trained healthcare provider using aseptic technique and without interruption. The preparation time from piercing the stopper until end of reconstitution on average takes 20 minutes and should not exceed 90 minutes.

a) Remove the vial of COSENTYX lyophilized powder from the refrigerator and allow to stand for 15 to 30 minutes to reach room temperature. Ensure the Sterile Water for Injection is at room temperature.

b) Slowly inject 1 mL of Sterile Water for Injection into the vial containing COSENTYX lyophilized powder and direct the stream of Sterile Water for Injection onto the lyophilized powder.

c) Tilt the vial at an angle of approximately 45 degrees and gently rotate between the fingertips for approximately 1 minute. Do not shake or invert the vial.

d) Allow the vial to stand for about 10 minutes at room temperature to allow for dissolution. Note that foaming may occur.

e) Tilt the vial at an angle of approximately 45 degrees and gently rotate between the fingertips for approximately 1 minute. Do not shake or invert the vial.

f) Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The reconstituted COSENTYX solution should be essentially free of visible particles, clear to opalescent, and colorless to slightly yellow. Do not use if the lyophilized powder has not fully dissolved or if the liquid contains visible particles, is cloudy or discolored.

g) Prepare the required number of vials (1 vial for the 150 mg dose or 2 vials for the 300 mg dose).

h) The COSENTYX reconstituted solution contains 150 mg of secukinumab in 1 mL of solution. After reconstitution, use the solution immediately or store in the refrigerator at 2ºC to 8ºC (36ºF to 46ºF) for up to 24 hours. Do not freeze.

i) If stored at 2ºC to 8ºC (36ºF to 46ºF), allow the reconstituted COSENTYX solution to reach room temperature (15 to 30 minutes) before administration. COSENTYX does not contain preservatives; therefore, administer within 1 hour after removal from 2ºC to 8ºC (36ºF to 46ºF) storage.

3 DOSAGE FORMS AND STRENGTHS

- Injection: 150 mg/mL as a clear to opalescent, colorless to slightly yellowish solution in a single-dose Sensoready pen
- Injection: 150 mg/mL as a clear to opalescent, colorless to slightly yellowish solution in a single-dose prefilled syringe
- Injection: 75 mg/0.5 mL as a clear to opalescent, colorless to slightly yellowish solution in a single-dose prefilled syringe (for pediatric patients less than 50 kg)
- For injection: 150 mg white lyophilized powder in a single-dose vial for reconstitution (for healthcare professional use only)

4 CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients in COSENTYX. Cases of anaphylaxis have been reported during treatment with COSENTYX *[see Warnings and Precautions (5.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Infections

COSENTYX may increase the risk of infections. In clinical trials, a higher rate of infections was observed in COSENTYX treated subjects compared to placebo-treated subjects. In placebo-controlled clinical trials in subjects with moderate to severe plaque psoriasis, higher rates of common infections, such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.5% versus 0.7%) and mucocutaneous infections with candida (1.2% versus 0.3%) were observed with COSENTYX compared with placebo. A similar increase in risk of infection was seen in placebo-controlled trials in subjects with psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. The incidence of some types of infections appeared to be dose-dependent in clinical studies *[see Adverse Reactions (6.1)]*. In the postmarketing setting, serious and some fatal infections have been reported in patients receiving COSENTYX.

Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, monitor the patient closely and discontinue COSENTYX until the infection resolves.

5.2 Pre-Treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Avoid administration of COSENTYX to patients with active TB infection. Initiate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients closely for signs and symptoms of active TB during and after treatment.

5.3 Inflammatory Bowel Disease

Caution should be used when prescribing COSENTYX to patients with inflammatory bowel disease. Exacerbations, in some cases serious, occurred in COSENTYX treated subjects during clinical trials in plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. In addition, new onset inflammatory bowel disease cases occurred in clinical trials with COSENTYX. In an exploratory trial in 59 subjects with active Crohn's disease, there were trends toward greater disease activity and increased adverse events in the secukinumab group as compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease *[see Adverse Reactions (6.1)]*.

5.4 Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated subjects in clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated *[see Contraindications (4), Adverse Reactions (6.1)]*.

5.5 Risk of Hypersensitivity in Latex-Sensitive Individuals

The removable caps of the COSENTYX Sensoready pen and the COSENTYX 1 mL and 0.5 mL prefilled syringes contain natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals. The safe use of COSENTYX Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

5.6 Immunizations

Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. COSENTYX may alter a patient`s immune response to live vaccines. Avoid use of live vaccines in patients treated with COSENTYX.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

- Infections *[see Warnings and Precautions (5.1)]*
- Inflammatory Bowel Disease *[see Warnings and Precautions (5.3)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adult Plaque Psoriasis

A total of 3430 plaque psoriasis subjects were treated with COSENTYX in controlled and uncontrolled clinical trials. Of these, 1641 subjects were exposed for at least 1 year.

Four placebo-controlled Phase 3 trials in plaque psoriasis subjects were pooled to evaluate the safety of COSENTYX in comparison to placebo up to 12 weeks after treatment initiation, in Trials PsO1, PsO2, PsO3, and PsO4. In total, 2077 subjects were evaluated (691 to COSENTYX 300 mg group, 692 to COSENTYX 150 mg group, and 694 to placebo group). Subjects randomized to COSENTYX received 300 mg or 150 mg doses subcutaneously at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks *[see Clinical Studies (14)]*.

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the COSENTYX groups than the placebo group during the 12-week placebo-controlled period of the placebo-controlled trials.

Table 2: Adverse Reactions Reported by Greater Than 1% of Subjects with Plaque Psoriasis Through Week 12 in Trials PsO1, PsO2, PsO3, and PsO4

Adverse Reactions	COSENTYX		Placebo (N = 694) n (%)
	300 mg (N = 691) n (%)	150 mg (N = 692) n (%)	
Nasopharyngitis	79 (11.4)	85 (12.3)	60 (8.6)
Diarrhea	28 (4.1)	18 (2.6)	10 (1.4)
Upper respiratory tract infection	17 (2.5)	22 (3.2)	5 (0.7)
Rhinitis	10 (1.4)	10 (1.4)	5 (0.7)
Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Pharyngitis	8 (1.2)	7 (1.0)	0 (0)
Urticaria	4 (0.6)	8 (1.2)	1 (0.1)
Rhinorrhea	8 (1.2)	2 (0.3)	1 (0.1)

Adverse reactions that occurred at rates less than 1% in the placebo-controlled period of Trials PsO1, PsO2, PsO3, and PsO4 through Week 12 included: sinusitis, tinea pedis, conjunctivitis, tonsillitis, oral candidiasis, impetigo, otitis media, otitis externa, inflammatory bowel disease, increased liver transaminases, and neutropenia.

Infections

In the placebo-controlled period of the clinical trials in plaque psoriasis (a total of 1382 subjects treated with COSENTYX and 694 subjects treated with placebo up to 12 weeks), infections were reported in 28.7% of subjects treated with COSENTYX compared with 18.9% of subjects treated with placebo. Serious infections occurred in 0.14% of subjects treated with COSENTYX and in 0.3% of subjects treated with placebo.

Over the entire treatment period (a total of 3430 plaque psoriasis subjects treated with COSENTYX for up to 52 weeks for the majority of subjects), infections were reported in 47.5% of subjects treated with COSENTYX (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of subjects treated with COSENTYX (0.015 per patient-year of follow-up).

Phase 3 data showed an increasing trend for some types of infection with increasing serum concentration of secukinumab. Candida infections, herpes viral infections, staphylococcal skin infections, and infections requiring treatment increased as serum concentration of secukinumab increased.

In the psoriasis open-label extension of Trials PsO1 and PsO2 (median follow-up of 3.9 years), representing 3582 subject-years of exposure, 74% of COSENTYX treated subjects reported infections (55 per 100 patient-years). Serious infections were reported in 4.5% of subjects (1.4 per 100 patient-years). Sepsis was reported in 5 subjects (0.2 per 100 patient-years).

Neutropenia was observed in controlled portion of clinical trials. Most cases of secukinumab-associated neutropenia were transient and reversible. No serious infections were associated with cases of neutropenia.

In the open-label extension of Trials PsO1 and PsO2, neutropenia (ANC < 1 $x10^9$/L) was reported in 1% of COSENTYX treated subjects (0.3 per 100 patient-years). Some cases of serious infections were associated with neutropenia; however the causal relationship was not established.

Inflammatory Bowel Disease

Cases of inflammatory bowel disease, in some cases serious, were observed in clinical trials with COSENTYX. In the plaque psoriasis program, with 3430 subjects exposed to COSENTYX over the entire treatment period for up to 52 weeks

(2725 patient-years), there were 3 cases (0.11 per 100 patient-years) of exacerbation of Crohn's disease, 2 cases (0.08 per 100 patient-years) of exacerbation of ulcerative colitis, and 2 cases (0.08 per 100 patient-years) of new onset ulcerative colitis. There were no cases in placebo subjects (N = 793; 176 patient-years) during the 12-week placebo-controlled period.

One case of exacerbation of Crohn's disease was reported in open-labeled portions of clinical trials in plaque psoriasis.

Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated subjects in clinical trials *[see Warnings and Precautions (5.4)]*.

Pediatric Plaque Psoriasis

The safety of COSENTYX was assessed in two Phase 3 trials in pediatric subjects with plaque psoriasis.

The first was a randomized, double-blind, placebo and active-controlled, 236-week trial (Trial PsO6) that enrolled 162 pediatric subjects 6 years of age and older, with severe plaque psoriasis (defined by PASI score ≥ 20, an IGA modified 2011 score of 4, and involving ≥ 10% of the body surface area) who were candidates for systemic therapy. The 162 subjects were randomized to receive placebo, a biologic active control, or COSENTYX. In the COSENTYX groups, subjects with body weight < 25 kg received 75 mg, subjects with body weight 25 to < 50 kg received either 75 mg or 150 mg (2 times the recommended dose), and subjects with body weight ≥ 50 kg received either 150 mg or 300 mg (2 times the recommended dose).

The second trial was a randomized, open-label, 208-week trial (Trial PsO7; NCT03668613) of 84 subjects 6 years of age and older with moderate to severe plaque psoriasis (defined by a PASI score ≥ 12, IGA mod 2011 score of ≥ 3, and BSA involvement of ≥ 10% at randomization) who were randomized into two COSENTYX arms [Arm 1: 75 mg for body weight (BW) < 50 kg or 150 mg for ≥ 50 kg and Arm 2: 75 mg for BW < 25 kg, 150 mg for BW ≥ 25 kg and < 50 kg, or 300 mg for BW ≥ 50 kg].

The safety profile reported in these trials was consistent with the safety profile reported in adult plaque psoriasis trials.

Infections

One case of methicillin-resistant Staphylococcus aureus (MRSA) toxic shock syndrome (TSS) was reported in a COSENTYX treated subject during the placebo-controlled period.

In the pediatric safety pool, which includes all subjects who took at least one dose of COSENTYX during the treatment periods [198 subjects (287 patient years)], 22 (11%) subjects reported ≥ CTCAE Grade 2 neutropenia (≥1,000 to < 1,500 cells/mm^3) with 57% of subjects followed for one year or more and 30% of subjects followed for two years or more. During the placebo-controlled period which included a total of 80 subjects treated with secukinumab and 41 subjects treated with placebo up to 12 weeks, ≥ CTCAE Grade 2 neutropenia was reported in 3 (4%) of the subjects treated with secukinumab compared with no subjects treated with placebo. No serious infections were associated with cases of neutropenia.

Psoriatic Arthritis

COSENTYX was studied in two placebo-controlled psoriatic arthritis trials with 1003 patients (703 patients on COSENTYX and 300 patients on placebo). Of the 703 patients who received COSENTYX, 299 patients received a subcutaneous loading dose of COSENTYX (PsA1) and 404 patients received an intravenous loading dose of secukinumab (PsA2) followed by COSENTYX administered by subcutaneous injection every four weeks. During the 16-week placebo-controlled period of the trials in patients with psoriatic arthritis, the overall proportion of patients with adverse events was similar in the secukinumab and placebo-treatment groups (59% and 58%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, upper respiratory tract infection, headache, nausea, and hypercholesterolemia. The safety profile observed in patients with psoriatic arthritis treated with COSENTYX is consistent with the safety profile in psoriasis.

Similar to the clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (29%) compared to placebo group (26%).

There were cases of Crohn's disease and ulcerative colitis that include patients who experienced either exacerbations or the development of new disease. There were three cases of inflammatory bowel disease, of which two patients received secukinumab and one received placebo.

Ankylosing Spondylitis

COSENTYX was studied in two placebo-controlled ankylosing spondylitis trials with 590 patients (394 patients on COSENTYX and 196 patients on placebo). Of the 394 patients who received COSENTYX, 145 patients received a subcutaneous load of COSENTYX (study AS1), and 249 received an intravenous loading dose of secukinumab (study AS2) followed by COSENTYX administered by subcutaneous injection every four weeks. During the 16-week placebo-controlled period of the trials in patients with ankylosing spondylitis, the overall proportion of patients with adverse events was higher in the secukinumab groups than the placebo-treatment groups (66% and 59%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, nausea, and upper respiratory tract infection. The safety profile observed in patients with ankylosing spondylitis treated with COSENTYX is consistent with the safety profile in psoriasis. In a third controlled study of AS (study AS3), the safety profile of the 300 mg dose of COSENTYX was consistent with the safety profile of the 150 mg dose of COSENTYX.

Similar to clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (31%) compared to the placebo group (18%).

In the original ankylosing spondylitis program, with 571 patients exposed to COSENTYX there were 8 cases of inflammatory bowel disease during the entire treatment period [5 Crohn's (0.7 per 100 patient-years) and 3 ulcerative colitis (0.4 per 100 patient-years)]. During the placebo-controlled 16-week period, there were 2 Crohn's disease exacerbations and 1 new onset ulcerative colitis case that was a serious adverse event in patients treated with COSENTYX compared to none of the patients treated with placebo. During the remainder of the study when all patients received COSENTYX, 1 patient developed Crohn's disease, 2 patients had Crohn's exacerbations, 1 patient developed ulcerative colitis, and 1 patient had an ulcerative colitis exacerbation.

Non-Radiographic Axial Spondyloarthritis

COSENTYX was studied in one randomized, double-blind, placebo-controlled non-radiographic axial spondyloarthritis trial with 555 patients (185 patients on with load COSENTYX, 184 patients on without load COSENTYX and 186 patients on placebo). The safety profile for patients with nr-axSpA treated with COSENTYX was overall similar to the safety profile seen in patients with AS and other previous experience with COSENTYX. Patients in nr-axSpA1 study who received the loading dosing regimen compared to those without the loading regimen, had higher incidence of infections and infestations (92 per 100 patient-years vs 72 per 100 patient years), including nasopharyngitis, upper respiratory tract infection and urinary tract infection, and gastrointestinal disorders (27 per 100 patient-years vs 22 per 100 patient-years), including gastritis, lower abdominal pain, colitis, diarrhea, and hematochezia.

6.2 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The immunogenicity of COSENTYX was evaluated using an electrochemiluminescence-based bridging immunoassay. Less than 1% of subjects treated with COSENTYX developed antibodies to secukinumab in up to 52 weeks of treatment. However, this assay has limitations in detecting anti-secukinumab antibodies in the presence of secukinumab; therefore, the incidence of antibody development might not have been reliably determined. Of the subjects who developed antidrug antibodies, approximately one-half had antibodies that were classified as neutralizing. Neutralizing antibodies were not associated with loss of efficacy.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to COSENTYX with the incidences of antibodies to other products may be misleading.

7 DRUG INTERACTIONS

CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation.

Upon initiation or discontinuation of COSENTYX in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment of the CYP450 substrate as needed *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Limited available human data with COSENTYX use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. In an embryo-fetal development study, no adverse developmental effects were observed in infants born to pregnant monkeys after subcutaneous administration of secukinumab during organogenesis at doses up to 30 times the maximum recommended human dose (MRHD) *(see Data)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown; however, the background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Data

Animal Data

An embryo-fetal development study was performed in cynomolgus monkeys with secukinumab. No malformations or embryo-fetal toxicity were observed in fetuses from pregnant monkeys that were administered secukinumab weekly by the subcutaneous route during the period of organogenesis at doses up to 30 times the MRHD (on a mg/kg basis at a maternal dose of 150 mg/kg).

A pre- and post-natal development toxicity study was performed in mice with a murine analog of secukinumab. No treatment-related effects on functional, morphological or immunological development were observed in fetuses from pregnant mice that were administered the murine analog of secukinumab on gestation days 6, 11, and 17 and on postpartum days 4, 10, and 16 at doses up to 150 mg/kg/dose.

8.2 Lactation

Risk Summary

It is not known whether secukinumab is excreted in human milk or absorbed systemically after ingestion. There are no data on the effects of COSENTYX on the breastfed child or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COSENTYX and any potential adverse effects on the breastfed child from COSENTYX or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of COSENTYX have been established in pediatric subjects aged 6 years and older with moderate to severe plaque psoriasis *[see Adverse Reactions (6.1), Clinical Studies (14.2)]*. Safety and effectiveness of COSENYX in pediatric patients with plaque psoriasis below the age of 6 years have not been established.

The safety and effectiveness of COSENTYX in pediatric patients in other indications have not been established.

8.5 Geriatric Use

Of the 3430 plaque psoriasis subjects exposed to COSENTYX in clinical trials, a total of 230 were 65 years or older, and 32 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 years and older was not sufficient to determine whether they responded differently from younger subjects.

10 OVERDOSAGE

Doses up to 30 mg/kg intravenously have been administered in clinical trials without dose-limiting toxicity. In the event of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

11 DESCRIPTION

Secukinumab, a recombinant human monoclonal IgG1/κ antibody, is an interleukin-17A antagonist. It is expressed in a recombinant Chinese Hamster Ovary (CHO) cell line. Secukinumab has a molecular mass of approximately 151 kDa; both heavy chains of secukinumab contain oligosaccharide chains.

COSENTYX Injection

COSENTYX injection is a sterile, preservative-free, clear to slightly opalescent, colorless to slightly yellow solution for subcutaneous use. COSENTYX is supplied in a single-dose Sensoready pen with a 27-gauge fixed ½-inch needle, or a single-dose prefilled syringe with a 27-gauge fixed ½-inch needle. The removable cap of the COSENTYX Sensoready pen or prefilled syringe contains natural rubber latex.

Each COSENTYX Sensoready pen or prefilled syringe contains 150 mg of secukinumab formulated in: L-histidine/histidine hydrochloride monohydrate (3.103 mg), L-methionine (0.746 mg), polysorbate 80 (0.2 mg), trehalose dihydrate (75.67 mg), and Sterile Water for Injection, USP, at pH of 5.8.

Each COSENTYX 75 mg/0.5 mL prefilled syringe contains 75 mg of secukinumab formulated in: L-histidine/histidine hydrochloride monohydrate (1.552 mg), L-methionine (0.373 mg), polysorbate 80 (0.1 mg), trehalose dihydrate (37.83 mg), and Sterile Water for Injection, USP, at pH of 5.8.

COSENTYX for Injection

COSENTYX for injection is supplied as a sterile, preservative free, white to slightly yellow, lyophilized powder in single-dose vials for subcutaneous use after reconstitution. Each COSENTYX vial contains 150 mg of secukinumab formulated in L-histidine/histidine hydrochloride monohydrate (4.656 mg), polysorbate 80 (0.6 mg), and sucrose (92.43 mg). Following reconstitution with 1 mL Sterile Water for Injection, USP, the resulting pH is approximately 5.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Secukinumab is a human IgG1 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Secukinumab inhibits the release of proinflammatory cytokines and chemokines.

12.2 Pharmacodynamics

Elevated levels of IL-17A are found in psoriatic plaques. Treatment with COSENTYX may reduce epidermal neutrophils and IL-17A levels in psoriatic plaques. Serum levels of total IL-17A (free and secukinumab-bound IL-17A) measured at Week 4 and Week 12 were increased following secukinumab treatment. These pharmacodynamic activities are based on small exploratory studies. The relationship between these pharmacodynamic activities and the mechanism(s) by which secukinumab exerts its clinical effects is unknown.

Increased numbers of IL-17A producing lymphocytes and innate immune cells and increased levels of IL-17A have been found in the blood of patients with psoriatic arthritis and ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis.

Immune Response to Non-Live Vaccines During Treatment

Healthy individuals who received a single 150 mg dose of COSENTYX 2 weeks prior to vaccination with a non-U.S. approved group C meningococcal polysaccharide conjugate vaccine and a non-U.S. approved inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive COSENTYX prior to vaccination. The clinical effectiveness of meningococcal and influenza vaccines has not been assessed in patients undergoing treatment with COSENTYX [see Warnings and Precautions (5.6)].

12.3 Pharmacokinetics

The pharmacokinetic (PK) properties of secukinumab observed in psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis patients were similar to the PK properties displayed in plaque psoriasis patients.

Absorption

Following a single subcutaneous dose of either 150 mg (one-half the recommended dose) or 300 mg in plaque psoriasis subjects, secukinumab reached peak mean (± SD) serum concentrations (C_{max}) of 13.7 ± 4.8 mcg/mL and 27.3 ± 9.5 mcg/mL, respectively, by approximately 6 days post dose.

Following multiple subcutaneous doses of secukinumab, the mean (± SD) serum trough concentrations of secukinumab ranged from 22.8 ± 10.2 mcg/mL (150 mg) to 45.4 ± 21.2 mcg/mL (300 mg) at Week 12. At the 300 mg dose at Week 4 and Week 12, the mean trough concentrations resulted from the Sensoready pen were 23% to 30% higher than those from the lyophilized powder and 23% to 26% higher than those from the prefilled syringe based on cross-study comparisons.

Steady-state concentrations of secukinumab were achieved by Week 24 following the every-4-week dosing regimens. The mean (± SD) steady-state trough concentrations ranged from 16.7 ± 8.2 mcg/mL (150 mg) to 34.4 ± 16.6 mcg/mL (300 mg).

In healthy subjects and subjects with plaque psoriasis, secukinumab bioavailability ranged from 55% to 77% following subcutaneous dose of 150 mg (one-half the recommended dose) or 300 mg.

Distribution

The mean volume of distribution during the terminal phase (Vz) following a single intravenous administration ranged from 7.10 to 8.60 L in plaque psoriasis subjects. Intravenous use is not recommended *[see Dosage and Administration (2)]*.

Secukinumab concentrations in interstitial fluid in lesional and non-lesional skin of plaque psoriasis subjects ranged from 27% to 40% of those in serum at 1 and 2 weeks after a single subcutaneous dose of secukinumab 300 mg.

Elimination

Metabolism

The metabolic pathway of secukinumab has not been characterized. As a human IgG1κ monoclonal antibody secukinumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Excretion

The mean systemic clearance (CL) ranged from 0.14 L/day to 0.22 L/day and the mean half-life ranged from 22 to 31 days in plaque psoriasis subjects following intravenous and subcutaneous administration across all psoriasis trials. Intravenous use is not recommended *[see Dosage and Administration (2)]*.

Dose Linearity

Secukinumab exhibited dose-proportional pharmacokinetics in subjects with psoriasis over a dose range from 25 mg (approximately 0.083 times the recommended dose) to 300 mg following subcutaneous administrations.

Weight

Secukinumab clearance and volume of distribution increase as body weight increases.

Specific Populations

Patients with Hepatic or Renal Impairment

No formal trial of the effect of hepatic or renal impairment on the pharmacokinetics of secukinumab was conducted.

Geriatric Patients

Population pharmacokinetic analysis indicated that the clearance of secukinumab was not significantly influenced by age in adult subjects with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis. Subjects who are 65 years or older had apparent clearance of secukinumab similar to subjects less than 65 years old.

Pediatric Patients

In a pool of the two pediatric trials, subjects with moderate to severe plaque psoriasis (6 years of age and older) were administered secukinumab at the recommended pediatric dosing regimen. At Week 24, secukinumab steady state mean ± SD serum trough concentrations were 32.6 ± 10.8 mcg/mL (n = 8), 19.8 ± 6.96 mcg/mL (n = 24), and 27.3 ± 10.1 mcg/mL (n = 36), in subjects weighing < 25 kg and receiving 75 mg of secukinumab, subjects weighing ≥ 25 and < 50 kg and receiving 75 mg of secukinumab, and subjects weighing ≥ 50 kg and receiving 150 mg of secukinumab, respectively.

Drug Interactions

Cytochrome P450 Substrates

In adult subjects with plaque psoriasis, midazolam (CYP3A4 substrate) pharmacokinetics was similar when administered alone, or when administered following either a single or five weekly subcutaneous administrations of 300 mg secukinumab *[see Drug Interactions (7.3)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of COSENTYX. Some published literature suggests that IL-17A directly promotes cancer cell invasion in vitro, whereas other reports indicate IL-17A promotes T-cell mediated tumor rejection. Depletion of IL-17A with a neutralizing antibody inhibited tumor development in mice. The relevance of experimental findings in mouse models for malignancy risk in humans is unknown.

No effects on fertility were observed in male and female mice that were administered a murine analog of secukinumab at subcutaneous doses up to 150 mg/kg once weekly prior to and during the mating period.

14 CLINICAL STUDIES

14.1 Adult Plaque Psoriasis

Four multicenter, randomized, double-blind, placebo-controlled trials (Trials PsO1, PsO2, PsO3, and PsO4) enrolled 2403 subjects (691 randomized to COSENTYX 300 mg, 692 to COSENTYX 150 mg, 694 to placebo, and 323 to a biologic active control) 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, and Psoriasis Area and Severity Index (PASI) score greater than or equal to 12, and who were candidates for phototherapy or systemic therapy.

- Trial PsO1 (NCT01365455) enrolled 738 subjects (245 randomized to COSENTYX 300 mg, 245 to COSENTYX 150 mg, and 248 to placebo). Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks. Subjects randomized to COSENTYX received 300 mg or 150 mg doses at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Subjects randomized to receive placebo that were non-responders at Week 12 were then crossed over to receive COSENTYX (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, and 16 followed by the same dose every 4 weeks. All subjects were followed for up to 52 weeks following first administration of study treatment.
- Trial PsO2 (NCT01358578) enrolled 1306 subjects (327 randomized to COSENTYX 300 mg, 327 to COSENTYX 150 mg, 326 to placebo, and 323 to a biologic active control). COSENTYX and placebo data are described. Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks. Subjects randomized to COSENTYX received 300 mg or 150 mg doses at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Subjects randomized to receive placebo that were non-responders at Week 12 then crossed over to receive COSENTYX (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, and 16 followed by the same dose every 4 weeks. All subjects were followed for up to 52 weeks following first administration of study treatment.
- Trial PsO3 (NCT01555125) enrolled 177 subjects (59 randomized to COSENTYX 300 mg, 59 to COSENTYX 150 mg, and 59 to placebo) and assessed safety, tolerability, and usability of COSENTYX self-administration via prefilled syringe for 12 weeks. Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks for up to 12 weeks total.
- Trial PsO4 (NCT01636687) enrolled 182 subjects (60 randomized to COSENTYX 300 mg, 61 to COSENTYX 150 mg, and 61 to placebo) and assessed safety, tolerability, and usability of COSENTYX self-administration via Sensoready pen for 12 weeks. Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks for up to 12 weeks total.

Endpoints

In all trials, the endpoints were the proportion of subjects who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline to Week 12 and treatment success (clear or almost clear) on the Investigator's Global Assessment modified 2011 (IGA). Other evaluated outcomes included the proportion of subjects who achieved a reduction in PASI score of at least 90% (PASI 90) from baseline at Week 12, maintenance of efficacy to Week 52, and improvements in itching, pain, and scaling at Week 12 based on the Psoriasis Symptom Diary©.

The PASI is a composite score that takes into consideration both the percentage of body surface area affected and the nature and severity of psoriatic changes within the affected regions (induration, erythema and scaling). The IGA is a 5-category scale, including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe" indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink coloration of lesions, no thickening of the plaque, and none to minimal focal scaling.

Baseline Characteristics

Across all treatment groups the baseline PASI score ranged from 11 to 72 with a median of 20 and the baseline IGA score ranged from "moderate" (62%) to "severe" (38%). Of the 2077 plaque psoriasis subjects who were included in the placebo-controlled trials, 79% were biologic-naïve (have never received a prior treatment with biologics) and 45% were non-biologic failures (failed to respond to a prior treatment with non-biologic therapies). Of the subjects who received a prior treatment with biologics, over one-third were biologic failures. Approximately 15% to 25% of trial subjects had a history of psoriatic arthritis.

Clinical Response

The results of Trials PsO1 and PsO2 are presented in Table 3.

Table 3: Clinical Outcomes at Week 12 in Adults with Plaque Psoriasis in Trials PsO1 and PsO2

	Trial PsO1			**Trial PsO2**		
	COSENTYX 300 mg (N = 245) n (%)	**COSENTYX 150 mg (N = 245) n (%)**	**Placebo (N = 248) n (%)**	**COSENTYX 300 mg (N = 327) n (%)**	**COSENTYX 150 mg (N = 327) n (%)**	**Placebo (N = 326) n (%)**
PASI 75 response	200 (82)	174 (71)	11 (4)	249 (76)	219 (67)	16 (5)
IGA of clear or almost clear	160 (65)	125 (51)	6 (2)	202 (62)	167 (51)	9 (3)

The results of Trials PsO3 and PsO4 are presented in Table 4.

Table 4: Clinical Outcomes at Week 12 in Adults with Plaque Psoriasis in Trials PsO3 and PsO4

	Trial PsO3			**Trial PsO4**		
	COSENTYX 300 mg (N = 59) n (%)	**COSENTYX 150 mg (N = 59) n (%)**	**Placebo (N = 59) n (%)**	**COSENTYX 300 mg (N = 60) n (%)**	**COSENTYX 150 mg (N = 61) n (%)**	**Placebo (N = 61) n (%)**
PASI 75 response	44 (75)	41 (69)	0 (0)	52 (87)	43 (70)	2 (3)
IGA of clear or almost clear	40 (68)	31 (53)	0 (0)	44 (73)	32 (52)	0 (0)

Examination of age, gender, and race subgroups did not identify differences in response to COSENTYX among these subgroups. Based on post-hoc sub-group analyses in subjects with moderate to severe psoriasis, subjects with lower body weight and lower disease severity may achieve an acceptable response with COSENTYX 150 mg.

PASI 90 response at Week 12 was achieved with COSENTYX 300 mg and 150 mg compared to placebo in 59% (145/245) and 39% (95/245) versus 1% (3/248) of subjects, respectively (Trial PsO1) and 54% (175/327) and 42% (137/327) versus 2% (5/326) of subjects, respectively (Trial PsO2). Similar results were seen in Trials PsO3 and PsO4.

With continued treatment over 52 weeks, subjects in Trial PsO1 who were PASI 75 responders at Week 12 maintained their responses in 81% (161/200) of the subjects treated with COSENTYX 300 mg and in 72% (126/174) of subjects treated with COSENTYX 150 mg. Trial PsO1 subjects who were clear or almost clear on the IGA at Week 12 also maintained their responses in 74% (119/160) of subjects treated with COSENTYX 300 mg and in 59% (74/125) of subjects treated with COSENTYX 150 mg. Similarly in Trial PsO2, PASI 75 responders maintained their responses in 84% (210/249) of subjects treated with COSENTYX 300 mg and in 82% (180/219) of subjects treated with COSENTYX 150 mg. Trial PsO2 subjects who were clear or almost clear on the IGA also maintained their responses in 80% (161/202) of subjects treated with COSENTYX 300 mg and in 68% (113/167) of subjects treated with COSENTYX 150 mg.

Among the subjects who chose to participate (39%) in assessments of patient reported outcomes, improvements in signs and symptoms related to itching, pain, and scaling, at Week 12 compared to placebo (Trials PsO1 and PsO2) were observed using the Psoriasis Symptom Diary©.

Psoriasis Lesions of Scalp

A randomized, placebo-controlled trial (Trial PsO5; NCT02267135) enrolled 102 subjects with moderate to severe psoriasis lesions of scalp, defined as having a Psoriasis Scalp Severity Index (PSSI) score of greater than or equal to 12, an IGA scalp only score of 3 or greater, and at least 30% of the scalp affected. In this trial, 62% of subjects had at least 50% of scalp surface area affected. The proportions of subjects achieving an IGA scalp only score of *0* or *1* (clear or almost clear) were 56.9% and 5.9% for the COSENTYX 300 mg and the placebo groups, respectively.

14.2 Pediatric Plaque Psoriasis

A 52-week, multicenter randomized, double-blind, placebo and active-controlled trial (Trial PsO6; NCT02471144) enrolled 162 pediatric subjects 6 years of age and older, with severe plaque psoriasis (as defined by a PASI score ≥ 20, an IGA modified 2011 score of 4, and involving ≥ 10% of the body surface area) who were candidates for systemic therapy.

Subjects were randomized to receive placebo, COSENTYX, or a biologic active control. In the COSENTYX groups, subjects with body weight < 25 kg received 75 mg, subjects with body weight 25 to < 50 kg received either 75 mg or 150 mg (2 times the recommended dose), and subjects with body weight ≥ 50 kg received either 150 mg or 300 mg (2 times the recommended dose). Subjects in the COSENTYX and placebo groups received treatment at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks. At Week 12, subjects randomized to placebo who were non-responders were switched to COSENTYX (dose based on body weight) and received COSENTYX at Weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at Week 16.

Overall, 60% of the subjects were female, 83% were Caucasian, the median body weight was 50.6 kg, and the mean age was 13.5 years with 23% of the subjects < 12 years. At baseline, the median PASI score was 26 (ranged from 17 to 60), and 99% of the subjects had an IGA modified 2011 score of 4 (‘severe’). Approximately 43% of the subjects had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The co-primary endpoints were the proportion of subjects who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline to Week 12 and the proportion of subjects who achieved an IGA modified 2011 score of ‘clear’ or ‘almost clear’ (0 or 1) with at least a 2 point improvement from baseline to Week 12. The key secondary endpoint was the proportion of subjects who achieved a reduction in PASI score of at least 90% (PASI 90) from baseline to Week 12.

Clinical Response

Table 5 presents the efficacy results at Week 12 by baseline weight strata for the approved dose.

Table 5: Clinical Outcomes at Week 12 in Pediatric Subjects with Severe Plaque Psoriasis in Trial PsO6

	Body Weight < 50 kg		**Body Weight ≥ 50 kg**		**Total**	
	COSENTYX 75 mg (N = 22) n (%)	**Placebo (N = 20) n (%)**	**COSENTYX 150 mg (N = 21) n (%)**	**Placebo (N = 21) n (%)**	**COSENTYX[a] (N = 43) n (%)**	**Placebo (N = 41) n (%)**
IGA of clear or almost clear	7 (32)	1 (5)	17 (81)	1 (5)	24 (56)	2 (5)
PASI 75 response	12 (55)	2 (10)	18 (86)	4 (19)	30 (70)	6 (15)
PASI 90 response	9 (41)	1 (5)	17 (81)	0 (0)	26 (60)	1 (2)

Non-responder imputation was used to handle missing values.
[a] COSENTYX treated subjects received 75 mg for subjects < 50 kg and 150 mg for subjects ≥ 50 kg body weight.

14.3 Psoriatic Arthritis

The safety and efficacy of COSENTYX were assessed in 1999 patients, in 3 randomized, double-blind, placebo-controlled studies (PsA1, PsA2 and PsA3) in adult patients, age 18 years and older with active psoriatic arthritis (greater than or equal to 3 swollen and greater than or equal to 3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease modifying anti-rheumatic drug (DMARD) therapy. Patients in these studies had a diagnosis of PsA of at least 5 years across all studies. At baseline, over 61% and 42% of the patients had enthesitis and dactylitis, respectively. Overall, 31% of patients discontinued previous treatment with anti-TNFα agents due to either lack of efficacy or intolerance. In addition, approximately 53% of patients from both studies had concomitant methotrexate (MTX) use. Patients with different subtypes of PsA were enrolled, including polyarticular arthritis with no evidence of rheumatoid nodules (80%), asymmetric peripheral arthritis (63%), distal interphalangeal involvement (58%), spondylitis with peripheral arthritis (20%) and arthritis mutilans (7%).

PsA1 Study (NCT 01752634) evaluated 397 patients, who were treated with COSENTYX 75 mg, 150 mg or 300 mg subcutaneous treatment at Weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks. Patients receiving placebo were re-randomized to receive COSENTYX (either 150 mg or 300 mg every 4 weeks) at Week 16 or Week 24 based on responder status. The primary endpoint was the percentage of patients achieving an ACR20 response at Week 24.

PsA2 Study (NCT 01392326) evaluated 606 patients, who were treated with secukinumab 10 mg/kg, intravenous treatment (or placebo) at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneous COSENTYX treatment (or placebo) every 4 weeks. Patients receiving placebo were re-randomized to receive COSENTYX (either 75 mg or 150 mg every 4 weeks) at Week 16 or Week 24 based on responder status.

PsA3 Study (NCT 02404350) evaluated 996 patients, who were treated with COSENTYX 150 mg or 300 mg subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or once every 4 weeks of COSENTYX 150 mg. Patients treated with placebo received COSENTYX, either 150 mg or 300 mg, subcutaneous, per baseline randomization, at Week 16 or Week 24 based upon responder status. The primary endpoint was ACR20 response at Week 16 with the key secondary endpoint the change from baseline in modified Total Sharp Score (mTSS) at Week 24.

Clinical Response

In PsA1, patients treated with 150 mg or 300 mg COSENTYX demonstrated a greater clinical response, including ACR20, ACR50, and ACR70 compared to placebo at Week 24 (Table 6). Responses were similar in patients regardless of concomitant methotrexate treatment. Responses were seen regardless of prior anti-TNFα exposure.

In patients with coexistent plaque psoriasis receiving COSENTYX (n = 99), the skin lesions of psoriasis improved with treatment, relative to placebo, as measured by the Psoriasis Area Severity Index (PASI).

Table 6: Responses[a] in PsA1 Study at Week 16 and Week 24

	COSENTYX 150 mg (N = 100)	**COSENTYX 300 mg (N = 100)**	**Placebo (N = 98)**	**Difference from Placebo (95% CI)**	
				COSENTYX 150 mg	**COSENTYX 300 mg**
ACR20 response					
Week 16 (%)	60	57	18	42 (30, 54)	38 (26, 51)
Week 24 (%)	51	54	15	36 (24, 48)	39 (27, 51)
ACR50 response					
Week 16 (%)	37	35	6	31 (21, 42)	28 (18, 39)
Week 24 (%)	35	35	7	28 (18, 38)	28 (17, 38)
ACR70 response					
Week 16 (%)	17	15	2	15 (7, 23)	13 (5, 20)
Week 24 (%)	21	20	1	20 (12, 28)	19 (11, 27)

[a]Patients who met escape criteria (less than 20% improvement in tender or swollen joint counts) at Week 16 were considered non-responders.

The percentage of patients achieving ACR20 response by visit is shown in Figure 1. Patients on placebo who received COSENTYX without a loading regimen achieved similar ACR20 responses over time (data not shown).

Figure 1: Percent of Patients Achieving ACR 20 Response[a] in PsA1 Study Through Week 24

[a]Patients who met escape criteria (less than 20% improvement in tender or swollen joint counts) at Week 16 were considered non-responders.

The improvements in the components of the ACR response criteria are shown in Table 7.

Table 7: Mean Change from Baseline in ACR Components at Week 16[a] (PsA1 Study)

	COSENTYX 150 mg (N = 100)	**COSENTYX 300 mg** (N = 100)	**Placebo** (N = 98)
No. of Swollen Joints			
Baseline	12.0	11.2	12.1
Mean change at Week 16	-4.86	-5.83	-3.22
Number of Tender Joints			
Baseline	24.1	20.2	23.5
Mean change at Week 16	-10.70	-10.01	-1.77
Patient's Assessment of Pain			
Baseline	58.9	57.7	55.4
Mean change at Week 16	-22.91	-23.97	-7.98
Patient Global Assessment			
Baseline	62.0	60.7	57.6
Mean change at Week 16	-25.47	-25.40	-8.25
Physician Global Assessment			
Baseline	56.7	55.0	55.0
Mean change at Week 16	-29.24	-34.71	-14.95
Disability Index (HAQ)			
Baseline	1.2200	1.2828	1.1684
Mean change at Week 16	-0.45	-0.55	-0.23
CRP (mg/L)			
Baseline	14.15	10.88	7.87
Mean Change at Week 16[b]	-8.41	-7.21	0.79

[a]Week 16 rather than Week 24 data are displayed to provide comparison between arms prior to placebo escape to COSENTYX.
[b]Mean Change based upon observed data.

Improvements in enthesitis and dactylitis scores were observed in each COSENTYX group compared to placebo at Week 24.

Radiographic Response

In PsA3 Study, inhibition of progression of structural damage was assessed radiographically and expressed by the modified mTSS and its components, the Erosion Score (ES) and Joint Space Narrowing Score (JSN), at Week 24 compared to baseline. Radiographs of hands, wrists, and feet were obtained at baseline, Week 16 and/or Week 24 and scored independently by at least two readers who were blinded to treatment group and visit number. COSENTYX 150 mg without load, 150 mg with load and 300 mg with load treatment significantly inhibited progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at Week 24. The percentage of patients with no disease progression (defined as a change from baseline in mTSS of less than or equal to 0.0) from randomization to Week 24 was 75.7%, 70.9%, and 76.5% for COSENTYX 150 mg without load, 150 mg, 300 mg, respectively versus 68.2% for placebo.

Table 8: Rate of Change per 24 Weeks in Modified Total Sharp Score

Treatment	N	Rate of Change per 24 weeks	Difference from Placebo (95% CI)
COSENTYX 150 mg without load	210	-0.10	-0.61 (-0.95, -0.26)
COSENTYX 150 mg with load	213	0.14	-0.37 (-0.71, -0.03)
COSENTYX 300 mg with load	217	0.03	-0.48 (-0.82, -0.14)
Placebo	296	0.51	--

Results from a linear mixed effects model that excluded data after escape for placebo subjects who received escape therapy at Week 16. The model assumes approximately linear progression over time and estimates a difference in rates (slopes) of progression over 24 weeks to compare treatment arms.

Physical Function

Improvement in physical function as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) demonstrated that the proportion of patients who achieved at least -0.3 improvement in HAQ-DI score from baseline was greater in the COSENTYX 150 mg and 300 mg groups compared to placebo at Week 16 and 24. At Week 16 in PsA1 study, estimated mean change from baseline was -0.23 in the placebo group compared with -0.45 in the COSENTYX 150 mg group and -0.55 in the COSENTYX 300 mg group.

14.4 Ankylosing Spondylitis

The safety and efficacy of COSENTYX were assessed in 816 patients in three randomized, double-blind, placebo-controlled studies (AS1, AS2 and AS3) in adult patients 18 years of age and older with active ankylosing spondylitis. Patients had active disease as defined by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) greater or equal to 4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease modifying anti-rheumatic drug (DMARD) therapy. At baseline, approximately 13% and 25% used concomitant methotrexate or sulfasalazine, respectively. Overall, 29% of patients discontinued previous treatment with anti-TNFα agents due to either lack of efficacy or intolerance.

AS1 Study (NCT01649375) evaluated 219 patients, who were treated with COSENTYX 75 mg or 150 mg subcutaneous treatment at Weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks. At Week 16, patients receiving placebo were re-randomized to either COSENTYX 75 mg or 150 mg every 4 weeks. The primary endpoint was the percentage of patients achieving an ASAS20 response at Week 16.

AS2 Study (NCT01358175) evaluated 371 patients, who were treated with secukinumab 10 mg/kg intravenous treatment at Weeks 0, 2, and 4 (for both treatment arms) or placebo, followed by either 75 mg or 150 mg subcutaneous COSENTYX treatment every 4 weeks or placebo. Patients receiving placebo were re-randomized to receive COSENTYX (either 75 mg or 150 mg every 4 weeks) at Week 16 or Week 24 based on responder status.

AS3 Study (NCT02008916) evaluated 226 patients, who were treated with secukinumab 10 mg/kg intravenous treatment at Weeks 0, 2, and 4 (for both treatment arms) or placebo, followed by either 150 mg or 300 mg subcutaneous COSENTYX treatment every 4 weeks or placebo. Patients receiving placebo were re-randomized to receive COSENTYX (either 150 mg or 300 mg every 4 weeks) at Week 16. The primary endpoint was the percentage of patients achieving an ASAS20 response at Week 16. Patients were blinded to the treatment regimen up to Week 52, and the study continued to Week 156.

Clinical Response

In AS1, patients treated with 150 mg COSENTYX demonstrated greater improvements in ASAS20 and ASAS40 responses compared to placebo at Week 16 (Table 9). Responses were similar in patients regardless of concomitant therapies.

Table 9: ASAS20 and ASAS40 Responses in All AS Patients at Week 16 in Study AS1

	COSENTYX 150 mg (n = 72)	**Placebo (n = 74)**	**Difference from placebo (95% CI)**
ASAS20 response, %	61	28	33 (18, 48)
ASAS40 response, %	36	11	25 (12, 38)

The improvements in the main components of the ASAS20 response criteria and other measures of disease activity are shown in Table 10.

Table 10: ASAS20 Components and Other Measures of Disease Activity at Week 16 (AS1 Study)

	COSENTYX 150 mg (N = 72)		**Placebo (N = 74)**	
	Baseline	**Week 16 change from baseline**	**Baseline**	**Week 16 change from baseline**
ASAS20 Response criteria				
-Patient Global Assessment of Disease Activity (0-100 mm)[1]	67.5	-27.7	70.5	-12.9
-Total spinal pain (0-100 mm)	66.2	-28.5	69.2	-10.9
-BASFI (0-10)[2]	6.2	-2.2	6.1	-0.7
-Inflammation (0-10)[3]	6.5	-2.5	6.5	-0.8
BASDAI Score[4]	6.6	-2.2	6.8	-0.9
BASMI[5]	3.6	-0.51	3.9	-0.22
hsCRP[6] (mg/L) Mean Change at Week 16	27.0	-17.2	15.9	0.8

1. Percent of subjects with at least a 20% and 10 unit improvement measured on a Visual Analog Scale (VAS) with 0 = none, 100 = severe
2. Bath Ankylosing Spondylitis Functional Index.
3. Inflammation is the mean of two patient-reported stiffness self-assessment in BASDAI.
4. Bath Ankylosing Spondylitis Disease Activity Index.
5. Bath Ankylosing Spondylitis Metrology Index.
6. High sensitivity C-reactive protein / mean change based upon observed data.

The percent of patients achieving ASAS20 responses by visit is shown in Figure 2. Patients on placebo who received COSENTYX without a loading regimen achieved similar ASAS20 responses over time (data not shown).

Figure 2: ASAS20 Responses in all AS1 Study Patients Over Time Up to Week 16

In AS3 Study, patients treated with COSENTYX (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses, regardless of dose, that were superior to placebo at Week 16 for the primary and most secondary endpoints. At Week 16, the ASAS20 and ASAS40 responses were 58.1% and 40.5% for 150 mg and 60.5% and 42.1% for 300 mg, respectively. The percent of patients achieving ASAS20 responses by visit is shown in Figure 3.

Figure 3: ASAS20 Responses in all AS3 Study Patients Over Time Up to Week 16

COSENTYX treated patients showed improvement compared to placebo-treated patients in health-related quality of life as assessed by ASQoL at Week 16.

14.5 Non-Radiographic Axial Spondyloarthritis

The safety and efficacy of COSENTYX were assessed in 555 patients in one randomized, double-blind, placebo-controlled Phase 3 study (nr-axSpA1, NCT02696031) in adult patients 18 years of age and older with active non-radiographic axial spondyloarthritis. Patients met ASAS criteria for axial spondyloarthritis and had active disease as defined by a BASDAI greater or equal to 4, a Visual Analogue Scale (VAS) for total back pain greater or equal to 40 (on a scale of 0-100 mm) despite NSAID therapy and no evidence of radiographic changes in the sacroiliac joints that would meet the modified New York criteria for AS. Patients also had to have objective signs of inflammation with a C-reactive protein (CRP) level above the upper limit of normal and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Approximately 10% and 15% of patients used concomitant methotrexate or sulfasalazine, respectively. Overall, 10% of patients had received previous treatment with anti-TNFα agents and discontinued these due to either lack of efficacy or intolerance.

Patients were treated with COSENTYX 150 mg subcutaneous treatment with load (Weeks 0, 1, 2, 3, and 4) or without a load (Weeks 0 and 4) followed by the same dose every 4 weeks or placebo. In the double-blind period, patients (n = 555) received either placebo or COSENTYX for 52 weeks. Starting Week 16, dose adjustment or addition of concomitant NSAIDs and DMARDs was permitted. Starting at Week 20, patients were allowed to switch to open-label COSENTYX 150 mg monthly or other biologic at the discretion of the investigator and patient. The primary endpoint was at least 40% improvement in Assessment of Spondyloarthritis International Society (ASAS40) at Week 52.

Clinical Response

In nr-axSpA1 Study, treatment with COSENTYX 150 mg resulted in significant improvements in the measure of disease activity compared to placebo at Week 16 and Week 52 (Table 11).

Table 11: Clinical Response in nr-axSpA1 Study at Week 16 and Week 52

Number of subjects with ASAS40 response (%)	**COSENTYX 150 mg without load (n = 184)**	**COSENTYX 150 mg with load (n = 185)**	**Placebo (n = 186)**	**Difference from Placebo (95% CI)**	
				COSENTYX 150 mg without load	**COSENTYX 150 mg with load**
Week 16	75 (41)	74 (40)	52 (28)	13 (3, 22)	12 (2, 22)
Week 52	70 (38)	62 (34)	36 (19)	19 (10, 28)	14 (5, 23)

Difference in proportions with 95% CI based on normal approximation.

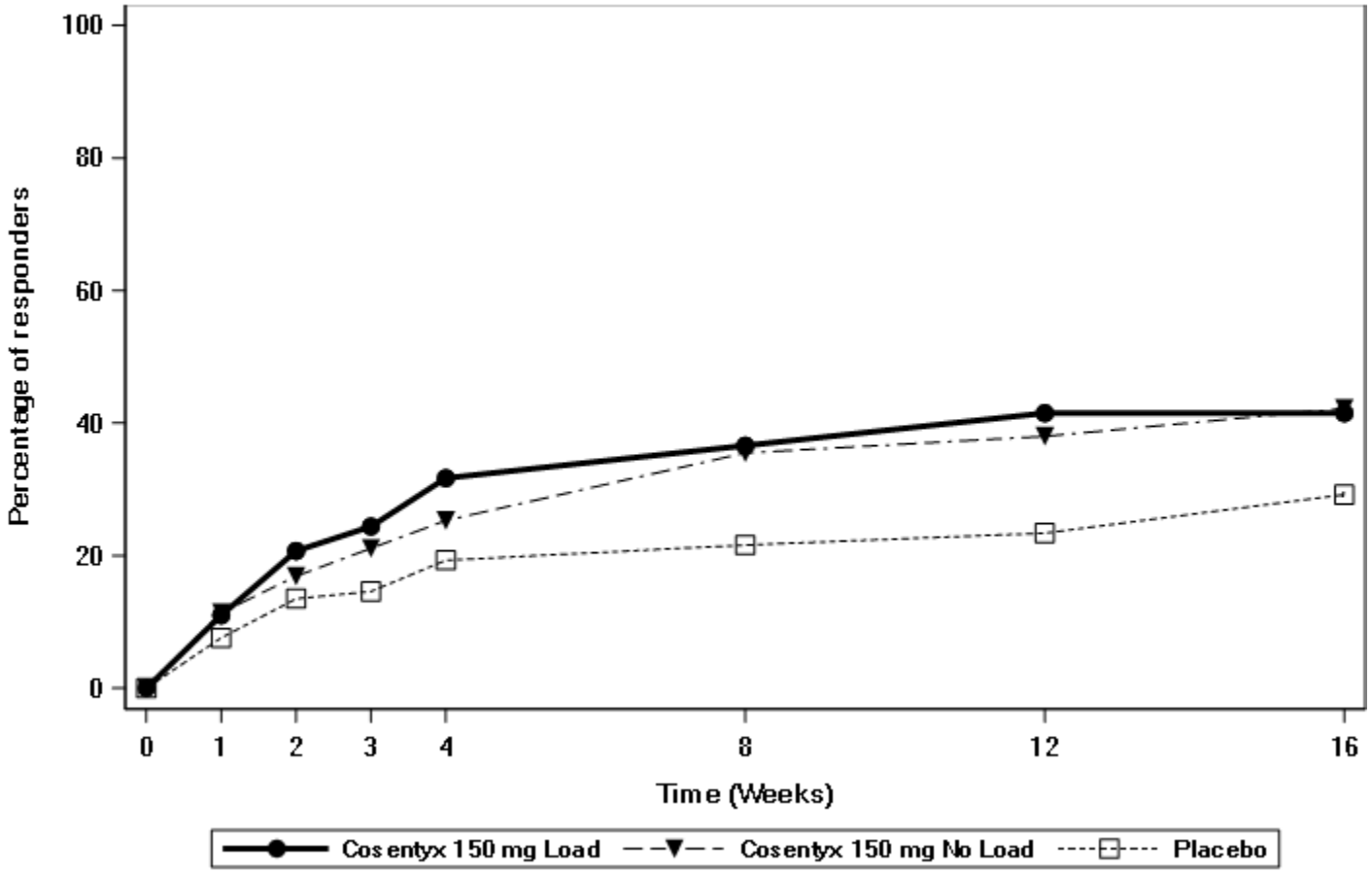
The results of the main components of the ASAS40 response criteria are shown in Table 12.

Table 12: Main Components of the ASAS40 Response Criteria and Other Measures of Disease Activity in nr-axSpA Patients at Baseline and Week 16 in nr-axSpA1 Study

	COSENTYX 150 mg without load (N = 184)		**COSENTYX 150 mg with load (N = 185)**		**Placebo (N = 186)**	
	Baseline	Week 16 change from baseline	Baseline	Week 16 change from baseline	Baseline	Week 16 change from baseline
ASAS40 Response criteria						
-Patient Global Assessment of Disease Activity (0-100 mm)	71.0	-26.2	72.6	-24.1	68.8	-13.8
-Total back pain (0-100 mm)	72.0	-25.5	73.3	-25.0	70.9	-15.6
-BASFI (0-10)	5.9	-1.6	6.2	-1.8	5.9	-1.0
-Inflammation (0-10)	6.8	-2.8	7.2	-2.8	6.6	-1.7
hsCRP (mg/L) Mean Change at Week 16	9.8	-4.7	13.4	-7.9	9.2	-2.4
BASDAI (0-10)	6.9	-2.4	7.1	-2.4	6.8	-1.5
-Spinal Pain	7.6	-3.0	7.8	-3.0	7.5	-2.0
-Peripheral pain and swelling (0-10)	6.6	-2.4	6.3	-2.3	6.1	-1.6
BASMI	2.8	-0.3	2.9	-0.3	2.8	-0.1

The percentage of patients achieving an ASAS40 response by visit is shown in Figure 4.

Figure 4: ASAS40 Responses in nr-axSpA1 Study Over Time up to Week 16



Health Related Quality of Life

COSENTYX treated patients showed improvement in both load and without load arms compared to placebo-treated patients at Week 16 in health-related quality of life as measured by ASQoL (LS mean change: Week 16: -3.5 and -3.6 vs -1.8, respectively).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

COSENTYX (secukinumab) injection is a clear to opalescent, colorless to slightly yellowish solution available as follows:

COSENTYX Sensoready pen:

• NDC 0078-0639-41: Carton of two 150 mg/mL (300 mg dose) single-dose Sensoready pens (injection)

• NDC 0078-0639-68: Carton of one 150 mg/mL single-dose Sensoready pen (injection)

COSENTYX prefilled syringe:

• NDC 0078-0639-98: Carton of two 150 mg/mL (300 mg dose) single-dose prefilled syringes (injection)

• NDC 0078-0639-97: Carton of one 150 mg/mL single-dose prefilled syringe (injection)

COSENTYX prefilled syringe (for pediatric patients less than 50 kg):

• NDC 0078-1056-97: Carton of one 75 mg/0.5 mL single-dose prefilled syringe (injection)

The removable cap of the COSENTYX 150 mg/mL Sensoready pen and prefilled syringe, and 75 mg/0.5 mL prefilled syringe contains natural rubber latex. Each Sensoready pen and prefilled syringe is equipped with a needle safety guard.

COSENTYX (secukinumab) for injection is a white lyophilized powder for healthcare professional use only available as follows:

• NDC 0078-0657-61: Carton of one 150 mg lyophilized powder in a single-dose vial (for injection)

16.2 Storage and Handling

Refrigerate COSENTYX Sensoready pens, prefilled syringes, and vials at 2ºC to 8ºC (36ºF to 46ºF). Keep the product in the original carton to protect from light until the time of use. Do not freeze. To avoid foaming do not shake. COSENTYX does not contain a preservative; discard any unused portion.

If necessary, COSENTYX Sensoready pens and 150 mg/mL prefilled syringes may be stored for up to 4 days at room temperature not to exceed 30°C (86°F). Write the date COSENTYX was removed from the refrigerator in the space provided on the carton. If unused and not stored above 30°C (86°F), COSENTYX Sensoready pens and 150 mg/mL prefilled syringes may be returned to the refrigerator. Throw away COSENTYX if it has been kept outside of the refrigerator and not been used in over 4 days.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Infections

Inform patients that COSENTYX may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to the doctor and contacting their doctor if they develop any symptoms of infection *[see Warnings and Precautions (5.1)]*.

Hypersensitivity

Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions (5.4)]*.

Risk of Hypersensitivity in Latex-Sensitive Individuals

Advise latex-sensitive patients that the removal caps of the COSENTYX Sensoready pen and the COSENTYX 1 mL and 0.5 mL prefilled syringes contain natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals *[see Warnings and Precautions (5.5)]*.

Immunization

Advise patients that vaccination with live vaccines is not recommended during COSENTYX treatment. Instruct patients to inform the healthcare practitioner that they are taking COSENTYX prior to a potential vaccination *[see Warnings and Precautions (5.6)]*.

Instructions on Injection Technique

If a patient or caregiver is to administer COSENTYX using the Sensoready pen or the prefilled syringe, instruct him/her in injection techniques and assess their ability to inject subcutaneously to ensure the proper administration of COSENTYX [*see Dosage and Administration (2.6), Medication Guide and Instructions for Use]*.

For pediatric patients, inform patients and caregivers that pediatric patients should not self-administer COSENTYX using the pre-filled syringe or the Sensoready pen.

Instruct patients or caregivers in the technique of proper syringe and needle disposal, and advise them not to reuse these items. Instruct patients to inject the full amount of COSENTYX according to the directions provided in the Medication Guide and Instructions for Use.

Manufactured by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

US License Number 1244

MEDICATION GUIDE

COSENTYX® (koe-sen-tix)

(secukinumab)

Injection, for subcutaneous use

What is the most important information I should know about COSENTYX?

COSENTYX is a medicine that affects your immune system. COSENTYX may increase your risk of having serious side effects, such as:

Infections. COSENTYX may lower the ability of your immune system to fight infections and may increase your risk of infections, sometimes serious.

- Your healthcare provider should check you for tuberculosis (TB) before starting treatment with COSENTYX.
- If your healthcare provider feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with COSENTYX and during treatment with COSENTYX.
- Your healthcare provider should watch you closely for signs and symptoms of TB during treatment with COSENTYX. **Do not take COSENTYX if you have an active TB infection.**

Before starting COSENTYX, tell your healthcare provider if you:

- are being treated for an infection
- have an infection that does not go away or that keeps coming back
- have TB or have been in close contact with someone with TB
- think you have an infection or have symptoms of an infection, such as:
  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in your phlegm
  - weight loss
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal

After starting COSENTYX, call your healthcare provider right away if you have any of the signs of infection listed above. Do not use COSENTYX if you have any signs of infection unless you are instructed to by your healthcare provider.

See **"What are the possible side effects of COSENTYX?"** for more information about side effects.

What is COSENTYX?

COSENTYX is a prescription medicine used to treat:

- people 6 years of age and older with moderate to severe plaque psoriasis that involves large areas or many areas of the body, and who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet or UV light alone or with systemic therapy)
- adults with active psoriatic arthritis
- adults with active ankylosing spondylitis
- adults with active non-radiographic axial spondyloarthritis and objective signs of inflammation

COSENTYX may improve your psoriasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis but it may also lower the ability of your immune system to fight infections.

It is not known if COSENTYX is safe and effective in children below the age of 6 with plaque psoriasis or in children for other conditions.

Do not use COSENTYX if you:

have had a severe allergic reaction to secukinumab or any of the other ingredients in COSENTYX. See the end of this Medication Guide for a complete list of ingredients in COSENTYX.

Before taking COSENTYX, tell your healthcare provider about all of your medical conditions, including if you: have any of the conditions or symptoms listed in the section **"What is the most important information I should know about COSENTYX?"**

- have inflammatory bowel disease (Crohn's disease or ulcerative colitis)

- are allergic to latex. The needle cap on the COSENTYX Sensoready® 150 mg/mL pen and 150 mg/mL and 75 mg/0.5 mL prefilled syringes contain latex.
- have recently received or are scheduled to receive an immunization (vaccine). People who take COSENTYX **should not** receive live vaccines. Children should be brought up to date with all vaccines before starting COSENTYX.
- are pregnant or plan to become pregnant. It is not known if COSENTYX can harm your unborn baby. You and your healthcare provider should decide if you will use COSENTYX.
- are breastfeeding or plan to breastfeed. It is not known if COSENTYX passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of your medicines to show your healthcare provider and pharmacist when you get a new medicine.

How should I use COSENTYX?

See the detailed "Instructions for Use" that comes with your COSENTYX for information on how to prepare and inject a dose of COSENTYX, and how to properly throw away (dispose of) used COSENTYX Sensoready pens and prefilled syringes.

- Use COSENTYX exactly as prescribed by your healthcare provider.
- COSENTYX comes in a Sensoready pen or prefilled syringes that you or your caregiver may use at home to give injections. Your healthcare provider will decide which type of COSENTYX is best for you to use at home.
- If your healthcare provider decides that you or a caregiver may give your injections of COSENTYX at home, you should receive training on the right way to prepare and inject COSENTYX. Do not try to inject COSENTYX yourself, until you or your caregiver has been shown how to inject COSENTYX by your healthcare provider.
- Children should not inject themselves with the Sensoready pen or the prefilled syringes. An adult caregiver should prepare and inject COSENTYX after receiving training on the right way to prepare and inject COSENTYX.
- Your healthcare provider will prescribe the dose of COSENTYX that is right for you or your child based on their body weight.
  - If your prescribed dose of COSENTYX is **75 mg**, you must give **1 injection** of COSENTYX 75 mg/0.5 mL for each dose.
  - If your prescribed dose of COSENTYX is **150 mg**, you must give **1 injection** of COSENTYX 150 mg/mL for each dose.
  - If your prescribed dose of COSENTYX is **300 mg**, you must give **2 injections** of COSENTYX 150 mg/mL for each dose.
- COSENTYX is given as an injection under your skin (subcutaneous injection), in your upper legs (thighs) or stomach-area (abdomen) by you or a caregiver. A caregiver may also give you an injection of COSENTYX in your upper outer arm.
- **Do not** give an injection in an area of the skin that is tender, bruised, red or hard, or in an area of skin that is affected by psoriasis.
- Each injection should be given at a different site. **Do not** use the 2-inch area around your navel (belly button).
- If you inject more COSENTYX than prescribed, call your healthcare provider or go to the nearest emergency room right away.

What are the possible side effects of COSENTYX?

COSENTYX may cause serious side effects including:

- See **"What is the most important information I should know about COSENTYX?"**
- **Inflammatory bowel disease.** New cases of inflammatory bowel disease or "flare-ups" can happen with COSENTYX, and can sometimes be serious. If you have inflammatory bowel disease (ulcerative colitis or Crohn's disease), tell your healthcare provider if you have worsening disease symptoms during treatment with COSENTYX or develop new symptoms of stomach pain or diarrhea.
- **Serious allergic reactions.** Get emergency medical help right away if you get any of the following symptoms of a serious allergic reaction:
  - feel faint
  - trouble breathing or throat tightness
  - skin rash

- o swelling of your face, eyelids, lips, mouth, tongue, or throat
- o chest tightness
- o hives (red, itchy bumps)

If you have a severe allergic reaction, do not give another injection of COSENTYX.

The most common side effects of COSENTYX include:

- o cold symptoms
- o diarrhea
- o upper respiratory infections

These are not all of the possible side effects of COSENTYX.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store COSENTYX?

- Store COSENTYX in a refrigerator, between 36°F to 46°F (2°C to 8°C).
- Keep COSENTYX in the original carton until ready for use to protect from light.
- COSENTYX Sensoready pen and COSENTYX 150 mg/mL prefilled syringe may be stored at room temperature, not to exceed temperatures above 86°F (30°C), for up to 4 days.
- Write the date COSENTYX Sensoready pen or COSENTYX 150 mg/mL prefilled syringe was removed from the refrigerator in the space provided on the carton.
- If unused and not stored above 30°C (86°F), COSENTYX Sensoready pens and 150 mg/mL prefilled syringe may be returned to the refrigerator.
- Throw away COSENTYX Sensoready pen or COSENTYX 150 mg/mL prefilled syringe if it has been kept outside of the refrigerator and not been used in over 4 days.
- Do not freeze COSENTYX.
- Do not shake COSENTYX.
- Throw away (dispose of) any unused COSENTYX Sensoready pen or prefilled syringes.

Keep COSENTYX and all medicines out of the reach of children.

General information about the safe and effective use of COSENTYX.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use COSENTYX for a condition for which it was not prescribed. Do not give COSENTYX to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your healthcare provider or pharmacist for information about COSENTYX that is written for health professionals.

What are the ingredients in COSENTYX?

Active ingredient: secukinumab

Inactive ingredients: Sensoready pen and prefilled syringes: L-histidine/histidine hydrochloride monohydrate, L-methionine, polysorbate 80, trehalose dihydrate, and sterile water for injection.

Vial: L-histidine/histidine hydrochloride monohydrate, polysorbate 80, and sucrose.

Manufactured by: Novartis Pharmaceuticals Corporation, East Hanover, New Jersey 07936

For more information, call 1-888-669-6682 or go to www.COSENTYX.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration Revised: May 2021

INSTRUCTIONS FOR USE

COSENTYX® (koe-sen-tix)

(secukinumab)

For Injection

The following information is intended for medical or healthcare professionals only.

IMPORTANT:

- The single-dose vial contains 150 mg of COSENTYX for reconstitution with Sterile Water for Injection (SWFI). Do not use the vial after the expiry date shown on the outer box or vial. If it has expired, return the entire pack to the pharmacy.
- The preparation of the solution for subcutaneous injection shall be done without interruption ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution on average takes 20 minutes and should not exceed 90 minutes.
- Throw away (dispose of) the used syringe right away after use. Do not re-use a syringe. See **"How should I dispose of a used syringe?"** at the end of this Instructions for Use.

How should I store COSENTYX?

- Store the vial of COSENTYX in the refrigerator between 2°C to 8°C (36°F to 46°F).

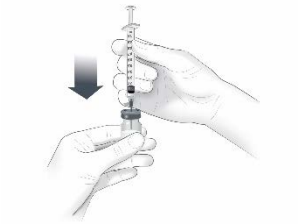
To prepare COSENTYX 150 mg for injection, please adhere to the following instructions:

Instructions for reconstitution of COSENTYX 150 mg for injection:

Step 1. Remove the vial of COSENTYX 150 mg for injection from the refrigerator and allow to stand for 15 to 30 minutes to reach room temperature. Ensure the Sterile Water for Injection (SWFI) is at room temperature.

Step 2. Reconstitute the lyophilized powder by slowly injecting 1 mL of Sterile Water for Injection (SWFI) into the vial. Direct the stream of SWFI onto the lyophilized powder (**See Figure A**).

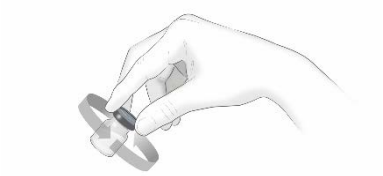
Figure A



Step 3. Tilt the vial to an angle of approximately 45 degrees and gently rotate between the fingertips for approximately 1 minute. Do not shake or invert the vial (**See Figure B**).

Step 4. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.

Figure B



Step 5. Tilt the vial to an angle of approximately 45 degrees and gently rotate between the fingertips for approximately 1 minute. Do not shake or invert the vial (**See Figure B**).

Step 6. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its color may vary from colorless to slightly yellow. Do not use if the lyophilized powder has not fully dissolved or if the liquid contains visible particles, is cloudy or is discolored.

Step 7. Prepare the required number of vials (1 vial for the 150 mg dose or 2 vials for the 300 mg dose).

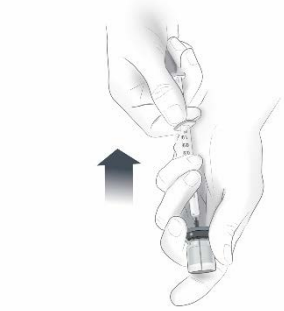
After preparation, use the solution for subcutaneous injection immediately or store at 2°C to 8°C (36°F to 46°F) for up to 24 hours. Do not freeze. After storage at 2°C to 8°C (36°F to 46°F), allow the reconstituted solution to come to room temperature (15 to 30 minutes) before administration. Administer the solution within 1 hour after removal from the 2°C to 8°C (36°F to 46°F) storage.

Instructions for administration of COSENTYX solution:

Step 1. Tilt the vial to an angle of approximately 45 degrees and position the needle tip at the very bottom of the solution in the vial when drawing the solution into the syringe. DO NOT invert the vial.

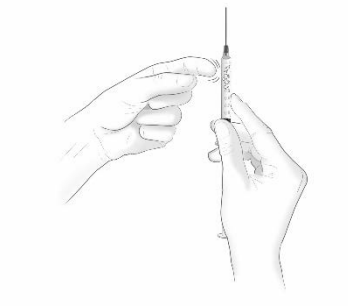
Step 2. Carefully withdraw slightly more than 1 mL of the solution for subcutaneous injection from the vial into a 1 mL graduated disposable syringe using a suitable needle (e.g., 21G x 2") **(See Figure C).** This needle will only be used for withdrawing COSENTYX into the disposable syringe. Prepare the required number of syringes (1 syringe for the 150 mg dose or 2 syringes for the 300 mg dose).

Figure C



Step 3. With the needle pointing upward, gently tap the syringe to move any air bubbles to the top **(See Figure D).**

Figure D



Step 4. Replace the attached needle with a 27G x ½" needle **(See Figure E).**

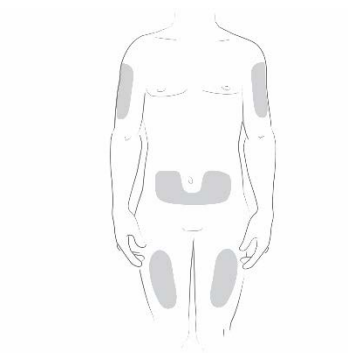
Step 5. Expel the air bubbles and advance the plunger to the 1 mL mark.

Step 6. Clean the injection site with an alcohol wipe.

Figure E

Step 7. Inject the COSENTYX solution subcutaneously into the front of thighs, lower abdomen [but not the area 2 inches around the navel (belly button)] or outer upper arms **(See Figure F).** Choose a different site each time an injection is administered. Do not inject into areas where the skin is tender, bruised, red, scaly or hard, or in an area of skin that is affected by psoriasis. Avoid areas with scars or stretch marks.

Figure F



How should I dispose of a used syringe?

Any remaining solution in the vial must not be used and must be discarded in accordance with local requirements. Vials are for single use only.

Put the used syringes and needles in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of)** the syringes and needles in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

1. made of a heavy-duty plastic,
2. can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
3. upright and stable during use,
4. leak-resistant, and
5. properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
US License Number 1244

Revised: May 2021

INSTRUCTIONS FOR USE

COSENTYX® (koe-sen-tix)

(secukinumab)

Injection

150 mg/mL single-dose Prefilled Syringe

Be sure that you read, understand, and follow this Instructions for Use before injecting COSENTYX. Your healthcare provider should show you how to prepare and inject COSENTYX properly using the prefilled syringe before you use it for the first time. Children should not inject COSENTYX themselves using the prefilled syringe. An adult caregiver should prepare and inject COSENTYX after receiving proper training in subcutaneous injection technique. Talk to your healthcare provider if you have any questions.

Important:

- **Do not use** the COSENTYX prefilled syringe if either the seal on the outside carton or the seal of the blister are broken. Keep the COSENTYX prefilled syringe in the sealed carton until you are ready to use it.
- **Do not shake** the COSENTYX prefilled syringe.
- **The needle caps of the prefilled syringes contain latex. Do not handle the prefilled syringes if you are sensitive to latex.**
- The prefilled syringe has a needle guard that will be activated to cover the needle after the injection is finished. The needle guard will help to prevent needle stick injuries to anyone who handles the prefilled syringe.
- Do not remove the needle cap until just before you give the injection.
- Avoid touching the syringe guard wings before use. Touching them may cause the syringe guard to be activated too early.
- Throw away (dispose of) the used COSENTYX prefilled syringe right away after use. **Do not re-use a COSENTYX prefilled syringe.** See **"How should I dispose of used COSENTYX prefilled syringes?"** at the end of this Instructions for Use.

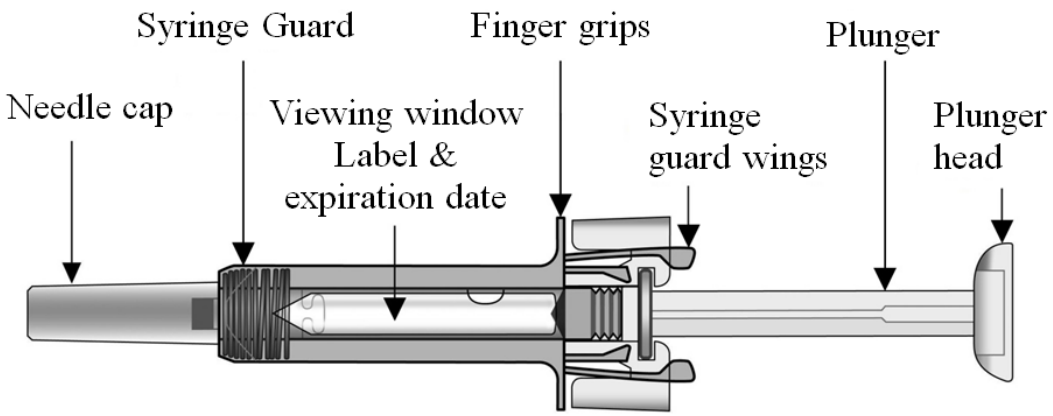
How should I store COSENTYX?

- Store your carton of COSENTYX prefilled syringes in a refrigerator, between 36°F to 46°F (2°C to 8°C).
- Keep COSENTYX prefilled syringes in the original carton until ready to use to protect from light.
- COSENTYX prefilled syringes may be stored at room temperature, not to exceed temperatures above 86°F (30°C), for up to 4 days.
- Write the date COSENTYX prefilled syringes was removed from the refrigerator in the space provided on the carton.
- If unused and not stored above 30°C (86°F), COSENTYX prefilled syringes may be returned to the refrigerator.
- Throw away COSENTYX if it has been kept outside of the refrigerator and not been used in over 4 days.
- Do not freeze COSENTYX prefilled syringes.
- Throw away (dispose of) any unused COSENTYX prefilled syringes.

Keep COSENTYX and all medicines out of the reach of children.

COSENTYX prefilled syringe parts (see Figure A):

Figure A



What you need for your injection:

Included in the carton:

A new COSENTYX prefilled syringe.

Each COSENTYX prefilled syringe contains **150 mg** of COSENTYX.

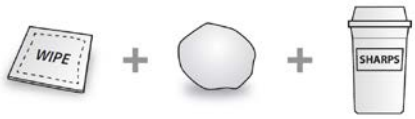
- If your **prescribed dose** of COSENTYX is **150 mg**, you must give **1 injection**.
- If your **prescribed dose** of COSENTYX is **300 mg**, you must give **2 injections**.

Not included in the carton **(see Figure B)**:

- 1 Alcohol wipe
- 1 Cotton ball or gauze
- Sharps disposal container

See "**How should I dispose of used COSENTYX prefilled syringes**?" at the end of this Instructions for Use.

Figure B



Prepare the COSENTYX 150 mg prefilled syringe

Step 1. Find a clean, well-lit, flat work surface.

Step 2. Take the carton containing the COSENTYX prefilled syringe out of the refrigerator and leave it **unopened** on your work surface for about 15 to 30 minutes so that it reaches room temperature.

Step 3. Wash your hands well with soap and water.

Step 4. Remove the COSENTYX prefilled syringe from the outer carton and take it out of the blister.

Step 5. Look through the viewing window on the COSENTYX prefilled syringe. The liquid inside should be clear. The color may be colorless to slightly yellow. You may see a small air bubble in the liquid. This is normal. **Do not use** the prefilled syringe if the liquid contains visible particles, or if the liquid is cloudy or discolored.

Step 6. **Do not use** the COSENTYX prefilled syringe if it is broken. Return the prefilled syringe and the package it came in to the pharmacy.

Step 7. **Do not use** the COSENTYX prefilled syringe if the expiration date has passed.

Choose and clean the injection site

- Areas of your body that you may use as injection sites include:
  - the front of your thighs **(see Figure C)**
  - the lower stomach-area (abdomen), but **not** the area 2 inches around your navel (belly button) **(see Figure C)**
  - the upper outer arms, if a caregiver is giving you the injection **(see Figure D)**
- Choose a different site for each injection of COSENTYX.
- **Do not** inject into areas where the skin is tender, bruised, red, scaly, or hard, or in an area of skin that is affected by psoriasis. Avoid areas with scars or stretch marks.

Figure C

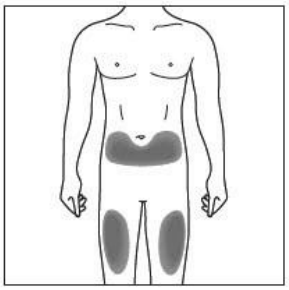
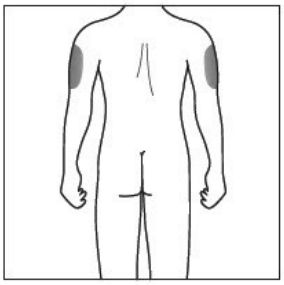


Figure D

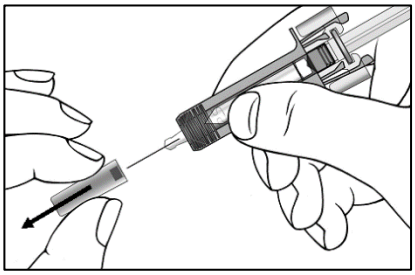


Step 8. Using a circular motion, clean the injection site with the alcohol wipe. Leave it to dry before injecting. Do not touch the cleaned area again before injecting.

Giving the injection

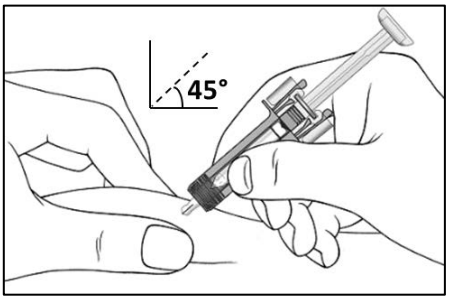
Step 9. Carefully remove the needle cap from the COSENTYX prefilled syringe **(see Figure E).** Throw away the needle cap. You may see a drop of liquid at the end of the needle. This is normal.

Figure E



Step 10. With one hand gently pinch the skin at the injection site. With your other hand insert the needle into your skin at a 45-degree angle as shown **(see Figure F).** Push the needle all the way in to make sure that you inject your full dose.

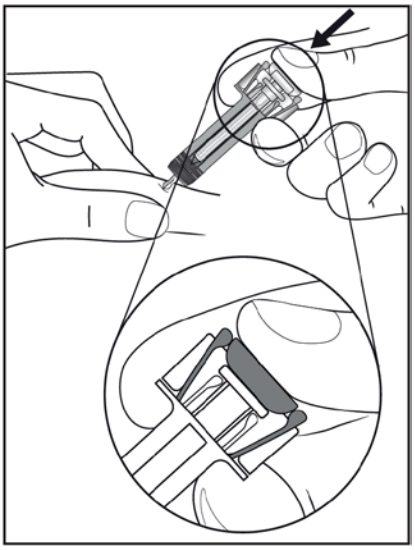
Figure F



Step 11. Hold the COSENTYX prefilled syringe finger grips as shown (**see Figure G**). Slowly press down on the plunger as far as it will go, so that the plunger head is completely between the syringe guard wings. This will make sure that the syringe guard has been activated.

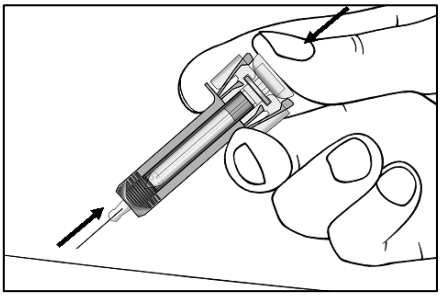
Step 12. Continue to press fully on the plunger for an additional 5 seconds. Hold the syringe in place for the full 5 seconds.

Figure G



Step 13. Keep the plunger fully depressed while you carefully pull the needle straight out from the injection site **(see Figure H).**

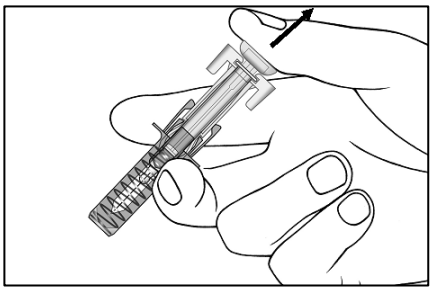
Figure H



Step 14. Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle **(see Figure I).**

Step 15. There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Figure I

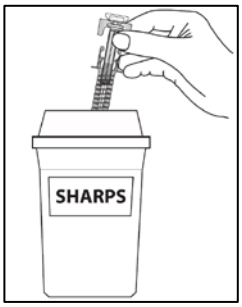


If your prescribed dose of COSENTYX is 300 mg, repeat steps 4 through 15 with a new COSENTYX prefilled syringe.

How should I dispose of used COSENTYX prefilled syringes?

Step 16. Put your used prefilled syringes in a FDA-cleared sharps disposal container right away after use **(see Figure J). Do not throw away (dispose of)** prefilled syringes in your household trash.

Figure J



If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles, syringes and prefilled syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Revised: May 2021

Manufactured by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
US License Number 1244

INSTRUCTIONS FOR USE

COSENTYX® (koe-sen-tix)

(secukinumab)

Injection

75 mg/0.5 mL single-dose Prefilled Syringe

Be sure that you read, understand, and follow this Instructions for Use before injecting COSENTYX. Your healthcare provider should show you how to prepare and inject COSENTYX properly using the prefilled syringe before you use it for the first time. Children should not inject COSENTYX themselves using the prefilled syringe. An adult caregiver should prepare and inject COSENTYX after receiving proper training in subcutaneous injection technique. Talk to your healthcare provider if you have any questions.

Important:

- **Do not use** the COSENTYX prefilled syringe if either the seal on the outside carton or the seal of the blister are broken. Keep the COSENTYX prefilled syringe in the sealed carton until you are ready to use it.
- Inject COSENTYX **within 1 hour** after taking it out of the refrigerator.
- **Do not shake** the COSENTYX prefilled syringe.
- **The needle cap of the prefilled syringe contains latex. Do not handle the prefilled syringe if you are sensitive to latex**.
- The prefilled syringe has a needle guard that will be activated to cover the needle after the injection is finished. The needle guard will help to prevent needle stick injuries to anyone who handles the prefilled syringe.
- Do not remove the needle cap until just before you give the injection.
- Avoid touching the syringe guard wings before use. Touching them may cause the syringe guard to be activated too early.
- Throw away (dispose of) the used COSENTYX prefilled syringe right away after use. **Do not re-use a COSENTYX prefilled syringe.** See "**How should I dispose of used COSENTYX prefilled syringes?**" at the end of this Instructions for Use.

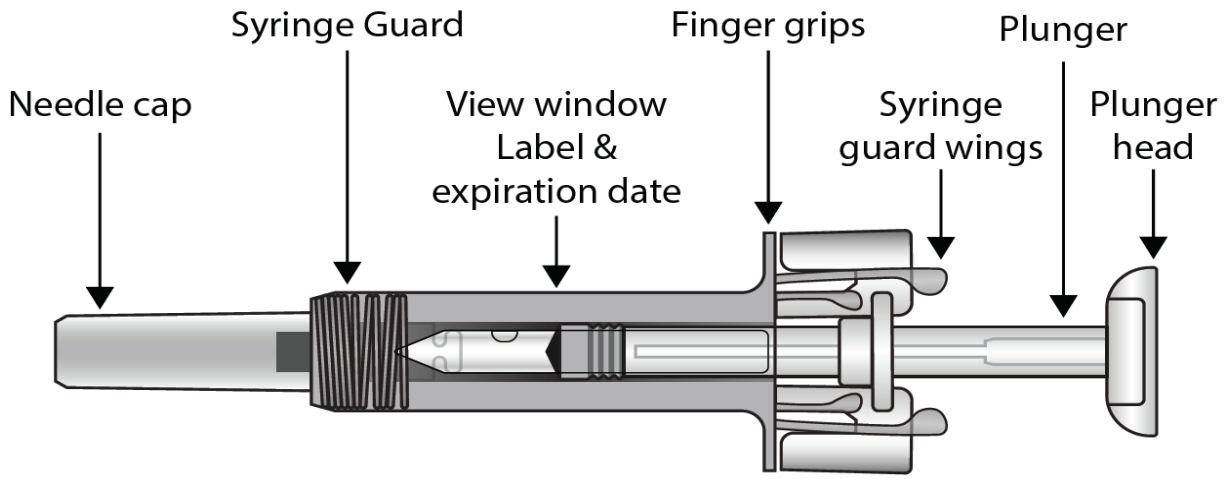
How should I store COSENTYX?

- Store your carton of COSENTYX prefilled syringe in a refrigerator, between 36°F to 46°F (2°C to 8°C).
- Keep COSENTYX prefilled syringe in the original carton until ready to use to protect from light.
- Do not freeze COSENTYX prefilled syringe.
- Throw away (dispose of) any unused COSENTYX prefilled syringes.

Keep COSENTYX and all medicines out of the reach of children.

COSENTYX prefilled syringe parts (**see Figure A**):

Figure A



What you need for your injection:

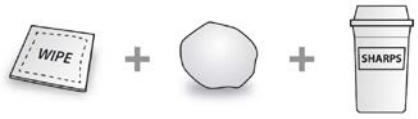
Included in the carton:
A new COSENTYX prefilled syringe.
Each COSENTYX prefilled syringe contains **75 mg** of COSENTYX.

Not included in the carton (**see Figure B**):

- 1 Alcohol wipe
- 1 Cotton ball or gauze
- Sharps disposal container

See "**How should I dispose of used COSENTYX prefilled syringes**?" at the end of this Instructions for Use.

Figure B



Prepare the COSENTYX 75 mg Prefilled Syringe

Step 1. Find a clean, well-lit, flat work surface.

Step 2. Take the carton containing the COSENTYX prefilled syringe out of the refrigerator and leave it **unopened** on your work surface for about 15 to 30 minutes so that it reaches room temperature.

Step 3. Wash your hands well with soap and water.

Step 4. Remove the COSENTYX prefilled syringe from the outer carton and take it out of the blister.

Step 5. Look through the viewing window on the COSENTYX prefilled syringe. The liquid inside should be clear. The color may be colorless to slightly yellow. You may see a small air bubble in the liquid. This is normal. **Do not use** the prefilled syringe if the liquid contains visible particles, or if the liquid is cloudy or discolored.

Step 6. **Do not use** the COSENTYX prefilled syringe if it is broken. Return the prefilled syringe and the package it came in to the pharmacy.

Step 7. **Do not use** the COSENTYX prefilled syringe if the expiration date has passed.

Choose and clean the injection site

- Areas of your body that you may use as injection sites include:
  - the front of your thighs (**see Figure C**)
  - the lower stomach-area (abdomen), but **not** the area 2 inches around your navel (belly button) (**see Figure C**)
  - the upper outer arms, (**see Figure D**)
- Choose a different site for each injection of COSENTYX.
- **Do not** inject into areas where the skin is tender, bruised, red, scaly, or hard, or in an area of skin that is affected by psoriasis. Avoid areas with scars or stretch marks.

Figure C

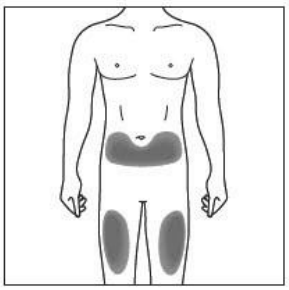
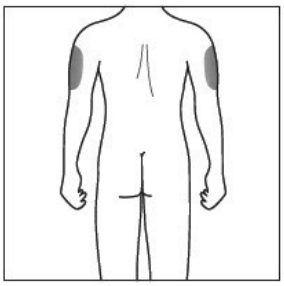


Figure D

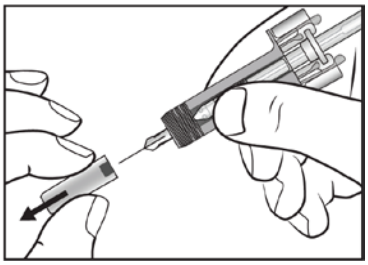


Step 8. Using a circular motion, clean the injection site with the alcohol wipe. Leave it to dry before injecting. Do not touch the cleaned area again before injecting.

Giving the injection

Step 9. Carefully remove the needle cap from the COSENTYX prefilled syringe (**see Figure E**). Throw away the needle cap. You may see a drop of liquid at the end of the needle. This is normal.

Figure E



Step 10. With one hand gently pinch the skin at the injection site. With your other hand insert the needle into your skin at a 45-degree angle as shown (**see Figure F**). Push the needle all the way in to make sure that you inject your full dose.

Figure F

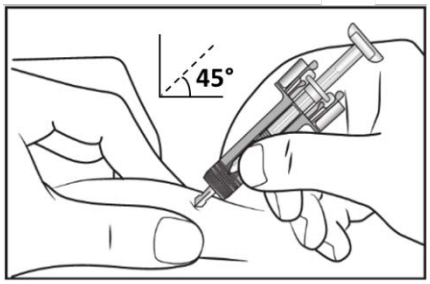
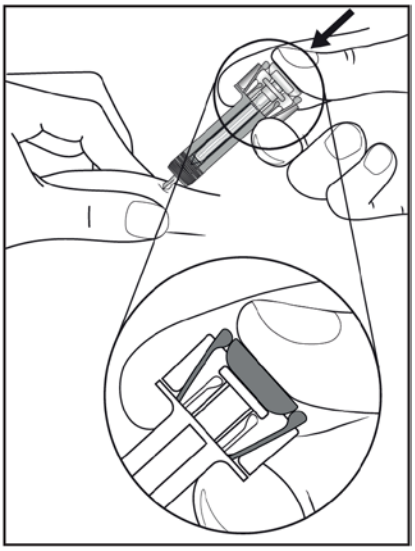


Figure G



Step 11. Hold the COSENTYX prefilled syringe finger grips as shown (**see Figure G**). Slowly press down on the plunger as far as it will go, so that the plunger head is completely between the syringe guard wings. This will make sure that the syringe guard has been activated.

Step 12. Continue to press fully on the plunger for an additional 5 seconds. Hold the syringe in place for the full 5 seconds.

Step 13. Keep the plunger fully depressed while you carefully pull the needle straight out from the injection site (**see Figure H**).

Figure H

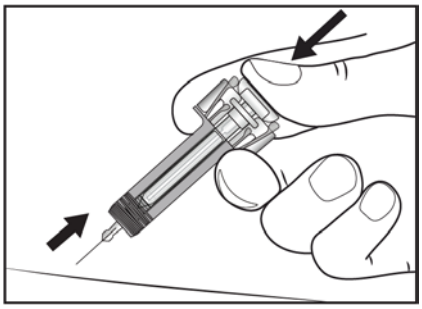
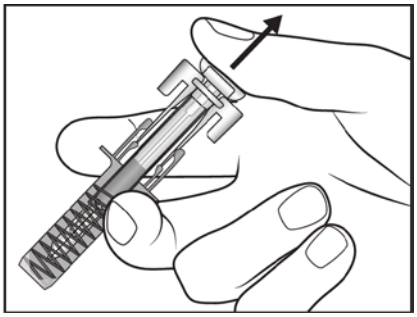


Figure I

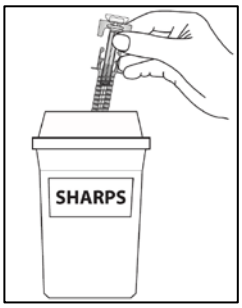
Step 14. Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle (**see Figure I**).



Step 15. There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

How should I dispose of used COSENTYX prefilled syringe?

Figure J



Step 16. Put your used prefilled syringe in a FDA-cleared sharps disposal container right away after use (**see Figure J**)**. Do not throw away (dispose of)** prefilled syringes in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

a. made of a heavy-duty plastic,

b. can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,

c. upright and stable during use,

d. leak-resistant, and

e. properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles, syringes and prefilled syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

Manufactured by:

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
US License Number 1244

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Issued: May 2021

INSTRUCTIONS FOR USE
COSENTYX® (koe-sen-tix)
(secukinumab)
Injection
150 mg/mL single-dose Sensoready® Pen

Be sure that you read, understand, and follow this Instructions for Use before injecting COSENTYX. Your healthcare provider should show you how to prepare and inject COSENTYX properly using the Sensoready Pen before you use it for the first time. Children should not inject COSENTYX themselves using the Sensoready pen. An adult caregiver should prepare and inject COSENTYX after receiving proper training in subcutaneous injection technique. Talk to your healthcare provider if you have any questions.

Important:

- **Do not use** the COSENTYX Sensoready Pen if either the seal on the outer carton or the seal on the pen is broken. Keep the COSENTYX Sensoready Pen in the sealed outer carton until you are ready to use it.
- **Do not shake** the COSENTYX Sensoready Pen.
- The caps of the Sensoready Pens contain latex. **Do not handle the Sensoready Pens if you are sensitive to latex**.
- If you drop your COSENTYX Sensoready Pen, **do not use** it if the Sensoready Pen looks damaged, or if you dropped it with the cap removed.
- Throw away (dispose of) the used COSENTYX Sensoready Pen right away after use. **Do not re-use a COSENTYX Sensoready Pen.** See "How should I dispose of used COSENTYX Sensoready Pens?" at the end of this Instructions for Use.

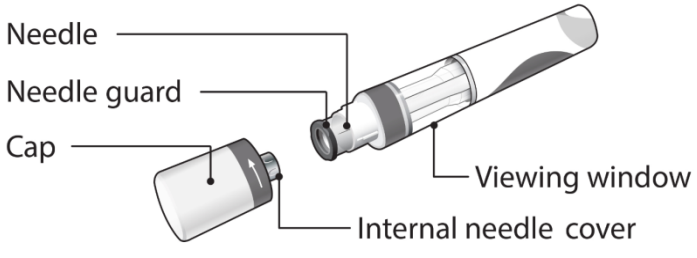
How should I store COSENTYX?

- Store your carton of COSENTYX Sensoready Pens in a refrigerator, between 36°F to 46°F (2°C to 8°C).
- Keep COSENTYX Sensoready Pens in the original carton until ready to use to protect from light.
- COSENTYX Sensoready pens may be stored at room temperature, not to exceed temperatures above 86°F (30°C), for up to 4 days.
- Write the date COSENTYX Sensoready pens was removed from the refrigerator in the space provided on the carton.
- If unused and not stored above 30°C (86°F), COSENTYX Sensoready pens may be returned to the refrigerator.
- Throw away COSENTYX if it has been kept outside of the refrigerator and not been used in over 4 days.
- Do not freeze COSENTYX Sensoready Pens.
- Throw away (dispose of) any unused COSENTYX Sensoready Pens.

Keep COSENTYX and all medicines out of the reach of children.

COSENTYX Sensoready Pen parts (see Figure A):

Figure A



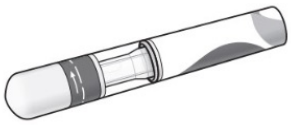
The COSENTYX Sensoready Pen is shown above with the cap removed. **Do not** remove the cap until you are ready to inject.

What you need for your injection:

Included in the carton:

A new COSENTYX Sensoready Pen (**see Figure B**).

Figure B



Each COSENTYX Sensoready Pen contains 150 mg of COSENTYX.

- If your **prescribed dose** of COSENTYX is **150 mg**, you must give **1 injection.**
- If your **prescribed dose** of COSENTYX is **300 mg**, you must give **2 injections**.

Not included in the carton **(see Figure C)**:

Figure C

- 1 Alcohol wipe
- 1 Cotton ball or gauze
- Sharps disposal container.

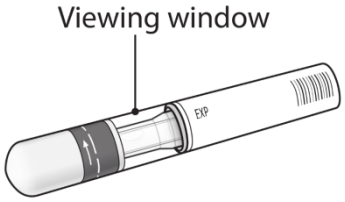
See "**How should I dispose of used COSENTYX Sensoready Pen**?" at the end of this Instructions for Use.

Before your injection:

Take the COSENTYX Sensoready Pen out of the refrigerator **15 to 30 minutes before injecting** to allow it to reach room temperature.

Step 1. Important safety checks before you inject **(see Figure D)**:

Figure D



- Look through the viewing window. The liquid should be clear. Its color may vary from colorless to slightly yellow.

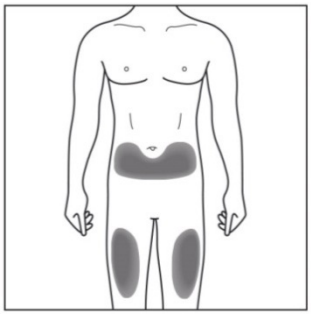
  Do not use if the liquid contains visible particles, is cloudy or is discolored. You may see a small air bubble, which is normal.

- Look at the **expiration date (EXP)** on your Sensoready Pen. **Do not use** your COSENTYX Sensoready Pen if the expiration date has passed.

Contact your pharmacist if the COSENTYX Sensoready Pen fails any of these checks.

Step 2. Choose your injection site:

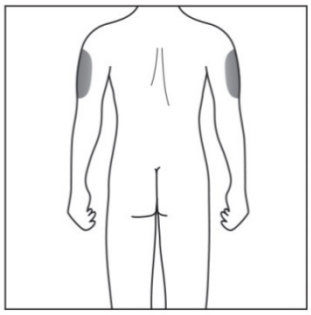
Figure E



- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 2 inches around your navel (belly button) **(see Figure E).**
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard, or in an area of skin that is affected by psoriasis. Avoid areas with scars or stretch marks.

- If a **caregiver** or **healthcare provider** is giving you your injection, they may also inject into your outer upper arm **(see Figure F).**

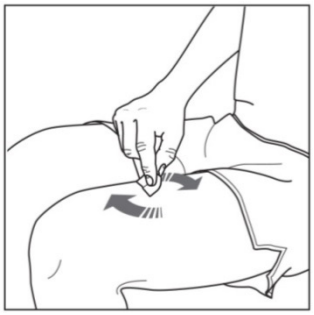
Figure F



Step 3. Cleaning your injection site:

- Wash your hands well with soap and water.
- Using a circular motion, clean the injection site with the alcohol wipe. Leave it to dry before injecting **(see Figure G).**
- Do not touch the cleaned area again before injecting.

Figure G

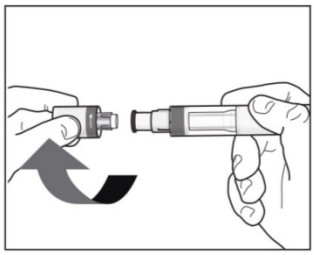


Your injection:

Step 4. Removing the cap:

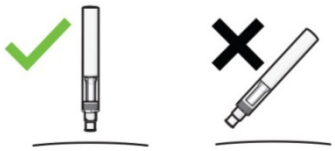
- Only remove the cap when you are ready to use the COSENTYX Sensoready Pen.
- Twist off the cap in the direction of the arrow **(see Figure H)**.
- Throw away the cap. **Do not try to re-attach the cap.**
- Use the COSENTYX Sensoready Pen within 5 minutes of removing the cap.

Figure H



Step 5. **Holding your COSENTYX Sensoready Pen:**

- Hold the COSENTYX Sensoready Pen at 90 degrees to the cleaned injection site **(see Figure I).**



Correct **Incorrect**

Figure I

Important: During the injection you will hear **2 loud clicks**:

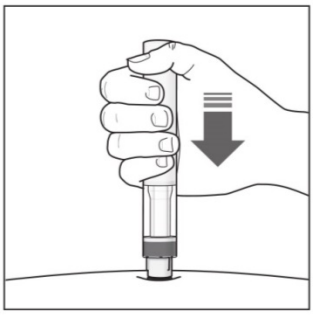
- The **1st click** indicates that **the injection has started**.
- Several seconds later a **2nd click** will indicate that **the injection is almost finished**.

You must keep holding the COSENTYX Sensoready Pen firmly against your skin until you see a **green indicator** fill the window and stop moving.

Step 6. Starting your injection:

- Press the COSENTYX Sensoready Pen firmly against the skin to start the injection **(see Figure J).**
- The **1st click** indicates the injection has started.
- **Keep holding** the COSENTYX Sensoready Pen firmly against your skin.
- The **green indicator** shows the progress of the injection.

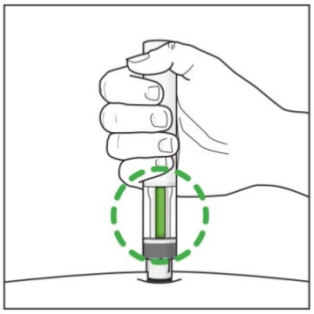
Figure J



Step 7. Completing your injection:

- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator** fills the window and has stopped moving **(see Figure K).**
- The COSENTYX Sensoready Pen can now be removed.

Figure K

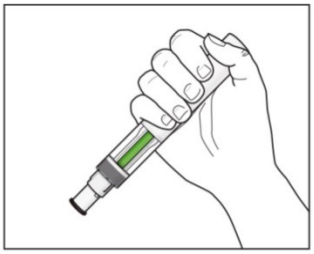


After your injection:

Step 8. Check the green indicator fills the window **(see Figure L)**:

- This means the medicine has been delivered. Contact your healthcare provider if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Figure L



If your prescribed dose of COSENTYX is 300 mg, repeat steps 1 through 8 with a new COSENTYX Sensoready Pen.

How should I dispose of used COSENTYX Sensoready Pens?

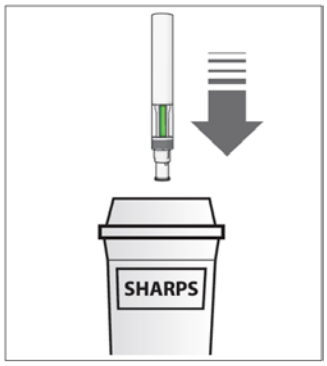
Step 9. Put your used Sensoready Pens in a FDA-cleared sharps disposal container right away after use **(see Figure M). Do not throw away (dispose of)** Sensoready Pens in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles, syringes, and Sensoready Pens. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

Figure M



This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: May 2021

Manufactured by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
US License Number 1244

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

The powder is a white solid lyophilisate.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Paediatric plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Psoriatic arthritis

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

Axial spondyloarthritis (axSpA)

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

Non-radiographic axial spondyloarthritis (nr-axSpA)
Cosentyx is indicated for the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs).

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

Posology

Adult plaque psoriasis
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Paediatric plaque psoriasis (adolescents and children from the age of 6 years)
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Table 1 Recommended dose for paediatric plaque psoriasis

Body weight at time of dosing	**Recommended Dose**
<25 kg	75 mg
25 to <50 kg	75 mg
≥50 kg	150 mg (*may be increased to 300 mg)

*Some patients may derive additional benefit from the higher dose.

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children with plaque psoriasis below the age of 6 years have not been established.

The safety and efficacy of Cosentyx in children below the age of 18 years in other indications have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The powder for solution for injection must be reconstituted before use.

The reconstitution, dose preparation and administration of the powder for solution for injection is to be done by a healthcare professional. For instructions on reconstitution of the medicinal product before administration, see section 6.6 and the Instructions for Use in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

Inflammatory bowel disease (including Crohn's disease and ulcerative colitis)

Cases of new or exacerbations of inflammatory bowel disease have been reported with secukinumab (see section 4.8). Secukinumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with secukinumab (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) are upper respiratory tract infections (most frequently nasopharyngitis, rhinitis).

Tabulated list of adverse reactions

ADRs from clinical studies and post-marketing reports (Table 2) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available data).

Over 18,000 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, axial spondyloarthritis and other autoimmune conditions), representing 30,565 patient years of exposure. Of these, over 11,700 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

Table 2 List of adverse reactions in clinical studies[1)] and post-marketing experience

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
		Tinea pedis
	Uncommon	Oral candidiasis
		Otitis externa
		Lower respiratory tract infections
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Common	Nausea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Exfoliative dermatitis[2)]
General disorders and administration site conditions	Common	Fatigue

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA, AS and nr-axSpA patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA, AS and nr-axSpA) treatment duration
[2)] Cases were reported in patients with psoriasis diagnosis

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to those observed in the psoriasis studies.

Neutropenia
In psoriasis phase III clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) was similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE grade 4) were reported.

Hypersensitivity reactions
In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

Immunogenicity
In psoriasis, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Paediatric population

Undesirable effects in paediatric patients from the age of 6 years with plaque psoriasis
The safety of secukinumab was assessed in two phase III studies in paediatric patients with plaque psoriasis. The first study (paediatric study 1) was a double-blind, placebo-controlled study of 162 patients from 6 to less than 18 years of age with severe plaque psoriasis. The second study (paediatric study 2) is an open-label study of 84 patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis. The safety profile reported in these two studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis. Inhibition of IL-17A was shown to be effective in the treatment of ankylosing spondylitis, thus establishing the key role of this cytokine in axial spondyloarthritis.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Adult plaque psoriasis
The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at week 12 (see Tables 3 and 4). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

Table 3 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in psoriasis studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 4 Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), speed of onset of PASI 75 response at week 4, and long-term PASI 90 response at week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to week 52.

Table 5 Summary of clinical response on CLEAR study

	Week 4		Week 16		Week 52	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 “clear” or “almost clear” response n (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

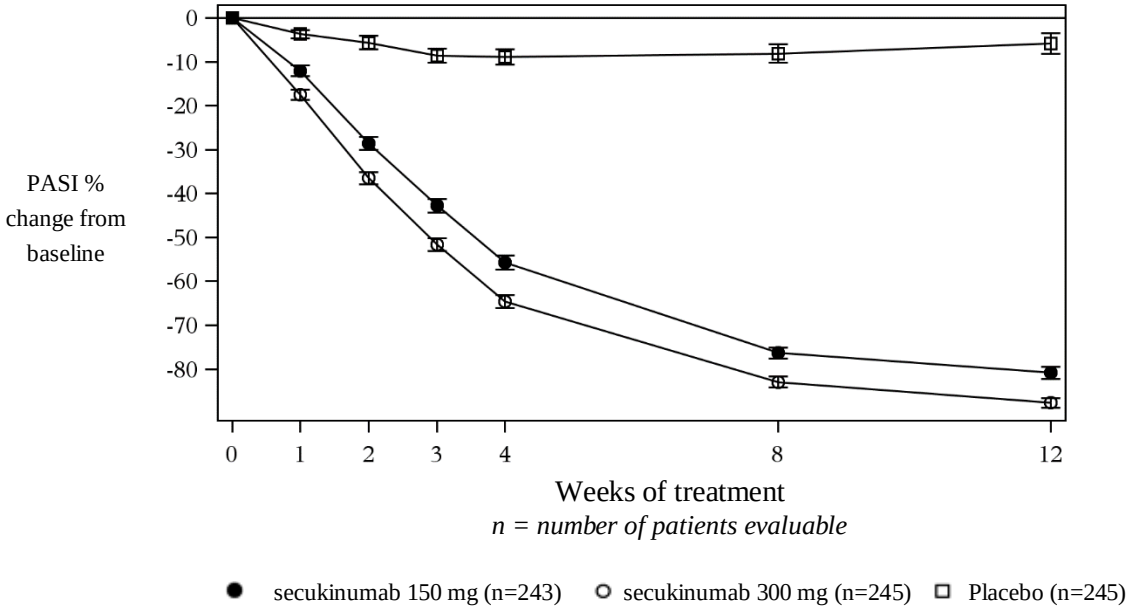
** p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

*** p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



Specific locations/forms of plaque psoriasis
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

Quality of life/patient-reported outcomes
Statistically significant improvements at week 12 (studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Statistically significant improvements at week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at week 16 and week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Psoriatic arthritis
The safety and efficacy of secukinumab were assessed in 1,999 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA of at least five years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For all studies, the primary endpoint was American College of Rheumatology (ACR) 20 response. For Psoriatic Arthritis study 1 (PsA study 1) and Psoriatic Arthritis study 2 (PsA study 2), the primary endpoint was at week 24. For Psoriatic Arthritis study 3 (PsA study 3), the primary endpoint was at week 16 with the key secondary endpoint, the change from baseline in modified Total Sharp Score (mTSS), at week 24.

In PsA study 1, PsA study 2 and PsA study 3, 29%, 35% and 30% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to secukinumab received 75 mg, 150 mg or 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

PsA study 3 (FUTURE 5) evaluated 996 patients, of whom 50.1% had concomitant MTX. Patients were randomised to receive secukinumab 150 mg, 300 mg or placebo subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month, or a once monthly injection of secukinumab 150 mg (without loading). Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were then crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

Signs and symptoms
Treatment with secukinumab resulted in significant improvement in measures of disease activity compared to placebo at weeks 16 and 24 (see Table 6).

Table 6 Clinical response in PsA study 2 and PsA study 3 at week 16 and week 24

	PsA study 2			PsA study 3		
	Placebo	150 mg[1]	300 mg[1]	Placebo	150 mg[1]	300 mg[1]
Number of patients randomised	98	100	100	332	220	222
ACR20 response n (%)						
Week 16	18 (18.4%)	60 (60.0%***)	57 (57.0%***)	91[◊] (27.4%)	122[◊] (55.5%***)	139[◊] (62.6%***)
Week 24	15[◊] (15.3%)	51[◊] (51.0%***)	54[◊] (54.0%***)	78 (23.5%)	117 (53.2%***)	141 (63.5%***)
ACR50 response n (%)						
Week 16	6 (6.1%)	37 (37.0%***)	35 (35.0%***)	27 (8.1%)	79 (35.9%*)	88 (39.6%*)
Week 24	7 (7.1%)	35 (35.0%)	35 (35.0%**)	29 (8.7%)	86 (39.1%***)	97 (43.7%***)
ACR70 response n (%)						
Week 16	2 (2.0%)	17 (17.0%**)	15 (15.0%**)	14 (4.2%)	40 (18.2%***)	45 (20.3%***)
Week 24	1 (1.0%)	21 (21.0%**)	20 (20.0%**)	13 (3.9%)	53 (24.1%***)	57 (25.7%***)
DAS28-CRP						
Week 16	-0.50	-1.45***	-1.51***	-0.63	-1.29*	-1.49*
Week 24	-0.96	-1.58**	-1.61**	-0.84	-1.57***	-1.68***
Number of patients with ≥3% BSA psoriasis skin involvement at baseline	43 (43.9%)	58 (58.0%)	41 (41.0%)	162 (48.8%)	125 (56.8%)	110 (49.5%)
PASI 75 response n (%)						
Week 16	3 (7.0%)	33 (56.9%***)	27 (65.9%***)	20 (12.3%)	75 (60.0%*)	77 (70.0%*)
Week 24	7 (16.3%)	28 (48.3%**)	26 (63.4%***)	29 (17.9%)	80 (64.0%***)	78 (70.9%***)
PASI 90 response n (%)						
Week 16	3 (7.0%)	22 (37.9%***)	18 (43.9%***)	15 (9.3%)	46 (36.8%*)	59 (53.6%*)
Week 24	4 (9.3%)	19 (32.8%**)	20 (48.8%***)	19 (11.7%)	51 (40.8%***)	60 (54.5%***)
Dactylitis resolution n (%) †						
Week 16	10 (37%)	21 (65.6%*)	26 (56.5%)	40 (32.3%)	46 (57.5%*)	54 (65.9%*)
Week 24	4 (14.8%)	16 (50.0%**)	26 (56.5%**)	42 (33.9%)	51 (63.8%***)	52 (63.4%***)

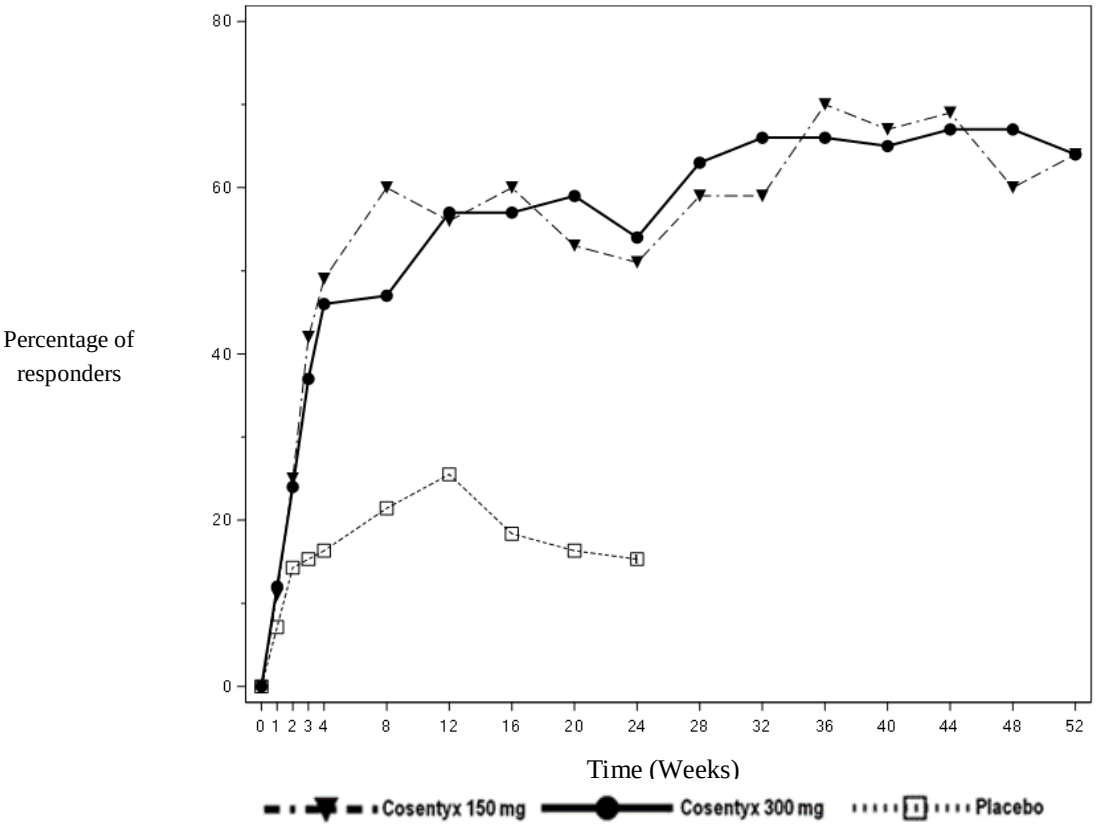
Enthesitis resolution n (%) ‡						
Week 16	17 (26.2%)	32 (50.0%**)	32 (57.1%***)	68 (35.4%)	77 (54.6%*)	78 (55.7%*)
Week 24	14 (21.5%)	27 (42.2%*)	27 (48.2%**)	66 (34.4%)	77 (54.6%***)	86 (61.4%***)

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 24 for PsA study 2, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints and all endpoints at week 16.
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 16 for PsA study 3, except for ACR70 which was an exploratory endpoint and all endpoints at week 24.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
◊Primary Endpoint
[1]Secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month
†In patients with dactylitis at baseline (n=27, 32, 46, respectively for PsA study 2 and n=124, 80, 82, respectively for PsA study 3)
‡In patients with enthesitis at baseline (n=65, 64, 56, respectively for PsA study 2 and n=192, 141, 140, respectively for PsA study 3)

The onset of action of secukinumab occurred as early as week 2. Statistically significant difference in ACR 20 versus placebo was reached at week 3.

The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

Figure 2 ACR20 response in PsA study 2 over time up to week 52



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. In PsA study 2, at week 24, secukinumab-treated patients with concomitant MTX use had a higher ACR 20 response (47.7% and 54.4% for 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (31.8% and 38.6% for 150 mg and 300 mg, respectively, compared to placebo 8.0%). Secukinumab-treated patients without concomitant MTX use had a higher ACR 20 response (53.6% and 53.6% for 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (37.5% and 32.1% for 150 mg and 300 mg, respectively, compared to placebo 6.3%).

In PsA study 2, both anti-TNFα-naive and anti-TNFα-IR secukinumab-treated patients had a significantly higher ACR 20 response compared to placebo at week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 64% and 58% for 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 30% and 46% for 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo ($p<0.05$) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. In PsA study 2, the proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the secukinumab-treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at week 24.

In PsA study 1 and PsA study 2, efficacy was maintained up to week 104. In PsA study 2, among 200 patients initially randomised to secukinumab 150 mg and 300 mg, 178 (89%) patients were still on treatment at week 52. Of the 100 patients randomised to secukinumab 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to secukinumab 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

Radiographic response
In PsA study 3, inhibition of progression of structural damage was assessed radiographically and expressed by the modified Total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing Score (JSN). Radiographs of hands, wrists, and feet were obtained at baseline, week 16 and/or week 24 and scored independently by at least two readers who were blinded to treatment group and visit number. Secukinumab 150 mg and 300 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at week 24 (Table 7).

Inhibition of progression of structural damage was also assessed in PsA study 1 at weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 7.

Table 7 Change in modified Total Sharp Score in psoriatic arthritis

	PsA study 3			PsA study 1	
	Placebo n=296	**secukinumab 150 mg[1] n=213**	**secukinumab 300 mg[1] n=217**	**Placebo n=179**	**secukinumab 150 mg[2] n=185**
Total score					
Baseline (SD)	15.0 (38.2)	13.5 (25.6)	12.9 (23.8)	28.4 (63.5)	22.3 (48.0)
Mean change at Week 24	0.50	0.13*	0.02*	0.57	0.13*

*p<0.05 based on nominal, but non adjusted, p-value
[1]secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month
[2]10 mg/kg at weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg

In PsA study 1, inhibition of structural damage was maintained with secukinumab treatment up to week 52.

In PsA study 3, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 80.3%, 88.5% and 73.6% for secukinumab 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed in anti-TNFα-naïve and anti-TNFα-IR patients and in patients treated with and without concomitant MTX.

In PsA study 1, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from week 24 to week 52 for secukinumab 10 mg/kg intravenous load – followed by 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at week 16 or week 24 was 85.7% and 86.8%, respectively.

Axial manifestations in PsA
A randomised, double-blind, placebo-controlled study (MAXIMISE) assessed the efficacy of secukinumab in 485 PsA patients with axial manifestations who were naive to biologic treatment and responded inadequately to NSAIDs. The primary variable of at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 12 was met. Treatment with secukinumab 300 mg and 150 mg compared to placebo also resulted in greater improvement in signs and symptoms (including decreases from baseline in spinal pain) and improvement in physical function (see Table 8).

Table 8 Clinical response on MAXIMISE study at week 12

	Placebo (n=164)	**150 mg (n=157)**	**300 mg (n=164)**
ASAS 20 response, % (95% CI)	31.2 (24.6, 38.7)	66.3 (58.4, 73.3)*	62.9 (55.2, 70.0)*
ASAS 40 response, % (95% CI)	12.2 (7.8, 18.4)	39.5 (32.1, 47.4)**	43.6 (36.2, 51.3)**
BASDAI 50, % (95% CI)	9.8 (5.9, 15.6)	32.7 (25.8, 40.5)**	37.4 (30.1, 45.4)**
Spinal pain, VAS (95% CI)	-13.6 (-17.2, -10.0)	-28.5 (-32.2, -24.8)**	-26.5 (-30.1, -22.9)**
Physical function, HAQ-DI (95% CI)	-0.155 (-0.224, -0.086)	-0.330 (-0.401, -0.259)**	-0.389 (-0.458, -0.320)**
* p<0.0001; versus placebo using multiple imputation. ** Comparison versus placebo was not adjusted for multiplicity. ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: Visual Analog Scale; HAQ-DI: Health Assessment Questionnaire – Disability Index.			

Improvement in ASAS 20 and ASAS 40 for both secukinumab doses were observed by week 4 and were maintained up to 52 weeks.

Physical function and health-related quality of life
In PsA study 2 and PsA study 3, patients treated with secukinumab 150 mg (p=0.0555 and p<0.0001) and 300 mg (p=0.0040 and p<0.0001) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24 and week 16, respectively. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA study 1.

Secukinumab-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively) and these improvements were maintained up to week 104 in PsA study 2.

Similar responses were seen in PsA study 1 and efficacy was maintained up to week 52.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS) / Radiographic axial spondyloarthritis
The safety and efficacy of secukinumab were assessed in 816 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in Ankylosing Spondylitis study 1 (AS study 1) and Ankylosing Spondylitis study 2 (AS study 2) had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 16.

In Ankylosing Spondylitis study 1 (AS study 1), Ankylosing Spondylitis study 2 (AS study 2), and Ankylosing Spondylitis study 3 (AS study 3), 27.0%, 38.8%, and 23.5% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

AS study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and all other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 75 mg or 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 75 mg or 150 mg subcutaneously) every month.

AS study 3 (MEASURE 3) evaluated 226 patients, of whom 13.3% and 23.5% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 150 mg or 300 mg subcutaneously every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 150 mg or 300 mg subcutaneously) every month. The primary endpoint was ASAS 20 at week 16. Patients were blinded to the treatment regimen up to week 52, and the study continued to week 156.

Signs and symptoms:
In AS study 2, treatment with secukinumab 150 mg resulted in greater improvement in measures of disease activity compared with placebo at week 16 (see Table 9).

Table 9 Clinical response in AS study 2 at week 16

Outcome (p-value versus placebo)	**Placebo (n = 74)**	**75 mg (n = 73)**	**150 mg (n = 72)**
ASAS 20 response, %	28.4	41.1	61.1***
ASAS 40 response, %	10.8	26.0	36.1***
hsCRP, (post-BSL/BSL ratio)	1.13	0.61	0.55***
ASAS 5/6, %	8.1	34.2	43.1***
ASAS partial remission, %	4.1	15.1	13.9
BASDAI 50, %	10.8	24.7*	30.6**
ASDAS-CRP major improvement	4.1	15.1*	25.0***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of secukinumab 150 mg occurred as early as week 1 for ASAS 20 and week 2 for ASAS 40 (superior to placebo) in AS study 2.

ASAS 20 responses were improved at week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; $p<0.05$) and anti-TNFα-IR patients (50.0% versus 24.1%; $p<0.05$) for secukinumab 150 mg compared with placebo, respectively.

In AS study 1 and AS study 2, secukinumab-treated patients (150 mg in AS study 2 and both regimens in AS study 1) demonstrated significantly improved signs and symptoms at week 16, with comparable magnitude of response and efficacy maintained up to week 52 in both anti-TNFα-naive and anti-TNFα-IR patients. In AS study 2, among 72 patients initially randomised to secukinumab 150 mg, 61 (84.7%) patients were still on treatment at week 52. Of the 72 patients randomised to secukinumab 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

In AS study 3, patients treated with secukinumab (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses regardless of dose that were superior to placebo at week 16 for the primary endpoint (ASAS 20). Overall, the efficacy response rates for the 300 mg group were consistently greater compared to the 150 mg group for the secondary endpoints. During the blinded period, the ASAS 20 and ASAS 40 responses were 69.7% and 47.6% for 150 mg and 74.3% and 57.4% for 300 mg at week 52, respectively. The ASAS 20 and ASAS 40 responses were maintained up to week 156 (69.5% and 47.6% for 150 mg versus 74.8% and 55.6% for 300 mg). Greater response rates favouring 300 mg were also observed for ASAS partial remission (ASAS PR) response at week 16 and were maintained up to week 156. Larger differences in response rates, favouring 300 mg over 150 mg, were observed in anti-TNFα-IR patients (n=36) compared to anti-TNFα-naïve patients (n=114).

Spinal mobility:
Patients treated with secukinumab 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at week 16 for both AS study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to week 52.

Physical function and health-related quality of life:
In AS study 1 and study 2, patients treated with secukinumab 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with secukinumab 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to week 52.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The safety and efficacy of secukinumab were assessed in 555 patients in one randomised, double-blind, placebo-controlled phase III study (PREVENT), consisting of a 2-year core phase and a 2-year extension phase, in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for ankylosing spondylitis (AS). Patients enrolled had active disease, defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, a Visual Analogue Scale (VAS) for total back pain of ≥40 (on a scale of 0-100 mm), despite current or previous non-steroidal anti-inflammatory drug (NSAID) therapy and increased C-reactive protein (CRP) and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Patients in this study had a diagnosis of axSpA for a mean of 2.1 to 3.0 years and 54% of the study participants were female.

In the PREVENT study, 9.7% of patients were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

In the PREVENT study, 9.9% and 14.8% of patients used concomitant MTX or sulfasalazine, respectively. In the double-blind period, patients received either placebo or secukinumab for 52 weeks. Patients randomised to secukinumab received 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4 followed by the same dose every month, or a once monthly injection of secukinumab 150 mg. The primary endpoint was at least 40% improvement in Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16 in anti-TNFα-naive patients.

Signs and symptoms:
In the PREVENT study, treatment with secukinumab 150 mg resulted in significant improvements in the measures of disease activity compared to placebo at week 16. These measures include ASAS 40, ASAS 5/6, BASDAI score, BASDAI 50, high-sensitivity CRP (hsCRP), ASAS 20 and ASAS partial remission response compared to placebo (Table 10). Responses were maintained up to week 52.

Table 10 Clinical response in the PREVENT study at week 16

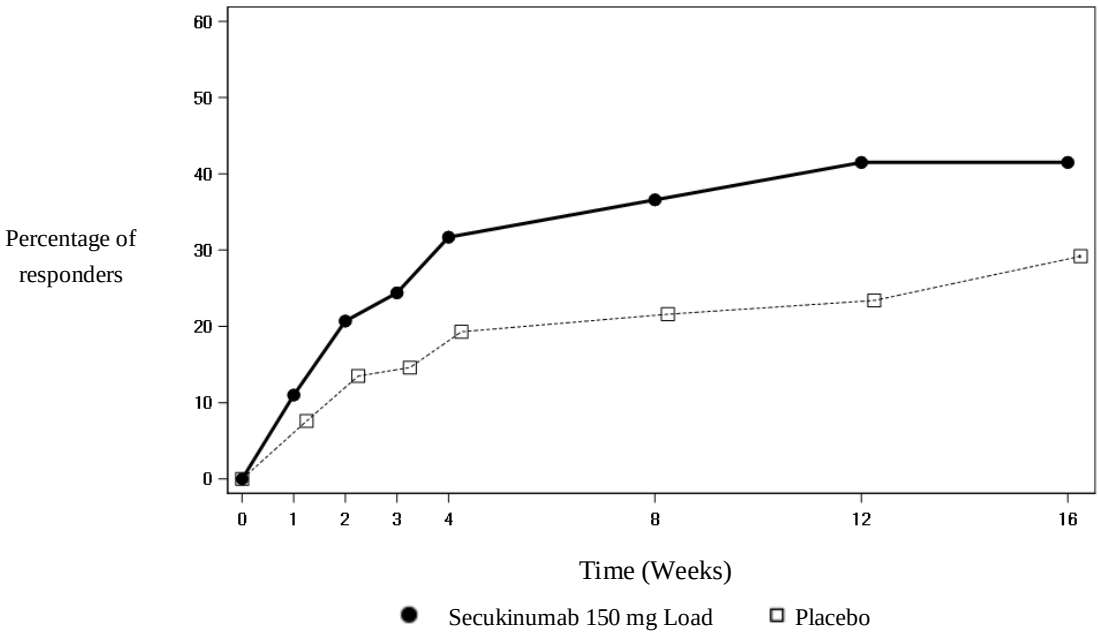
Outcome (p-value versus placebo)	**Placebo**	**150 mg[1]**
Number of anti-TNFα-naive patients randomised	**171**	**164**
ASAS 40 response, %	29.2	41.5*
Total number of patients randomised	**186**	**185**
ASAS 40 response, %	28.0	40.0*
ASAS 5/6, %	23.7	40.0*
BASDAI, LS mean change from baseline score	-1.46	-2.35*
BASDAI 50, %	21.0	37.3*
hsCRP, (post-BSL/BSL ratio)	0.91	0.64*
ASAS 20 response, %	45.7	56.8*
ASAS partial remission, %	7.0	21.6*

*p<0.05 versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy
Non-responder imputation used for missing binary endpoint
[1]secukinumab 150 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; BSL: baseline; LS: Least square

The onset of action of secukinumab 150 mg occurred as early as week 3 for ASAS 40 in anti-TNFα naive patients (superior to placebo) in the PREVENT study. The percentage of patients achieving an ASAS 40 response in anti-TNFα naive patients by visit is shown in Figure 3.

Figure 3 ASAS 40 responses in anti-TNFα naive patients in the PREVENT study over time up to week 16



ASAS 40 responses were also improved at week 16 in anti-TNFα-IR patients for secukinumab 150 mg compared with placebo.

Physical function and health-related quality of life:
Patients treated with secukinumab 150 mg showed statistically significant improvements by week 16 compared to placebo-treated patients in physical function as assessed by the BASFI (week 16: -1.75 versus -1.01, $p<0.05$). Patients treated with secukinumab reported significant improvements compared to placebo-treated patients by week 16 in health-related quality of life as measured by ASQoL (LS mean change: week 16: -3.45 versus -1.84, $p<0.05$) and SF-36 Physical Component Summary (SF-36 PCS) (LS mean change: week 16: 5.71 versus 2.93, $p<0.05$). These improvements were sustained up to week 52.

Spinal mobility:
Spinal mobility was assessed by BASMI up to week 16. Numerically greater improvements were demonstrated in patients treated with secukinumab compared with placebo-treated patients at weeks 4, 8, 12 and 16.

Inhibition of inflammation in magnetic resonance imaging (MRI):
Signs of inflammation were assessed by MRI at baseline and week 16 and expressed as change from baseline in Berlin SI-joint oedema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with secukinumab. Mean change from baseline in Berlin SI-joint oedema score was -1.68 for patients treated with secukinumab 150 mg (n=180) versus -0.39 for the placebo-treated patients (n=174) ($p<0.05$).

Paediatric population

Paediatric plaque psoriasis
Secukinumab has been shown to improve signs and symptoms, and health-related quality of life in paediatric patients 6 years and older with plaque psoriasis (see Tables 12 and 14).

Severe plaque psoriasis
The safety and efficacy of secukinumab were assessed in a randomised, double-blind, placebo and etanercept-controlled phase III study in paediatric patients from 6 to <18 years of age with severe plaque psoriasis, as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and BSA involvement of ≥10%, who were candidates for systemic therapy. Approximately 43% of the patients had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The paediatric psoriasis study 1 evaluated 162 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg), high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg), or placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or etanercept. Patients randomised to etanercept received 0.8 mg/kg weekly (up to a maximum of 50 mg). Patient distribution by weight and age at randomisation is described in Table 11.

Table 11 Patient distribution by weight and age for paediatric psoriasis study 1

Randomisation strata	**Description**	**Secukinumab low dose n=40**	**Secukinumab high dose n=40**	**Placebo n=41**	**Etanercept n=41**	**Total N=162**
Age	6-<12 years	8	9	10	10	37
	≥12-<18 years	32	31	31	31	125
Weight	<25 kg	2	3	3	4	12
	≥25-<50 kg	17	15	17	16	65
	≥50 kg	21	22	21	21	85

Patients randomised to receive placebo who were non-responders at week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at week 16. The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

During the 12 week placebo-controlled period, the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 'clear' or 'almost clear' (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at week 4, the difference becoming more prominent at week 12. The response was maintained throughout the 52 week time period (see Table 12). Improvement in PASI 50, 90, 100 responder rates and Children's Dermatology Life Quality Index (CDLQI) scores of 0 or 1 were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept (see Table 12).

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 12 Summary of clinical response in severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 1)*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n**/m (%)	'control' n**/m (%)	odds ratio estimate (95% CI)	p-value
At week 12* **					
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08, 114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31, 98.93)	<0.0001
	secukinumab low dose vs. etanercept	32/40 (80.0)	26/41 (63.4)	2.25 (0.73, 7.38)	
	secukinumab high dose vs. etanercept	31/40 (77.5)	26/41 (63.4)	1.92 (0.64, 6.07)	
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02, 538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48, 329.52)	<0.0001
	secukinumab low dose vs. etanercept	28/40 (70.0)	14/41 (34.1)	4.49 (1.60, 13.42)	
	secukinumab high dose vs. etanercept	24/40 (60.0)	14/41 (34.1)	2.86 (1.05, 8.13)	
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83, 6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22, 4850.13)	<0.0001
	secukinumab low dose vs. etanercept	29/40 (72.5)	12/41 (29.3)	7.03 (2.34, 23.19)	
	secukinumab high dose vs. etanercept	27/40 (67.5)	12/41 (29.3)	5.32 (1.82, 16.75)	
At week 52					
PASI 75	secukinumab low dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.12 (0.91, 12.52)	
	secukinumab high dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.09 (0.90, 12.39)	
IGA 0/1	secukinumab low dose vs. etanercept	29/40 (72.5)	23/41 (56.1)	2.02 (0.73, 5.77)	
	secukinumab high dose vs. etanercept	30/40 (75.0)	23/41 (56.1)	2.26 (0.81, 6.62)	
PASI 90	secukinumab low dose vs. etanercept	30/40 (75.0)	21/41 (51.2)	2.85 (1.02, 8.38)	
	secukinumab high dose vs. etanercept	32/40 (80.0)	21/41 (51.2)	3.69 (1.27, 11.61)	

* non-responder imputation was used to handle missing values
** n is the number of responders, m = number of patients evaluable
*** extended visit window at week 12
Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at week 12 (low dose 44.7%, high dose 50%, placebo 15%). Over time up to and including week 52 both secukinumab dose groups were numerically higher than the etanercept group (low dose 60.6%, high dose 66.7%, etanercept 44.4%).

Moderate to severe plaque psoriasis
Secukinumab was predicted to be effective for the treatment of paediatric patients with moderate plaque psoriasis based on the demonstrated efficacy and exposure response relationship in adult patients with moderate to severe plaque psoriasis, and the similarity of the disease course, pathophysiology, and drug effect in adult and paediatric patients at the same exposure levels.

Moreover, the safety and efficacy of secukinumab was assessed in an open-label, two-arm, parallel-group, multicentre phase III study in paediatric patients from 6 to <18 years of age with moderate to severe plaque psoriasis, as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and BSA involvement of ≥10%, who were candidates for systemic therapy.

The paediatric psoriasis study 2 evaluated 84 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) or high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Patient distribution by weight and age at randomisation is described in Table 13.

Table 13 Patient distribution by weight and age for paediatric psoriasis study 2

Sub-groups	Description	Secukinumab low dose n=42	Secukinumab high dose n=42	Total N=84
Age	6-<12 years	17	16	33
	≥12-<18 years	25	26	51
Weight	<25 kg	4	4	8
	≥25-<50 kg	13	12	25
	≥50 kg	25	26	51

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically significant improvement compared to historical placebo for the co-primary endpoints. The estimated posterior probability of a positive treatment effect was 100%.

All patients were followed for efficacy for at least 24 weeks following first administration (see Table 14). Efficacy (defined as PASI 75 response and IGA mod 2011 'clear' or 'almost clear' [0 or 1]) was observed as early as the first post-baseline visit at week 2 and the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) increased throughout the 24 week time period. Improvement in PASI 90 and PASI 100 were also observed at week 12 and increased throughout the 24 week time period.

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 14 Summary of clinical response in moderate to severe paediatric psoriasis at weeks 12 and 24 (paediatric psoriasis study 2)*

	Week 12		Week 24	
	Secukinumab low dose	Secukinumab high dose	Secukinumab low dose	Secukinumab high dose
Number of patients	42	42	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)	40 (95.2%)	40 (95.2%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)	37 (88.1%)	39 (92.9%)
PASI 90 response n (%)	29 (69%)	32 (76.2%)	37 (88.1%)	37 (88.1%)
PASI 100 response n (%)	25 (59.5%)	23 (54.8%)	28 (66.7%)	28 (66.7%)
* non-responder imputation was used to handle missing values				

These outcomes in the paediatric moderate to severe plaque psoriasis population confirmed the predictive assumptions based on the efficacy and exposure response relationship in adult patients, mentioned above.

In the low dose group, 50% and 70.7% of patients achieved a CDLQI 0 or 1 score at weeks 12 and 24, respectively. In the high dose group, 61.9% and 60.5% achieved a CDLQI 0 or 1 score at weeks 12 and 24, respectively.

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 years (see section 4.2 for information on paediatric use).

The European Medicines Agency has deferred the obligation to submit the results of studies with Cosentyx in chronic idiopathic arthritis for paediatric patients aged from 2 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis were similar.

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Special populations

Elderly patients
Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment
No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

Paediatric population
In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough concentration of 19.8 ± 6.96 µg/ml (n=24) after 75 mg of secukinumab and patients weighing ≥50 kg had mean ±SD trough concentration of 27.3 ± 10.1 µg/ml (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6 ± 10.8 µg/ml at week 24 after 75 mg dose.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans (adult or paediatric) based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Histidine
Histidine hydrochloride monohydrate
Polysorbate 80

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

After reconstitution

Chemical and physical in-use stability has been demonstrated for 24 hours at 2ºC to 8ºC.
From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
For storage conditions after reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Cosentyx is supplied in a colourless glass vial with a grey coated rubber stopper and aluminium cap with a white flip-off component containing 150 mg of secukinumab.

Cosentyx is available in packs containing one vial.

6.6 Special precautions for disposal and other handling

The single-use vial contains 150 mg secukinumab for reconstitution with sterile water for injections. The resulting solution should be clear and colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Reconstitution
Cosentyx 150 mg powder for solution for injection must be prepared by a healthcare professional. The preparation of the solution for subcutaneous injection must be done without interruption and ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution takes 20 minutes on average and should not exceed 90 minutes.

1. Bring the vial of powder to room temperature and ensure that the sterile water for injections is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injections into a 1 ml graduated disposable syringe and adjust to 1.0 ml.
3. Remove the plastic cap from the vial.
4. Insert the syringe needle into the vial containing the powder through the centre of the rubber stopper and reconstitute the powder by slowly injecting 1.0 ml of sterile water for injections into the vial. The stream of sterile water for injections should be directed onto the powder.
5. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.
6. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.
7. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.
8. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its colour may vary from colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.
9. Prepare the required number of vials (2 vials for the 300 mg dose).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Use in the paediatric population

For paediatric patients receiving the 75 mg dose, it is currently recommended to use the single-use vial containing 150 mg secukinumab for reconstitution with sterile water for injections. Slightly more than 0.5 ml of the reconstituted solution for subcutaneous injection have to be withdrawn and the rest of the solution must be discarded immediately. Detailed instructions for use are provided in the package leaflet.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 January 2015
Date of latest renewal: 03 September 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
Cosentyx 300 mg solution for injection in pre-filled syringe
Cosentyx 150 mg solution for injection in pre-filled pen
Cosentyx 300 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cosentyx 150 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 150 mg secukinumab in 1 ml.

Cosentyx 300 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 300 mg secukinumab in 2 ml.

Cosentyx 150 mg solution for injection in pre-filled pen

Each pre-filled pen contains 150 mg secukinumab in 1 ml.

Cosentyx 300 mg solution for injection in pre-filled pen

Each pre-filled pen contains 300 mg secukinumab in 2 ml.

Secukinumab is a recombinant fully human monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adult plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Paediatric plaque psoriasis

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

Psoriatic arthritis

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

Axial spondyloarthritis (axSpA)

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy.

Non-radiographic axial spondyloarthritis (nr-axSpA)
Cosentyx is indicated for the treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs).

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Cosentyx is indicated.

Posology

Adult plaque psoriasis
The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Paediatric plaque psoriasis (adolescents and children from the age of 6 years)
The recommended dose is based on body weight (Table 1) and administered by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 75 mg dose is given as one subcutaneous injection of 75 mg. Each 150 mg dose is given as one subcutaneous injection of 150 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Table 1 Recommended dose for paediatric plaque psoriasis

Body weight at time of dosing	**Recommended Dose**
<25 kg	75 mg
25 to <50 kg	75 mg
≥50 kg	150 mg (*may be increased to 300 mg)

*Some patients may derive additional benefit from the higher dose.

The 150 mg solution for injection in pre-filled syringe is not indicated for administration to paediatric patients with a weight <50 kg. The 150 mg powder for solution for injection presentation is appropriate for administration to this population.

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Each 300 mg dose is given as one subcutaneous injection of 300 mg or as two subcutaneous injections of 150 mg.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children with plaque psoriasis below the age of 6 years have not been established.

The safety and efficacy of Cosentyx in children below the age of 18 years in other indications have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The solution in the syringe or pen must not be shaken.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx or be injected by a caregiver if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients or caregivers should be instructed to inject the full amount of Cosentyx according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection, e.g. active tuberculosis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Secukinumab has the potential to increase the risk of infections. Serious infections have been observed in patients receiving secukinumab in the post-marketing setting. Caution should be exercised when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and secukinumab should not be administered until the infection resolves.

In clinical studies, infections have been observed in patients receiving secukinumab (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of secukinumab, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

No increased susceptibility to tuberculosis was reported from clinical studies. However, secukinumab should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of secukinumab in patients with latent tuberculosis.

Inflammatory bowel disease (including Crohn's disease and ulcerative colitis)

Cases of new or exacerbations of inflammatory bowel disease have been reported with secukinumab (see section 4.8). Secukinumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, secukinumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity reactions

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving secukinumab. If an anaphylactic or other serious allergic reactions occur, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive individuals – Cosentyx 150 mg solution for injection in pre-filled syringe and 150 mg solution for injection in pre-filled pen only

The removable needle cap of Cosentyx 150 mg solution for injection in pre-filled syringe and Cosentyx 150 mg solution for injection in pre-filled pen contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable needle cap. Nevertheless, the use of Cosentyx 150 mg solution for injection in pre-filled syringe and Cosentyx 150 mg solution for injection in pre-filled pen in latex-sensitive individuals has not been studied and there is therefore a potential risk of hypersensitivity reactions which cannot be completely ruled out.

Vaccinations

Live vaccines should not be given concurrently with secukinumab.

Patients receiving secukinumab may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that secukinumab does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Prior to initiating therapy with Cosentyx, it is recommended that paediatric patients receive all age-appropriate immunisations as per current immunisation guidelines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of secukinumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated. Secukinumab was administered concomitantly with methotrexate (MTX), sulfasalazine and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). Caution should be exercised when considering concomitant use of other immunosuppressants and secukinumab (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with secukinumab (see also section 4.4).

In a study in adult subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when secukinumab was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and axial spondyloarthritis).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx during pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) are upper respiratory tract infections (most frequently nasopharyngitis, rhinitis).

Tabulated list of adverse reactions

ADRs from clinical studies and post-marketing reports (Table 2) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available data).

Over 18,000 patients have been treated with secukinumab in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, axial spondyloarthritis and other autoimmune conditions), representing 30,565 patient years of exposure. Of these, over 11,700 patients were exposed to secukinumab for at least one year. The safety profile of secukinumab is consistent across all indications.

Table 2 List of adverse reactions in clinical studies[1)] and post-marketing experience

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections
	Common	Oral herpes
		Tinea pedis
	Uncommon	Oral candidiasis
		Otitis externa
		Lower respiratory tract infections
	Not known	Mucosal and cutaneous candidiasis (including oesophageal candidiasis)
Blood and lymphatic system disorders	Uncommon	Neutropenia
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Common	Rhinorrhoea
Gastrointestinal disorders	Common	Diarrhoea
	Common	Nausea
	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Exfoliative dermatitis[2)]
General disorders and administration site conditions	Common	Fatigue

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA, AS and nr-axSpA patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA, AS and nr-axSpA) treatment duration
[2)] Cases were reported in patients with psoriasis diagnosis

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with secukinumab and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with secukinumab compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with secukinumab and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with secukinumab for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with secukinumab (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with secukinumab (0.015 per patient-year of follow-up).

Infection rates observed in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies were similar to those observed in the psoriasis studies.

Neutropenia
In psoriasis phase III clinical studies, neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of secukinumab were reported in the remaining 3 cases.

The frequency of neutropenia in psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) was similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE grade 4) were reported.

Hypersensitivity reactions
In clinical studies, urticaria and rare cases of anaphylactic reaction to secukinumab were observed (see also section 4.4).

Immunogenicity
In psoriasis, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) clinical studies, less than 1% of patients treated with secukinumab developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Paediatric population

Undesirable effects in paediatric patients from the age of 6 years with plaque psoriasis
The safety of secukinumab was assessed in two phase III studies in paediatric patients with plaque psoriasis. The first study (paediatric study 1) was a double-blind, placebo-controlled study of 162 patients from 6 to less than 18 years of age with severe plaque psoriasis. The second study (paediatric study 2) is an open-label study of 84 patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis. The safety profile reported in these two studies was consistent with the safety profile reported in adult plaque psoriasis patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis) and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis. Increased numbers of IL-17A producing lymphocytes have also been found in patients with non-radiographic axial spondyloarthritis. Inhibition of IL-17A was shown to be effective in the treatment of ankylosing spondylitis, thus establishing the key role of this cytokine in axial spondyloarthritis.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Adult plaque psoriasis
The safety and efficacy of secukinumab were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of secukinumab 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis study 1 (ERASURE) evaluated 738 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Psoriasis study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both study 1 and study 2, patients randomised to receive placebo who were non-responders at week 12 then crossed over to receive secukinumab (either 150 mg or 300 mg) at weeks 12, 13, 14, and 15, followed by the same dose every month starting at week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled syringe. Psoriasis study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of secukinumab self-administration via the pre-filled pen. In both study 3 and study 4, patients randomised to secukinumab received 150 mg or 300 mg doses at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

Psoriasis study 5 (SCULPTURE) evaluated 966 patients. All patients received secukinumab 150 mg or 300 mg doses at weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at week 12 (see Tables 3 and 4). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at week 16, therefore this dose is recommended.

Table 3 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in psoriasis studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 4 Summary of clinical response on psoriasis study 2 (FIXTURE)

	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at week 16 (primary endpoint), speed of onset of PASI 75 response at week 4, and long-term PASI 90 response at week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to week 52.

Table 5 Summary of clinical response on CLEAR study

	Week 4		Week 16		Week 52	
	Secukinumab 300 mg	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***	**Secukinumab 300 mg**	**Ustekinumab***
Number of patients	334	335	334	335	334	335
PASI 75 response n (%)	166 (49.7%)**	69 (20.6%)	311 (93.1%)	276 (82.4%)	306 (91.6%)	262 (78.2%)
PASI 90 response n (%)	70 (21.0%)	18 (5.4%)	264 (79.0%)**	192 (57.3%)	250 (74.9%)***	203 (60.6%)
PASI 100 response n (%)	14 (4.2%)	3 (0.9%)	148 (44.3%)	95 (28.4%)	150 (44.9%)	123 (36.7%)
IGA mod 2011 “clear” or “almost clear” response n (%)	128 (38.3%)	41 (12.2%)	278 (83.2%)	226 (67.5%)	261 (78.1%)	213 (63.6%)

* Patients treated with secukinumab received 300 mg doses at weeks 0, 1, 2 3 and 4, followed by the same dose every 4 weeks until week 52. Patients treated with ustekinumab received 45 mg or 90 mg at weeks 0 and 4, then every 12 weeks until week 52 (dosed by weight as per approved posology)

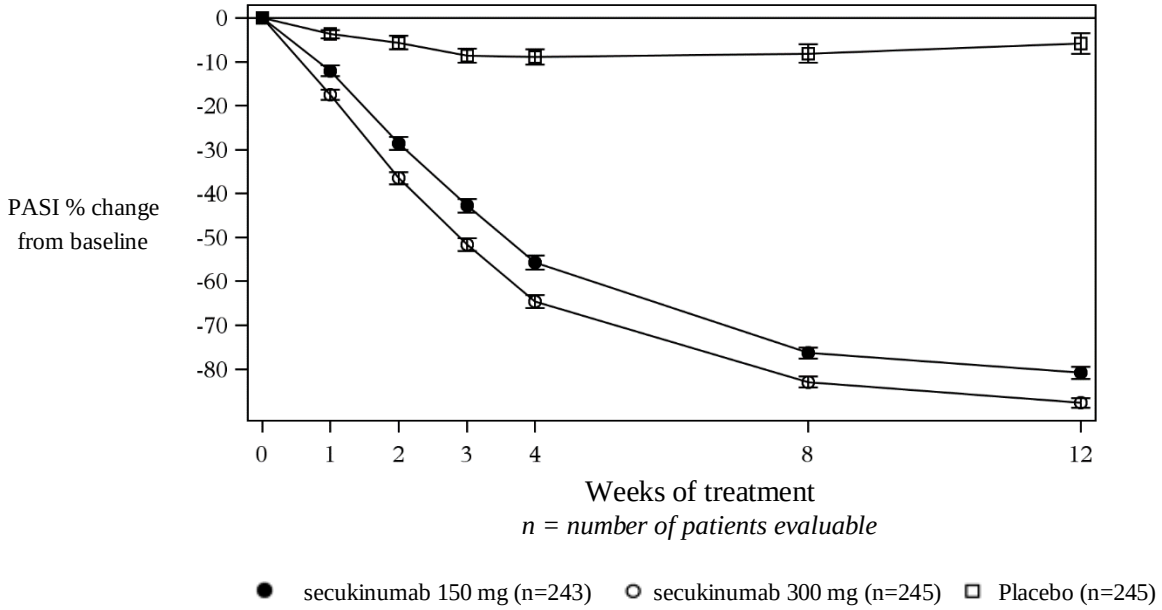
** p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at week 16 and secondary endpoint of PASI 75 at week 4

*** p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at week 52

Secukinumab was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Secukinumab was associated with a fast onset of efficacy with a 50% reduction in mean PASI by week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in study 1 (ERASURE)



Specific locations/forms of plaque psoriasis
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE study, secukinumab was superior to placebo at week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE study, secukinumab was superior to placebo at week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response ("clear" or "almost clear") for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to week 24.

Quality of life/patient-reported outcomes
Statistically significant improvements at week 12 (studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at week 12. These improvements were maintained for 52 weeks (studies 1 and 2).

Forty percent of the participants in studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Statistically significant improvements at week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at week 16 and week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Psoriatic arthritis
The safety and efficacy of secukinumab were assessed in 1,999 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA of at least five years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 61% and 42% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For all studies, the primary endpoint was American College of Rheumatology (ACR) 20 response. For Psoriatic Arthritis study 1 (PsA study 1) and Psoriatic Arthritis study 2 (PsA study 2), the primary endpoint was at week 24. For Psoriatic Arthritis study 3 (PsA study 3), the primary endpoint was at week 16 with the key secondary endpoint, the change from baseline in modified Total Sharp Score (mTSS), at week 24.

In PsA study 1, PsA study 2 and PsA study 3, 29%, 35% and 30% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to secukinumab received 75 mg, 150 mg or 300 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

PsA study 3 (FUTURE 5) evaluated 996 patients, of whom 50.1% had concomitant MTX. Patients were randomised to receive secukinumab 150 mg, 300 mg or placebo subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month, or a once monthly injection of secukinumab 150 mg (without loading). Patients randomised to receive placebo who were non-responders at week 16 (early rescue) were then crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at week 16 were crossed over to receive secukinumab (either 150 mg or 300 mg subcutaneously) at week 24 followed by the same dose every month.

Signs and symptoms
Treatment with secukinumab resulted in significant improvement in measures of disease activity compared to placebo at weeks 16 and 24 (see Table 6).

Table 6 Clinical response in PsA study 2 and PsA study 3 at week 16 and week 24

	PsA study 2			PsA study 3		
	Placebo	150 mg[1]	300 mg[1]	Placebo	150 mg[1]	300 mg[1]
Number of patients randomised	98	100	100	332	220	222
ACR20 response n (%)						
Week 16	18 (18.4%)	60 (60.0%***)	57 (57.0%***)	91[◊] (27.4%)	122[◊] (55.5%***)	139[◊] (62.6%***)
Week 24	15[◊] (15.3%)	51[◊] (51.0%***)	54[◊] (54.0%***)	78 (23.5%)	117 (53.2%***)	141 (63.5%***)
ACR50 response n (%)						
Week 16	6 (6.1%)	37 (37.0%***)	35 (35.0%***)	27 (8.1%)	79 (35.9%*)	88 (39.6%*)
Week 24	7 (7.1%)	35 (35.0%)	35 (35.0%**)	29 (8.7%)	86 (39.1%***)	97 (43.7%***)
ACR70 response n (%)						
Week 16	2 (2.0%)	17 (17.0%**)	15 (15.0%**)	14 (4.2%)	40 (18.2%***)	45 (20.3%***)
Week 24	1 (1.0%)	21 (21.0%**)	20 (20.0%**)	13 (3.9%)	53 (24.1%***)	57 (25.7%***)
DAS28-CRP						
Week 16	-0.50	-1.45***	-1.51***	-0.63	-1.29*	-1.49*
Week 24	-0.96	-1.58**	-1.61**	-0.84	-1.57***	-1.68***
Number of patients with ≥3% BSA psoriasis skin involvement at baseline	43 (43.9%)	58 (58.0%)	41 (41.0%)	162 (48.8%)	125 (56.8%)	110 (49.5%)
PASI 75 response n (%)						
Week 16	3 (7.0%)	33 (56.9%***)	27 (65.9%***)	20 (12.3%)	75 (60.0%*)	77 (70.0%*)
Week 24	7 (16.3%)	28 (48.3%**)	26 (63.4%***)	29 (17.9%)	80 (64.0%***)	78 (70.9%***)
PASI 90 response n (%)						
Week 16	3 (7.0%)	22 (37.9%***)	18 (43.9%***)	15 (9.3%)	46 (36.8%*)	59 (53.6%*)
Week 24	4 (9.3%)	19 (32.8%**)	20 (48.8%***)	19 (11.7%)	51 (40.8%***)	60 (54.5%***)
Dactylitis resolution n (%) †						
Week 16	10 (37%)	21 (65.6%*)	26 (56.5%)	40 (32.3%)	46 (57.5%*)	54 (65.9%*)
Week 24	4 (14.8%)	16 (50.0%**)	26 (56.5%**)	42 (33.9%)	51 (63.8%***)	52 (63.4%***)

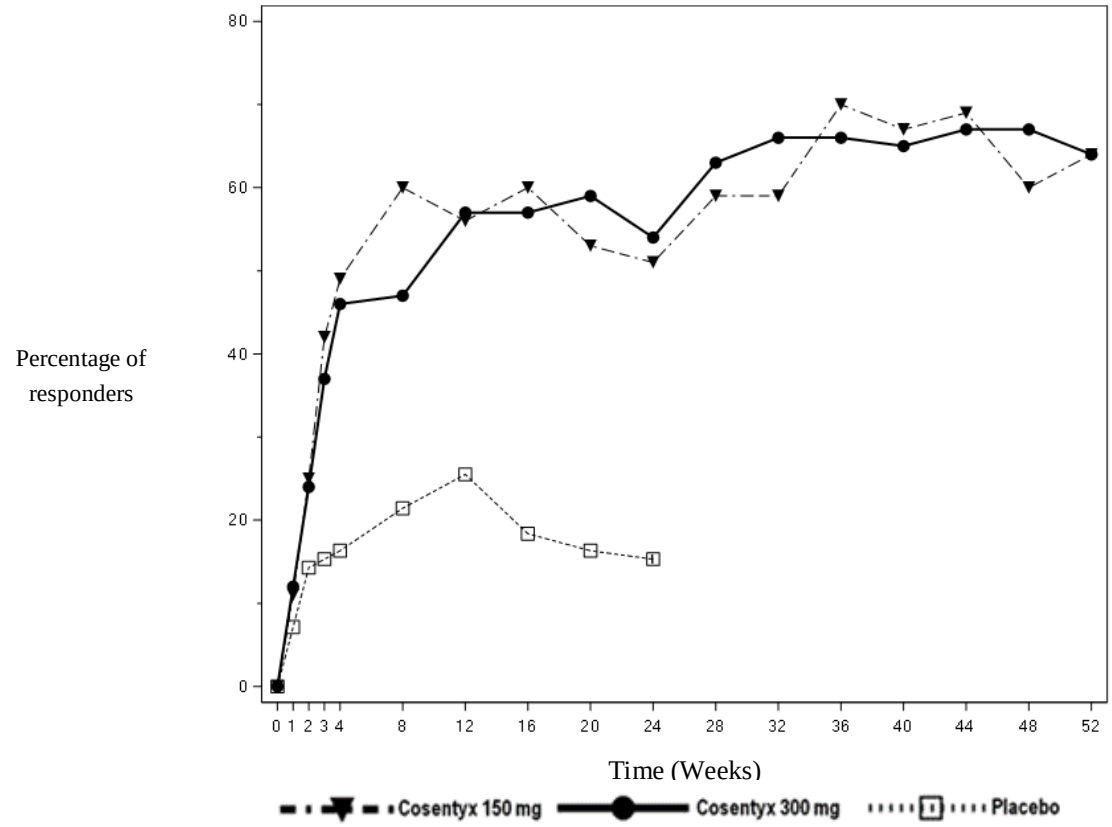
Enthesitis resolution n (%) ‡						
Week 16	17 (26.2%)	32 (50.0%**)	32 (57.1%***)	68 (35.4%)	77 (54.6%*)	78 (55.7%*)
Week 24	14 (21.5%)	27 (42.2%*)	27 (48.2%**)	66 (34.4%)	77 (54.6%***)	86 (61.4%***)

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 24 for PsA study 2, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints and all endpoints at week 16.
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy at week 16 for PsA study 3, except for ACR70 which was an exploratory endpoint and all endpoints at week 24.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
◊Primary Endpoint
[1]Secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month
†In patients with dactylitis at baseline (n=27, 32, 46, respectively for PsA study 2 and n=124, 80, 82, respectively for PsA study 3)
‡In patients with enthesitis at baseline (n=65, 64, 56, respectively for PsA study 2 and n=192, 141, 140, respectively for PsA study 3)

The onset of action of secukinumab occurred as early as week 2. Statistically significant difference in ACR 20 versus placebo was reached at week 3.

The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

Figure 2 ACR20 response in PsA study 2 over time up to week 52



Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. In PsA study 2, at week 24, secukinumab-treated patients with concomitant MTX use had a higher ACR 20 response (47.7% and 54.4% for 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (31.8% and 38.6% for 150 mg and 300 mg, respectively, compared to placebo 8.0%). Secukinumab-treated patients without concomitant MTX use had a higher ACR 20 response (53.6% and 53.6% for 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (37.5% and 32.1% for 150 mg and 300 mg, respectively, compared to placebo 6.3%).

In PsA study 2, both anti-TNFα-naive and anti-TNFα-IR secukinumab-treated patients had a significantly higher ACR 20 response compared to placebo at week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 64% and 58% for 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 30% and 46% for 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo ($p<0.05$) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. In PsA study 2, the proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the secukinumab-treated patients (59.0% and 61.0% for 150 mg and 300 mg, respectively) compared to placebo (26.5%) at week 24.

In PsA study 1 and PsA study 2, efficacy was maintained up to week 104. In PsA study 2, among 200 patients initially randomised to secukinumab 150 mg and 300 mg, 178 (89%) patients were still on treatment at week 52. Of the 100 patients randomised to secukinumab 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to secukinumab 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.

Radiographic response
In PsA study 3, inhibition of progression of structural damage was assessed radiographically and expressed by the modified Total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing Score (JSN). Radiographs of hands, wrists, and feet were obtained at baseline, week 16 and/or week 24 and scored independently by at least two readers who were blinded to treatment group and visit number. Secukinumab 150 mg and 300 mg treatment significantly inhibited the rate of progression of peripheral joint damage compared with placebo treatment as measured by change from baseline in mTSS at week 24 (Table 7).

Inhibition of progression of structural damage was also assessed in PsA study 1 at weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 7.

Table 7 Change in modified Total Sharp Score in psoriatic arthritis

	PsA study 3			PsA study 1	
	Placebo n=296	**secukinumab 150 mg[1] n=213**	**secukinumab 300 mg[1] n=217**	**Placebo n=179**	**secukinumab 150 mg[2] n=185**
Total score					
Baseline (SD)	15.0 (38.2)	13.5 (25.6)	12.9 (23.8)	28.4 (63.5)	22.3 (48.0)
Mean change at Week 24	0.50	0.13*	0.02*	0.57	0.13*

*p<0.05 based on nominal, but non adjusted, p-value
[1]secukinumab 150 mg or 300 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month
[2]10 mg/kg at weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg

In PsA study 1, inhibition of structural damage was maintained with secukinumab treatment up to week 52.

In PsA study 3, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 80.3%, 88.5% and 73.6% for secukinumab 150 mg, 300 mg and placebo, respectively. An effect of inhibition of structural damage was observed in anti-TNFα-naïve and anti-TNFα-IR patients and in patients treated with and without concomitant MTX.

In PsA study 1, the percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to week 24 was 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from week 24 to week 52 for secukinumab 10 mg/kg intravenous load – followed by 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at week 16 or week 24 was 85.7% and 86.8%, respectively.

Axial manifestations in PsA
A randomised, double-blind, placebo-controlled study (MAXIMISE) assessed the efficacy of secukinumab in 485 PsA patients with axial manifestations who were naive to biologic treatment and responded inadequately to NSAIDs. The primary variable of at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 12 was met. Treatment with secukinumab 300 mg and 150 mg compared to placebo also resulted in greater improvement in signs and symptoms (including decreases from baseline in spinal pain) and improvement in physical function (see Table 8).

Table 8 Clinical response on MAXIMISE study at week 12

	Placebo (n=164)	**150 mg (n=157)**	**300 mg (n=164)**
ASAS 20 response, % (95% CI)	31.2 (24.6, 38.7)	66.3 (58.4, 73.3)*	62.9 (55.2, 70.0)*
ASAS 40 response, % (95% CI)	12.2 (7.8, 18.4)	39.5 (32.1, 47.4)**	43.6 (36.2, 51.3)**
BASDAI 50, % (95% CI)	9.8 (5.9, 15.6)	32.7 (25.8, 40.5)**	37.4 (30.1, 45.4)**
Spinal pain, VAS (95% CI)	-13.6 (-17.2, -10.0)	-28.5 (-32.2, -24.8)**	-26.5 (-30.1, -22.9)**
Physical function, HAQ-DI (95% CI)	-0.155 (-0.224, -0.086)	-0.330 (-0.401, -0.259)**	-0.389 (-0.458, -0.320)**
* p<0.0001; versus placebo using multiple imputation. ** Comparison versus placebo was not adjusted for multiplicity. ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; VAS: Visual Analog Scale; HAQ-DI: Health Assessment Questionnaire – Disability Index.			

Improvement in ASAS 20 and ASAS 40 for both secukinumab doses were observed by week 4 and were maintained up to 52 weeks.

Physical function and health-related quality of life
In PsA study 2 and PsA study 3, patients treated with secukinumab 150 mg (p=0.0555 and p<0.0001) and 300 mg (p=0.0040 and p<0.0001) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24 and week 16, respectively. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA study 1.

Secukinumab-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively) and these improvements were maintained up to week 104 in PsA study 2.

Similar responses were seen in PsA study 1 and efficacy was maintained up to week 52.

Axial spondyloarthritis (axSpA)
Ankylosing spondylitis (AS) / Radiographic axial spondyloarthritis
The safety and efficacy of secukinumab were assessed in 816 patients in three randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in Ankylosing Spondylitis study 1 (AS study 1) and Ankylosing Spondylitis study 2 (AS study 2) had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of SpondyloArthritis International Society (ASAS 20) criteria at week 16.

In Ankylosing Spondylitis study 1 (AS study 1), Ankylosing Spondylitis study 2 (AS study 2), and Ankylosing Spondylitis study 3 (AS study 3), 27.0%, 38.8%, and 23.5% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

AS study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at week 8. Patients randomised to placebo who were non-responders at week 16 (early rescue) and all other placebo patients at week 24 were crossed over to receive secukinumab (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 75 mg or 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 75 mg or 150 mg subcutaneously) every month.

AS study 3 (MEASURE 3) evaluated 226 patients, of whom 13.3% and 23.5% used concomitant MTX or sulfasalazine, respectively. Patients randomised to secukinumab received 10 mg/kg intravenously at weeks 0, 2, and 4, followed by either 150 mg or 300 mg subcutaneously every month. At week 16, patients who were randomised to placebo at baseline were re-randomised to receive secukinumab (either 150 mg or 300 mg subcutaneously) every month. The primary endpoint was ASAS 20 at week 16. Patients were blinded to the treatment regimen up to week 52, and the study continued to week 156.

Signs and symptoms:
In AS study 2, treatment with secukinumab 150 mg resulted in greater improvement in measures of disease activity compared with placebo at week 16 (see Table 9).

Table 9 Clinical response in AS study 2 at week 16

Outcome (p-value versus placebo)	**Placebo (n = 74)**	**75 mg (n = 73)**	**150 mg (n = 72)**
ASAS 20 response, %	28.4	41.1	61.1***
ASAS 40 response, %	10.8	26.0	36.1***
hsCRP, (post-BSL/BSL ratio)	1.13	0.61	0.55***
ASAS 5/6, %	8.1	34.2	43.1***
ASAS partial remission, %	4.1	15.1	13.9
BASDAI 50, %	10.8	24.7*	30.6**
ASDAS-CRP major improvement	4.1	15.1*	25.0***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of secukinumab 150 mg occurred as early as week 1 for ASAS 20 and week 2 for ASAS 40 (superior to placebo) in AS study 2.

ASAS 20 responses were improved at week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; $p<0.05$) and anti-TNFα-IR patients (50.0% versus 24.1%; $p<0.05$) for secukinumab 150 mg compared with placebo, respectively.

In AS study 1 and AS study 2, secukinumab-treated patients (150 mg in AS study 2 and both regimens in AS study 1) demonstrated significantly improved signs and symptoms at week 16, with comparable magnitude of response and efficacy maintained up to week 52 in both anti-TNFα-naive and anti-TNFα-IR patients. In AS study 2, among 72 patients initially randomised to secukinumab 150 mg, 61 (84.7%) patients were still on treatment at week 52. Of the 72 patients randomised to secukinumab 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

In AS study 3, patients treated with secukinumab (150 mg and 300 mg) demonstrated improved signs and symptoms, and had comparable efficacy responses regardless of dose that were superior to placebo at week 16 for the primary endpoint (ASAS 20). Overall, the efficacy response rates for the 300 mg group were consistently greater compared to the 150 mg group for the secondary endpoints. During the blinded period, the ASAS 20 and ASAS 40 responses were 69.7% and 47.6% for 150 mg and 74.3% and 57.4% for 300 mg at week 52, respectively. The ASAS 20 and ASAS 40 responses were maintained up to week 156 (69.5% and 47.6% for 150 mg versus 74.8% and 55.6% for 300 mg). Greater response rates favouring 300 mg were also observed for ASAS partial remission (ASAS PR) response at week 16 and were maintained up to week 156. Larger differences in response rates, favouring 300 mg over 150 mg, were observed in anti-TNFα-IR patients (n=36) compared to anti-TNFα-naïve patients (n=114).

Spinal mobility:
Patients treated with secukinumab 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at week 16 for both AS study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to week 52.

Physical function and health-related quality of life:
In AS study 1 and study 2, patients treated with secukinumab 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with secukinumab 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to week 52.

Non-radiographic axial spondyloarthritis (nr-axSpA)
The safety and efficacy of secukinumab were assessed in 555 patients in one randomised, double-blind, placebo-controlled phase III study (PREVENT), consisting of a 2-year core phase and a 2-year extension phase, in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) with no radiographic evidence of changes in the sacroiliac joints that would meet the modified New York criteria for ankylosing spondylitis (AS). Patients enrolled had active disease, defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, a Visual Analogue Scale (VAS) for total back pain of ≥40 (on a scale of 0-100 mm), despite current or previous non-steroidal anti-inflammatory drug (NSAID) therapy and increased C-reactive protein (CRP) and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI). Patients in this study had a diagnosis of axSpA for a mean of 2.1 to 3.0 years and 54% of the study participants were female.

In the PREVENT study, 9.7% of patients were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

In the PREVENT study, 9.9% and 14.8% of patients used concomitant MTX or sulfasalazine, respectively. In the double-blind period, patients received either placebo or secukinumab for 52 weeks. Patients randomised to secukinumab received 150 mg subcutaneously at weeks 0, 1, 2, 3 and 4 followed by the same dose every month, or a once monthly injection of secukinumab 150 mg. The primary endpoint was at least 40% improvement in Assessment of SpondyloArthritis International Society (ASAS 40) at Week 16 in anti-TNFα-naive patients.

Signs and symptoms:
In the PREVENT study, treatment with secukinumab 150 mg resulted in significant improvements in the measures of disease activity compared to placebo at week 16. These measures include ASAS 40, ASAS 5/6, BASDAI score, BASDAI 50, high-sensitivity CRP (hsCRP), ASAS 20 and ASAS partial remission response compared to placebo (Table 10). Responses were maintained up to week 52.

Table 10 Clinical response in the PREVENT study at week 16

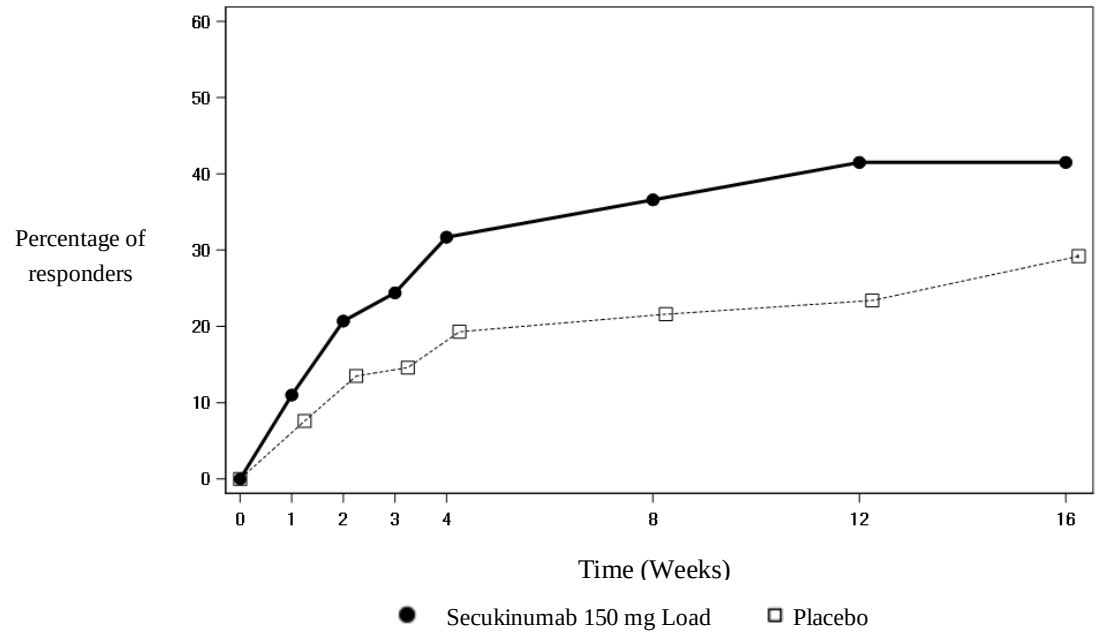
Outcome (p-value versus placebo)	**Placebo**	**150 mg[1]**
Number of anti-TNFα-naive patients randomised	**171**	**164**
ASAS 40 response, %	29.2	41.5*
Total number of patients randomised	**186**	**185**
ASAS 40 response, %	28.0	40.0*
ASAS 5/6, %	23.7	40.0*
BASDAI, LS mean change from baseline score	-1.46	-2.35*
BASDAI 50, %	21.0	37.3*
hsCRP, (post-BSL/BSL ratio)	0.91	0.64*
ASAS 20 response, %	45.7	56.8*
ASAS partial remission, %	7.0	21.6*

*p<0.05 versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy
Non-responder imputation used for missing binary endpoint
[1]secukinumab 150 mg s.c. at weeks 0, 1, 2, 3, and 4 followed by the same dose every month

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; BSL: baseline; LS: Least square

The onset of action of secukinumab 150 mg occurred as early as week 3 for ASAS 40 in anti-TNFα naive patients (superior to placebo) in the PREVENT study. The percentage of patients achieving an ASAS 40 response in anti-TNFα naive patients by visit is shown in Figure 3.

Figure 3 ASAS 40 responses in anti-TNFα naive patients in the PREVENT study over time up to week 16



ASAS 40 responses were also improved at week 16 in anti-TNFα-IR patients for secukinumab 150 mg compared with placebo.

Physical function and health-related quality of life:
Patients treated with secukinumab 150 mg showed statistically significant improvements by week 16 compared to placebo-treated patients in physical function as assessed by the BASFI (week 16: -1.75 versus -1.01, $p<0.05$). Patients treated with secukinumab reported significant improvements compared to placebo-treated patients by week 16 in health-related quality of life as measured by ASQoL (LS mean change: week 16: -3.45 versus -1.84, $p<0.05$) and SF-36 Physical Component Summary (SF-36 PCS) (LS mean change: week 16: 5.71 versus 2.93, $p<0.05$). These improvements were sustained up to week 52.

Spinal mobility:
Spinal mobility was assessed by BASMI up to week 16. Numerically greater improvements were demonstrated in patients treated with secukinumab compared with placebo-treated patients at weeks 4, 8, 12 and 16.

Inhibition of inflammation in magnetic resonance imaging (MRI):
Signs of inflammation were assessed by MRI at baseline and week 16 and expressed as change from baseline in Berlin SI-joint oedema score for sacroiliac joints and ASspiMRI-a score and Berlin spine score for the spine. Inhibition of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with secukinumab. Mean change from baseline in Berlin SI-joint oedema score was -1.68 for patients treated with secukinumab 150 mg (n=180) versus -0.39 for the placebo-treated patients (n=174) ($p<0.05$).

Paediatric population

Paediatric plaque psoriasis
Secukinumab has been shown to improve signs and symptoms, and health-related quality of life in paediatric patients 6 years and older with plaque psoriasis (see Tables 12 and 14).

Severe plaque psoriasis
The safety and efficacy of secukinumab were assessed in a randomised, double-blind, placebo and etanercept-controlled phase III study in paediatric patients from 6 to <18 years of age with severe plaque psoriasis, as defined by a PASI score ≥20, an IGA mod 2011 score of 4, and BSA involvement of ≥10%, who were candidates for systemic therapy. Approximately 43% of the patients had prior exposure to phototherapy, 53% to conventional systemic therapy, 3% to biologics, and 9% had concomitant psoriatic arthritis.

The paediatric psoriasis study 1 evaluated 162 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg), high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg), or placebo at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks, or etanercept. Patients randomised to etanercept received 0.8 mg/kg weekly (up to a maximum of 50 mg). Patient distribution by weight and age at randomisation is described in Table 11.

Table 11 Patient distribution by weight and age for paediatric psoriasis study 1

Randomisation strata	**Description**	**Secukinumab low dose n=40**	**Secukinumab high dose n=40**	**Placebo n=41**	**Etanercept n=41**	**Total N=162**
Age	6-<12 years	8	9	10	10	37
	≥12-<18 years	32	31	31	31	125
Weight	<25 kg	2	3	3	4	12
	≥25-<50 kg	17	15	17	16	65
	≥50 kg	21	22	21	21	85

Patients randomised to receive placebo who were non-responders at week 12 were switched to either the secukinumab low or high dose group (dose based on body weight group) and received study drug at weeks 12, 13, 14, and 15, followed by the same dose every 4 weeks starting at week 16. The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

During the 12 week placebo-controlled period, the efficacy of both the low and the high dose of secukinumab was comparable for the co-primary endpoints. The odds ratio estimates in favour of both secukinumab doses were statistically significant for both the PASI 75 and IGA mod 2011 0 or 1 responses.

All patients were followed for efficacy and safety during the 52 weeks following the first dose. The proportion of patients achieving PASI 75 and IGA mod 2011 'clear' or 'almost clear' (0 or 1) responses showed separation between secukinumab treatment groups and placebo at the first post-baseline visit at week 4, the difference becoming more prominent at week 12. The response was maintained throughout the 52 week time period (see Table 12). Improvement in PASI 50, 90, 100 responder rates and Children's Dermatology Life Quality Index (CDLQI) scores of 0 or 1 were also maintained throughout the 52 week time period.

In addition, PASI 75, IGA 0 or 1, PASI 90 response rates at weeks 12 and 52 for both secukinumab low and high dose groups were higher than the rates for patients treated with etanercept (see Table 12).

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable although the efficacy of the high dose was higher for patients ≥50 kg. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 12 Summary of clinical response in severe paediatric psoriasis at weeks 12 and 52 (paediatric psoriasis study 1)*

Response criterion	Treatment comparison 'test' vs. 'control'	'test' n**/m (%)	'control' n**/m (%)	odds ratio estimate (95% CI)	p-value
At week 12* **					
PASI 75	secukinumab low dose vs. placebo	32/40 (80.0)	6/41 (14.6)	25.78 (7.08, 114.66)	<0.0001
	secukinumab high dose vs. placebo	31/40 (77.5)	6/41 (14.6)	22.65 (6.31, 98.93)	<0.0001
	secukinumab low dose vs. etanercept	32/40 (80.0)	26/41 (63.4)	2.25 (0.73, 7.38)	
	secukinumab high dose vs. etanercept	31/40 (77.5)	26/41 (63.4)	1.92 (0.64, 6.07)	
IGA 0/1	secukinumab low dose vs. placebo	28/40 (70.0)	2/41 (4.9)	51.77 (10.02, 538.64)	<0.0001
	secukinumab high dose vs. placebo	24/40 (60.0)	2/41 (4.9)	32.52 (6.48, 329.52)	<0.0001
	secukinumab low dose vs. etanercept	28/40 (70.0)	14/41 (34.1)	4.49 (1.60, 13.42)	
	secukinumab high dose vs. etanercept	24/40 (60.0)	14/41 (34.1)	2.86 (1.05, 8.13)	
PASI 90	secukinumab low dose vs. placebo	29/40 (72.5)	1/41 (2.4)	133.67 (16.83, 6395.22)	<0.0001
	secukinumab high dose vs. placebo	27/40 (67.5)	1/41 (2.4)	102.86 (13.22, 4850.13)	<0.0001
	secukinumab low dose vs. etanercept	29/40 (72.5)	12/41 (29.3)	7.03 (2.34, 23.19)	
	secukinumab high dose vs. etanercept	27/40 (67.5)	12/41 (29.3)	5.32 (1.82, 16.75)	
At week 52					
PASI 75	secukinumab low dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.12 (0.91, 12.52)	
	secukinumab high dose vs. etanercept	35/40 (87.5)	28/41 (68.3)	3.09 (0.90, 12.39)	
IGA 0/1	secukinumab low dose vs. etanercept	29/40 (72.5)	23/41 (56.1)	2.02 (0.73, 5.77)	
	secukinumab high dose vs. etanercept	30/40 (75.0)	23/41 (56.1)	2.26 (0.81, 6.62)	
PASI 90	secukinumab low dose vs. etanercept	30/40 (75.0)	21/41 (51.2)	2.85 (1.02, 8.38)	
	secukinumab high dose vs. etanercept	32/40 (80.0)	21/41 (51.2)	3.69 (1.27, 11.61)	

* non-responder imputation was used to handle missing values
** n is the number of responders, m = number of patients evaluable
*** extended visit window at week 12
Odds ratio, 95% confidence interval, and p-value are from an exact logistic regression model with treatment group, baseline body-weight category and age category as factors

A higher proportion of paediatric patients treated with secukinumab reported improvement in health-related quality of life as measured by a CDLQI score of 0 or 1 compared to placebo at week 12 (low dose 44.7%, high dose 50%, placebo 15%). Over time up to and including week 52 both secukinumab dose groups were numerically higher than the etanercept group (low dose 60.6%, high dose 66.7%, etanercept 44.4%).

Moderate to severe plaque psoriasis
Secukinumab was predicted to be effective for the treatment of paediatric patients with moderate plaque psoriasis based on the demonstrated efficacy and exposure response relationship in adult patients with moderate to severe plaque psoriasis, and the similarity of the disease course, pathophysiology, and drug effect in adult and paediatric patients at the same exposure levels.

Moreover, the safety and efficacy of secukinumab was assessed in an open-label, two-arm, parallel-group, multicentre phase III study in paediatric patients from 6 to <18 years of age with moderate to severe plaque psoriasis, as defined by a PASI score ≥12, an IGA mod 2011 score of ≥3, and BSA involvement of ≥10%, who were candidates for systemic therapy.

The paediatric psoriasis study 2 evaluated 84 patients who were randomised to receive low dose secukinumab (75 mg for body weight <50 kg or 150 mg for body weight ≥50 kg) or high dose secukinumab (75 mg for body weight <25 kg, 150 mg for body weight between ≥25 kg and <50 kg, or 300 mg for body weight ≥50 kg) at weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks. Patient distribution by weight and age at randomisation is described in Table 13.

Table 13 Patient distribution by weight and age for paediatric psoriasis study 2

Sub-groups	Description	Secukinumab low dose n=42	Secukinumab high dose n=42	Total N=84
Age	6-<12 years	17	16	33
	≥12-<18 years	25	26	51
Weight	<25 kg	4	4	8
	≥25-<50 kg	13	12	25
	≥50 kg	25	26	51

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) response at week 12.

The efficacy of both the low and the high dose of secukinumab was comparable and showed statistically significant improvement compared to historical placebo for the co-primary endpoints. The estimated posterior probability of a positive treatment effect was 100%.

All patients were followed for efficacy for at least 24 weeks following first administration (see Table 14). Efficacy (defined as PASI 75 response and IGA mod 2011 'clear' or 'almost clear' [0 or 1]) was observed as early as the first post-baseline visit at week 2 and the proportion of patients who achieved a PASI 75 response and IGA mod 2011 'clear' or 'almost clear' (0 or 1) increased throughout the 24 week time period. Improvement in PASI 90 and PASI 100 were also observed at week 12 and increased throughout the 24 week time period.

Beyond week 12, efficacy of both the low and the high dose of secukinumab was comparable. The safety profiles of the low dose and the high dose were comparable and consistent with the safety profile in adults.

Table 14 Summary of clinical response in moderate to severe paediatric psoriasis at weeks 12 and 24 (paediatric psoriasis study 2)*

	Week 12		Week 24	
	Secukinumab low dose	Secukinumab high dose	Secukinumab low dose	Secukinumab high dose
Number of patients	42	42	42	42
PASI 75 response n (%)	39 (92.9%)	39 (92.9%)	40 (95.2%)	40 (95.2%)
IGA mod 2011 'clear' or 'almost clear' response n (%)	33 (78.6%)	35 (83.3%)	37 (88.1%)	39 (92.9%)
PASI 90 response n (%)	29 (69%)	32 (76.2%)	37 (88.1%)	37 (88.1%)
PASI 100 response n (%)	25 (59.5%)	23 (54.8%)	28 (66.7%)	28 (66.7%)
* non-responder imputation was used to handle missing values				

These outcomes in the paediatric moderate to severe plaque psoriasis population confirmed the predictive assumptions based on the efficacy and exposure response relationship in adult patients, mentioned above.

In the low dose group, 50% and 70.7% of patients achieved a CDLQI 0 or 1 score at weeks 12 and 24, respectively. In the high dose group, 61.9% and 60.5% achieved a CDLQI 0 or 1 score at weeks 12 and 24, respectively.

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 years (see section 4.2 for information on paediatric use).

The European Medicines Agency has deferred the obligation to submit the results of studies with Cosentyx in chronic idiopathic arthritis for paediatric patients aged from 2 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Most pharmacokinetics properties observed in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis were similar.

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Following a single subcutaneous injection of 300 mg solution for injection in pre-filled syringe in plaque psoriasis patients, secukinumab systemic exposure was similar to what was observed previously with two injections of 150 mg.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Special populations

Elderly patients
Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment
No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact secukinumab, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of secukinumab.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

Paediatric population
In a pool of the two paediatric studies, patients with moderate to severe plaque psoriasis (6 to less than 18 years of age) were administered secukinumab at the recommended paediatric dosing regimen. At week 24, patients weighing ≥25 and <50 kg had a mean ± SD steady-state trough concentration of 19.8 ± 6.96 µg/ml (n=24) after 75 mg of secukinumab and patients weighing ≥50 kg had mean ±SD trough concentration of 27.3 ± 10.1 µg/ml (n=36) after 150 mg of secukinumab. The mean ± SD steady-state trough concentration in patients weighing <25 kg (n=8) was 32.6 ± 10.8 µg/ml at week 24 after 75 mg dose.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans (adult or paediatric) based on conventional studies of safety pharmacology, repeated dose and reproductive toxicity, or tissue cross-reactivity.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose dihydrate
Histidine
Histidine hydrochloride monohydrate
Methionine
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months
If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cosentyx 150 mg solution for injection in pre-filled syringe

Cosentyx 150 mg solution for injection in pre-filled syringe is supplied in a pre-filled 1 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber assembled in an automatic needle guard of polycarbonate.

Cosentyx 150 mg solution for injection in pre-filled syringe is available in unit packs containing 1 or 2 pre-filled syringes and in multipacks containing 6 (3 packs of 2) pre-filled syringes.

Cosentyx 300 mg solution for injection in pre-filled syringe

Cosentyx 300 mg solution for injection in pre-filled syringe is supplied in a pre-filled 2.25 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of synthetic polyisoprene rubber assembled in an automatic needle guard of polycarbonate.

Cosentyx 300 mg solution for injection in pre-filled syringe is available in unit packs containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.

Cosentyx 150 mg solution for injection in pre-filled pen

Cosentyx 150 mg solution for injection in pre-filled pen is supplied in a single-use pre-filled syringe assembled into a triangular-shaped pen with transparent window and label. The pre-filled syringe inside the pen is a 1 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber.

Cosentyx 150 mg solution for injection in pre-filled pen is available in unit packs containing 1 or 2 pre-filled pens and in multipacks containing 6 (3 packs of 2) pre-filled pens.

Cosentyx 300 mg solution for injection in pre-filled pen

Cosentyx 300 mg solution for injection in pre-filled pen is supplied in a single-use pre-filled syringe assembled into a squared-shaped pen with transparent window and label. The pre-filled syringe inside the pen is a 2.25 ml glass syringe with a silicone-coated bromobutyl rubber plunger stopper, staked 27G x ½″ needle and rigid needle shield of synthetic polyisoprene rubber.

Cosentyx 300 mg solution for injection in pre-filled pen is available in unit packs containing 1 pre-filled pen and in multipacks containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cosentyx 150 mg solution for injection in pre-filled syringe

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. The syringe should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Cosentyx 300 mg solution for injection in pre-filled syringe

Cosentyx 300 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. The syringe should be taken out of the refrigerator 30-45 minutes before injecting to allow it to reach room temperature.

Cosentyx 150 mg solution for injection in pre-filled pen

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled pen for individual use. The pen should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Cosentyx 300 mg solution for injection in pre-filled pen

Cosentyx 300 mg solution for injection is supplied in a single-use pre-filled pen for individual use. The pen should be taken out of the refrigerator 30-45 minutes before injecting to allow it to reach room temperature.

Prior to use, a visual inspection of the pre-filled syringe or pre-filled pen is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown.
Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

Cosentyx 150 mg solution for injection in pre-filled syringe

EU/1/14/980/002
EU/1/14/980/003
EU/1/14/980/006

Cosentyx 300 mg solution for injection in pre-filled syringe

EU/1/14/980/008-009

Cosentyx150 mg solution for injection in pre-filled pen

EU/1/14/980/004
EU/1/14/980/005
EU/1/14/980/007

Cosentyx 300 mg solution for injection in pre-filled pen

EU/1/14/980/010-011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 January 2015
Date of latest renewal: 03 September 2019

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Novartis Pharma S.A.S.
Centre de Biotechnologie
8, rue de l'Industrie
F-68330 Huningue
France

Sandoz GmbH
Business Unit Biologics Technical Development and Manufacturing Drug Substance Schaftenau (BTDM DSS)
Biochemiestrasse 10
6336 Langkampfen
Austria

Name and address of the manufacturer responsible for batch release

Powder for solution for injection
Novartis Pharma GmbH
Roonstraße 25
90429 Nuremberg
Germany

Solution for injection in pre-filled syringe / Solution for injection in pre-filled pen
Novartis Pharma GmbH
Roonstraße 25
90429 Nuremberg
Germany

Sandoz GmbH
Biochemiestrasse 10
6336 Langkampfen
Austria

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – vial

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

3. LIST OF EXCIPIENTS

Also contains: Sucrose, histidine, histidine hydrochloride monohydrate, polysorbate 80.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg powder for solution for injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
2 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/002	Pack containing 1 pre-filled syringe
EU/1/14/980/003	Pack containing 2 pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 6 (3 packs of 2) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/006 Multipack containing 6 (3 x 2) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 pre-filled syringes. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/006 Multipack containing 6 (3 x 2) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled SensoReady pen
2 pre-filled SensoReady pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/004	Pack containing 1 pre-filled pen
EU/1/14/980/005	Pack containing 2 pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 6 (3 packs of 2) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/007 Multipack containing 6 (3 x 2) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 pre-filled pens. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/007 Multipack containing 6 (3 x 2) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

SensoReady pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/008 Pack containing 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/009 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/009 Multipack containing 3 (3 x 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 300 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled UnoReady pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/010 Pack containing 1 pre-filled pen

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/011 Multipack containing 3 (3 x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 300 mg secukinumab in 2 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/011 Multipack containing 3 (3 x 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 300 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

UnoReady pen

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Cosentyx 150 mg powder for solution for injection

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Cosentyx is given via injection under your skin (known as a subcutaneous injection) by a healthcare professional.

Make sure you discuss with your doctor when you will have your injections and your follow-up appointments.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older
- The recommended dose given by subcutaneous injection is based on body weight as follows:
  - Weight below 25 kg: 75 mg using the powder for solution for injection.
  - Weight 25 kg or above and below 50 kg: 75 mg using the powder for solution for injection.
  - Weight 50 kg or above: 150 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
    Your doctor may increase the dose to 300 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
- Each 75 mg dose **is given as one injection of 75 mg**. Each 150 mg dose **is given as one injection of 150 mg**. Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Psoriatic arthritis
For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have missed a Cosentyx injection, talk to your doctor.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- athlete's foot (tinea pedis)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

Rare (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer box or vial after "EXP".

Before reconstitution: Store the vial in the refrigerator between 2°C and 8°C.

After reconstitution: The solution can be used immediately or can be stored at 2°C to 8°C for up to 24 hours. Do not freeze. The solution should be administered within one hour after removal from 2°C to 8°C storage.

Do not use this medicine if you notice that the powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each vial of powder for solution for injection contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.
- The other ingredients are sucrose, histidine, histidine hydrochloride monohydrate and polysorbate 80.

What Cosentyx looks like and contents of the pack
Cosentyx powder for solution for injection is a white solid powder in a glass vial.
Cosentyx is supplied in a pack containing one vial.

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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu

Instructions for use of Cosentyx powder for solution for injection

The following information is intended for medical or healthcare professionals only.

The preparation of the solution for subcutaneous injection must be done without interruption and ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution takes 20 minutes on average and should not exceed 90 minutes.

To prepare Cosentyx 150 mg powder for solution for injection, please adhere to the following instructions:

Instructions for reconstitution of Cosentyx 150 mg powder for solution for injection:

1. Bring the vial of powder to room temperature and ensure that the sterile water for injections is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injections into a 1 ml graduated disposable syringe and adjust to 1.0 ml.
3. Remove the plastic cap from the vial.
4. Insert the syringe needle into the vial containing the powder through the centre of the rubber stopper and reconstitute the powder by slowly injecting 1.0 ml of sterile water for injections into the vial. The stream of sterile water for injections should be directed onto the powder.

5. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

6. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.
7. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

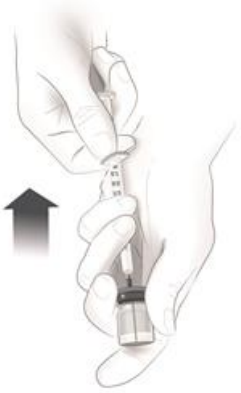
8. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its colour may vary from colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.

9. Prepare the required number of vials (1 vial for the 75 mg dose, 1 vial for the 150 mg dose, 2 vials for the 300 mg dose).

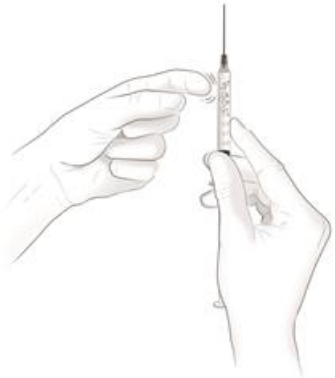
After storage at 2°C to 8°C, the solution should be allowed to come to room temperature for approximately 20 minutes before administration.

Instructions for administration of Cosentyx solution

1. Tilt the vial to an angle of approximately 45° and position the needle tip at the very bottom of the solution in the vial when drawing the solution into the syringe. DO NOT invert the vial.



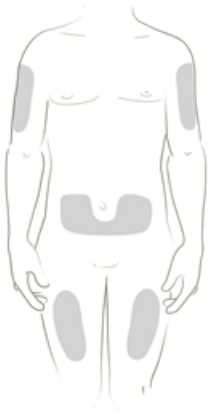
2. For the 150 mg and 300 mg doses, carefully withdraw slightly more than 1.0 ml of the solution for subcutaneous injection from the vial into a 1 ml graduated disposable syringe using a suitable needle (e.g. 21G x 2″). This needle will only be used for withdrawing Cosentyx into the disposable syringe. Prepare the required number of syringes (2 syringes for the 300 mg dose). For a child receiving the 75 mg dose, carefully withdraw slightly more than 0.5 ml of the solution for subcutaneous injection and discard the rest immediately.
3. With the needle pointing upward, gently tap the syringe to move any air bubbles to the top.



4. Replace the attached needle with a 27G x ½″ needle.

5. Expel the air bubbles and advance the plunger to the 1.0 ml mark for the 150 mg dose. Expel the air bubbles and advance the plunger to the 0.5 ml mark for the 75 mg dose.
6. Clean the injection site with an alcohol swab.

7. Inject the Cosentyx solution subcutaneously into the front of thighs, lower abdomen (but not the area 5 centimetres around the navel) or outer upper arms. Choose a different site each time an injection is administered. Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



8. Any remaining solution in the vial must not be used and should be discarded in accordance with local requirements. Vials are for single use only. Dispose of the used syringe in a sharps container (closable, puncture-resistant container). For the safety and health of you and others, needles and used syringes must never be re-used.

Package leaflet: Information for the patient

Cosentyx 150 mg solution for injection in pre-filled syringe

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx 150 mg pre-filled syringe" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older

- The recommended dose given by subcutaneous injection is based on body weight as follows:
  - Weight below 25 kg: 75 mg using the powder for solution for injection.
  - Weight 25 kg or above and below 50 kg: 75 mg using the powder for solution for injection.
  - Weight 50 kg or above: 150 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
    Your doctor may increase the dose to 300 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
- Each 75 mg dose **is given as one injection of 75 mg**. Each 150 mg dose **is given as one injection of 150 mg**. Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Psoriatic arthritis

For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- athlete's foot (tinea pedis)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

Rare (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 150 mg solution for injection in pre-filled syringe is available in unit packs containing 1 or 2 pre-filled syringe(s) and in multipacks containing 6 (3 packs of 2) pre-filled syringes.
Not all pack sizes may be marketed.

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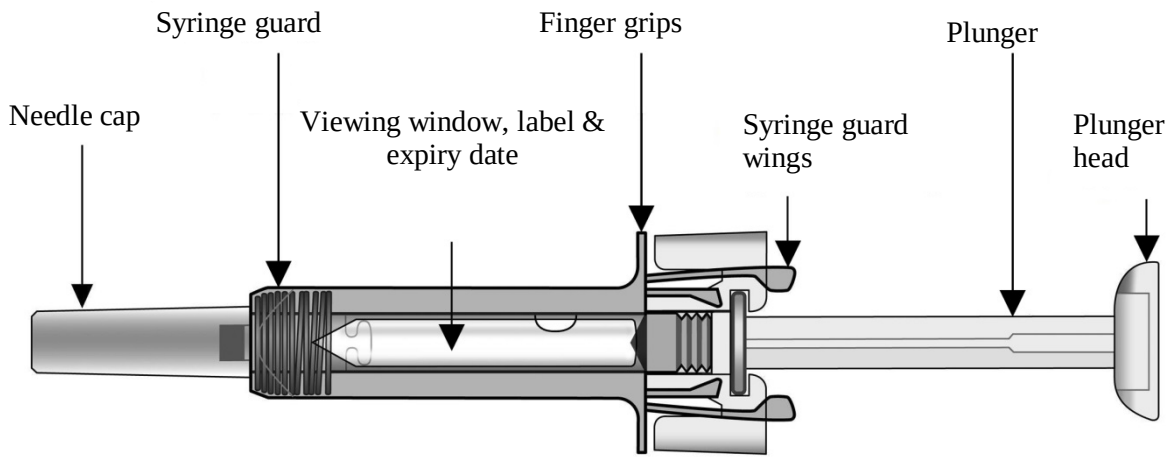
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 150 mg pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself or a person in your care until you have been trained by your doctor, nurse or pharmacist. The box contains Cosentyx 150 mg pre-filled syringe(s) individually sealed in a plastic blister.

Your Cosentyx 150 mg pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Important safety information

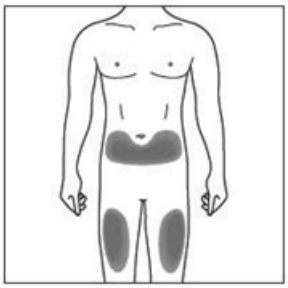
Caution: Keep the syringe out of the sight and reach of children.

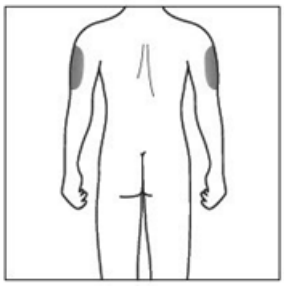
1. The needle cap of the syringe may contain dry rubber (latex), which should not be handled by persons sensitive to this substance.
2. Do not open the sealed outer box until you are ready to use this medicine.
3. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
4. Never leave the syringe lying around where others might tamper with it.
5. Do not shake the syringe.
6. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
7. Do not remove the needle cap until just before you give the injection.
8. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx 150 mg pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (15-30 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

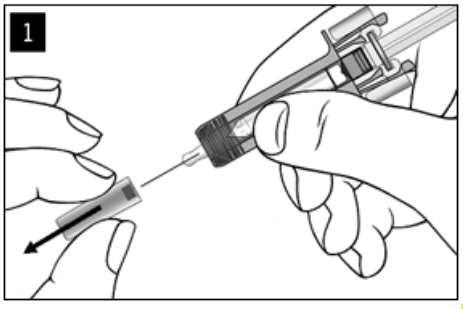
If a caregiver is giving you the injection, the outer upper arms may also be used.

Preparing the Cosentyx 150 mg pre-filled syringe ready for use

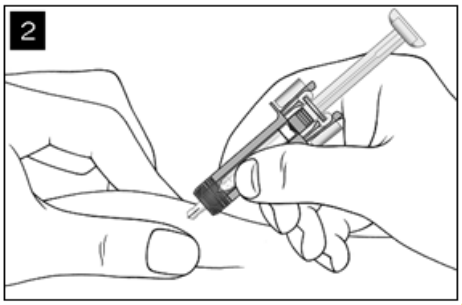
Note: For a 150 mg dose, prepare 1 pre-filled syringe and inject the content. For a 300 mg dose, prepare 2 pre-filled syringes and inject the contents of both.

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 15-30 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister by holding the syringe guard body.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

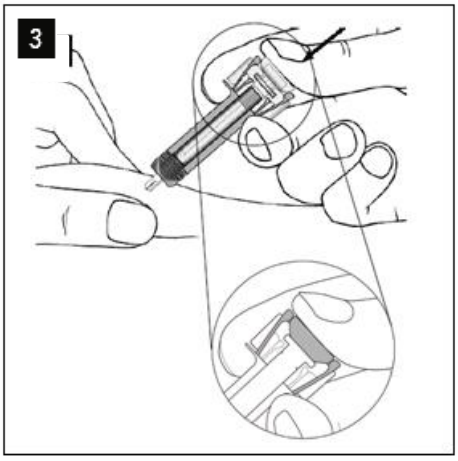
How to use the Cosentyx 150 mg pre-filled syringe



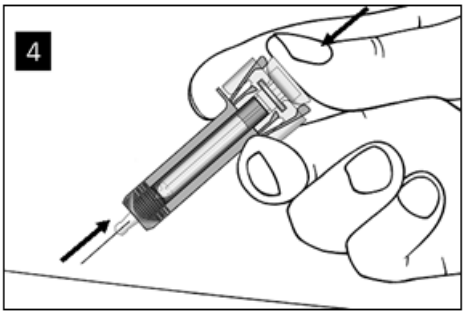
Carefully remove the needle cap from the syringe by holding the syringe guard body. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



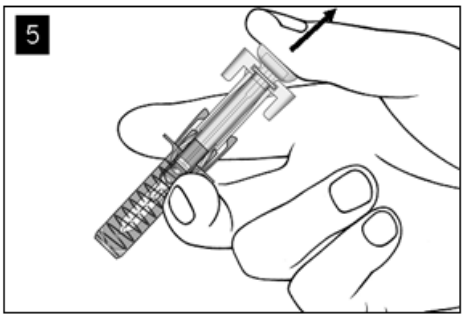
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions

Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the patient

Cosentyx 150 mg solution for injection in pre-filled pen

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of the Cosentyx SensoReady pen 150 mg" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Children aged 6 years and older

- The recommended dose given by subcutaneous injection is based on body weight as follows:
  - Weight below 25 kg: 75 mg using the powder for solution for injection.
  - Weight 25 kg or above and below 50 kg: 75 mg using the powder for solution for injection.
  - Weight 50 kg or above: 150 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
    Your doctor may increase the dose to 300 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
- Each 75 mg dose **is given as one injection of 75 mg**. Each 150 mg dose **is given as one injection of 150 mg**. Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Psoriatic arthritis

For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as two injections of 150 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- athlete's foot (tinea pedis)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

Rare (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the pen after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the pen sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled pen contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 150 mg solution for injection in pre-filled pen is available in unit packs containing 1 or 2 pre-filled pen(s) and in multipacks containing 6 (3 packs of 2) pre-filled pens.
Not all pack sizes may be marketed.

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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu

Instructions for use of the Cosentyx SensoReady pen 150 mg

Cosentyx SensoReady pen 150 mg

Solution for injection in a pre-filled pen

Secukinumab

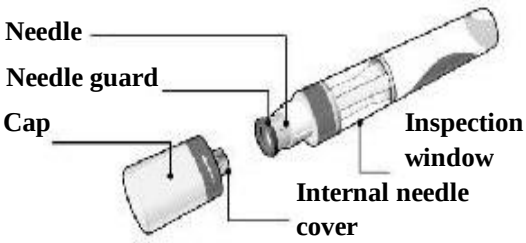
Patient Instructions for Use

Read ALL the way through these instructions before injecting.

These instructions are to help you to inject correctly using the Cosentyx SensoReady pen.

It is important not to try to inject yourself or the person in your care until you have been trained by your doctor, nurse or pharmacist.

Your Cosentyx SensoReady pen 150 mg:



Cosentyx SensoReady pen 150 mg shown with the cap removed. **Do not** remove the cap until you are ready to inject.

Store your boxed pen in a **refrigerator** between 2°C and 8°C and **out of the reach of children**.

- **Do not freeze** the pen.
- **Do not shake** the pen.
- Do not use the pen if it has been **dropped** with the cap removed.

For a more comfortable injection, take the pen out of the refrigerator **15-30 minutes before injecting** to allow it to reach room temperature.

What you need for your injection:

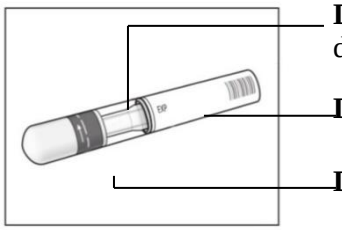
Included in the carton:

A new and unused Cosentyx SensoReady pen 150 mg (1 pen is needed for a 150 mg dose and 2 pens are needed for a 300 mg dose).

Not included in the carton:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Before your injection:

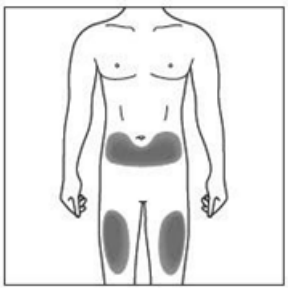


1. Important safety checks before you inject:
The liquid should be clear. Its colour may vary from colourless to slightly yellow.
Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. You may see a small air bubble, which is normal.

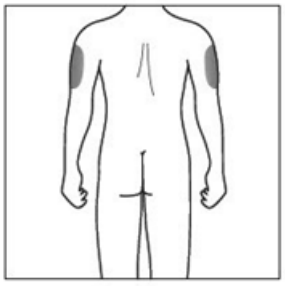
Do not use the pen if the **expiry date** has passed.

Do not use if the **safety seal** has been broken.

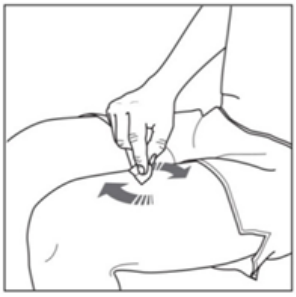
Contact your pharmacist if the pen fails any of these checks.



2a. Choose your injection site:
- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

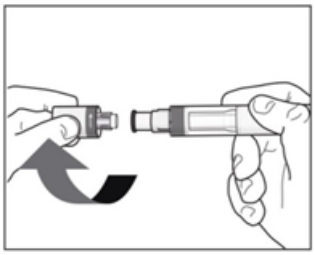


2b. Caregivers and healthcare professionals only:
- If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your outer upper arm.



3. Cleaning your injection site:
- Wash your hands with soap and hot water.
- Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting.
- Do not touch the cleaned area again before injecting.

Your injection:

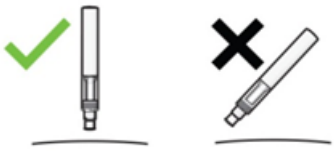


4. Removing the cap:

- Only remove the cap when you are ready to use the pen.
- Twist off the cap in the direction of the arrows.
- Once removed, throw away the cap. **Do not try to re-attach the cap.**
- Use the pen within 5 minutes of removing the cap.

5. Holding your pen:

- Hold the pen at 90 degrees to the cleaned injection site.



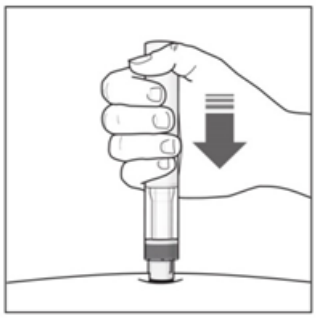
Correct **Incorrect**

YOU MUST READ THIS BEFORE INJECTING.

During the injection you will hear **2 loud clicks**.

The **1st click** indicates that the injection has started. Several seconds later a **2nd click** will indicate that the injection is **almost** finished.

You must keep holding the pen firmly against your skin until you see a **green indicator** fill the window and stop moving.



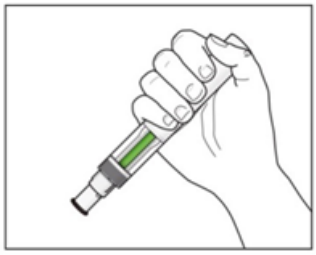
6. Starting your injection:

- Press the pen firmly against the skin to start the injection.
- The **1st click** indicates the injection has started.
- **Keep holding** the pen firmly against your skin.
- The **green indicator** shows the progress of the injection.

7. Completing your injection:

- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator** fills the window and has stopped moving.
- The pen can now be removed.

After your injection:



8. Check the green indicator fills the window:

- This means the medicine has been delivered. Contact your doctor if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

9. Disposing of your Cosentyx SensoReady pen:

- Dispose of the used pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar).
- Never try to reuse your pen.

Package leaflet: Information for the patient

Cosentyx 300 mg solution for injection in pre-filled syringe

secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx 300 mg pre-filled syringe" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

Children aged 6 years and older

- The recommended dose given by subcutaneous injection is based on body weight as follows:
  - Weight below 25 kg: 75 mg using the powder for solution for injection.
  - Weight 25 kg or above and below 50 kg: 75 mg using the powder for solution for injection.
  - Weight 50 kg or above: 150 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
    Your doctor may increase the dose to 300 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
- Each 75 mg dose **is given as one injection of 75 mg**. Each 150 mg dose **is given as one injection of 150 mg**. Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Psoriatic arthritis

For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as one injection of 300 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- athlete's foot (tinea pedis)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

Rare (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 300 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 300 mg solution for injection in pre-filled syringe is available in a pack containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.
Not all pack sizes may be marketed.

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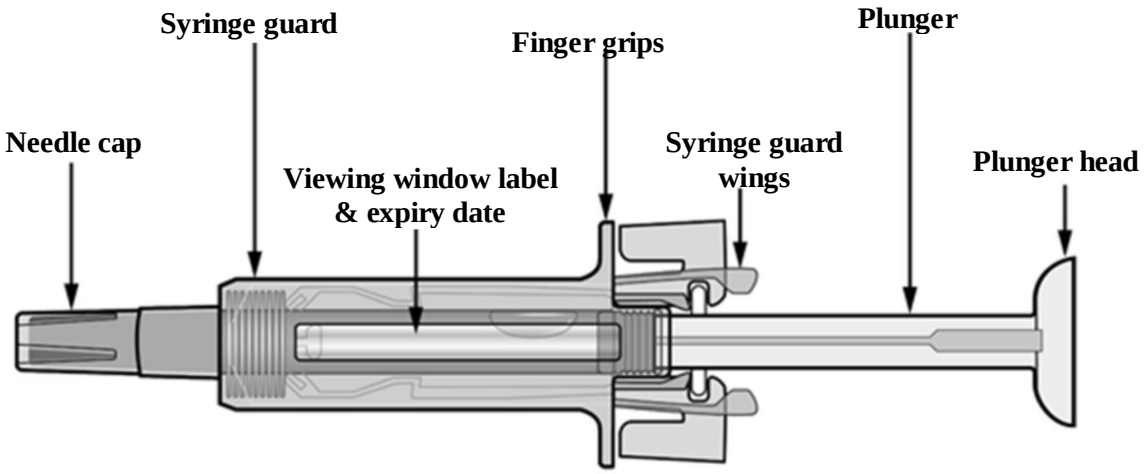
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx 300 mg pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. The box contains the Cosentyx 300 mg pre-filled syringe individually sealed in a plastic blister.

Your Cosentyx 300 mg pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Important safety information

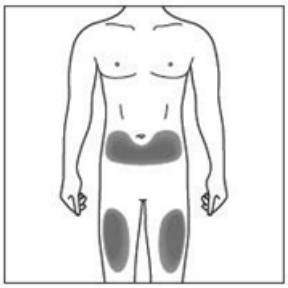
Caution: Keep the syringe out of the sight and reach of children.

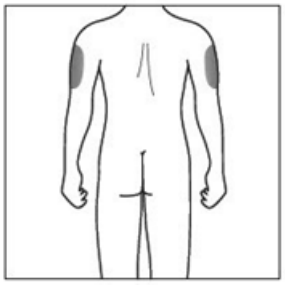
1. Do not open the sealed outer box until you are ready to use this medicine.
2. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
3. Never leave the syringe lying around where others might tamper with it.
4. Do not shake the syringe.
5. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
6. Do not remove the needle cap until just before you give the injection.
7. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx 300 mg pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (30-45 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

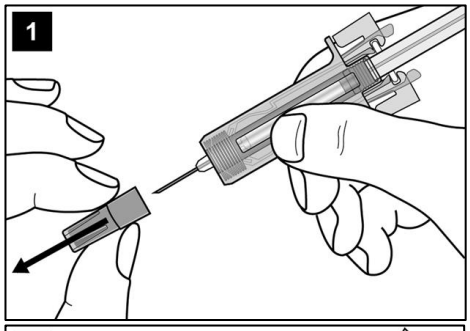
- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

If a caregiver is giving you the injection, the outer upper arms may also be used.

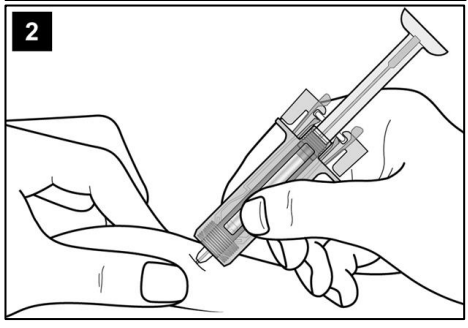
Preparing the Cosentyx 300 mg pre-filled syringe ready for use

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 30-45 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister by holding the syringe guard body.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

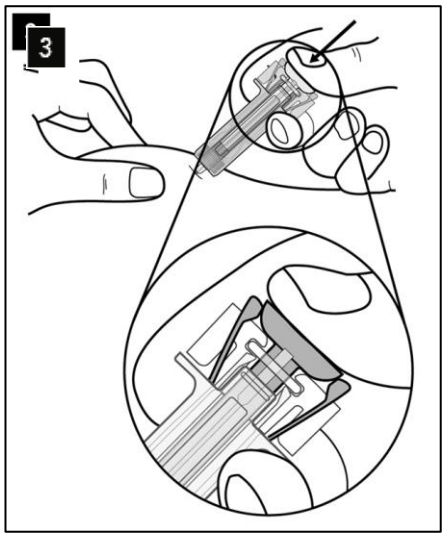
How to use the Cosentyx 300 mg pre-filled syringe



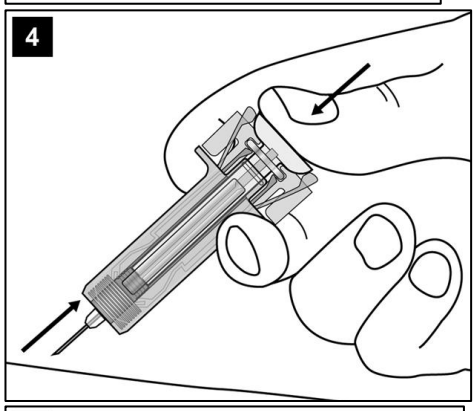
Carefully remove the needle cap from the syringe by holding the syringe guard body. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



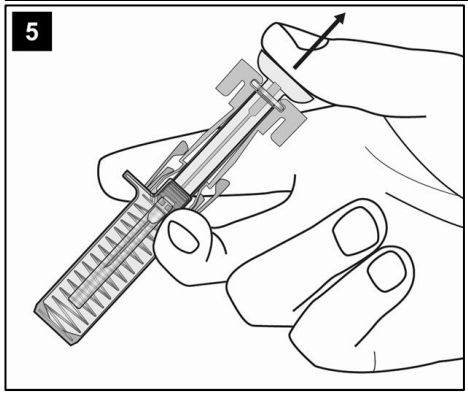
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



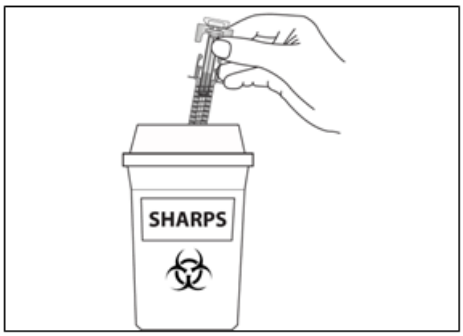
Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions



Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the patient

Cosentyx 300 mg solution for injection in pre-filled pen
secukinumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody which belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis, psoriatic arthritis and axial spondyloarthritis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis

Plaque psoriasis
Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults, adolescents and children (6 years of age and older) with moderate to severe plaque psoriasis.

Using Cosentyx in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Axial spondyloarthritis, including ankylosing spondylitis (radiographic axial spondyloarthritis) and non-radiographic axial spondyloarthritis
Cosentyx is used to treat conditions called "ankylosing spondylitis" and "non-radiographic axial spondyloarthritis". These conditions are inflammatory diseases primarily affecting the spine which cause inflammation of the spinal joints. If you have ankylosing spondylitis or non-radiographic axial spondyloarthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis and active non-radiographic axial spondyloarthritis.

Using Cosentyx in ankylosing spondylitis and non-radiographic axial spondyloarthritis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, nurse or pharmacist before using Cosentyx:
- if you currently have an infection
- if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have an inflammatory disease affecting your gut called Crohn's disease.
- if you have an inflammation of your large intestine called ulcerative colitis.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice abdominal cramps and pain, diarrhoea, weight loss, blood in the stool or any other signs of bowel problems.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children younger than 6 years of age with plaque psoriasis because it has not been studied in this age group.

Cosentyx is not recommended for children and adolescents (under 18 years of age) in other indications because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy, breast-feeding and fertility
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose.
  Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx is unlikely to influence your ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of the Cosentyx UnoReady pen 300 mg" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

Plaque psoriasis
Adult
- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

Children aged 6 years and older

- The recommended dose given by subcutaneous injection is based on body weight as follows:
  - Weight below 25 kg: 75 mg using the powder for solution for injection.
  - Weight 25 kg or above and below 50 kg: 75 mg using the powder for solution for injection.
  - Weight 50 kg or above: 150 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
    Your doctor may increase the dose to 300 mg using the powder for solution for injection, the pre-filled syringe or the pre-filled pen.
- Each 75 mg dose **is given as one injection of 75 mg**. Each 150 mg dose **is given as one injection of 150 mg**. Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Psoriatic arthritis

For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as one injection of 300 mg**.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as one injection of 300 mg.

For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg.

Ankylosing spondylitis (Radiographic axial spondyloarthritis)

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Based on your response, your doctor may increase your dose to 300 mg. Each 300 mg dose is given as one injection of 300 mg.

Non-radiographic axial spondyloarthritis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at weeks 1, 2, 3 and 4 followed by monthly injections.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis, psoriatic arthritis or axial spondyloarthritis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Your doctor will decide if and when you may restart the treatment.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhoea)
- athlete's foot (tinea pedis)
- headache
- nausea
- fatigue

Uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- itchy rash (urticaria)
- lower respiratory tract infections
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

Rare (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)
- redness and shedding of skin over a larger area of the body, which may be itchy or painful (exfoliative dermatitis)

Not known (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the pen after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the pen sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.
If necessary, Cosentyx can be left out of the refrigerator for a single period of up to 4 days at room temperature, not above 30°C.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled pen contains 300 mg secukinumab.
- The other ingredients are trehalose dihydrate, histidine, histidine hydrochloride monohydrate, methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow.
Cosentyx 300 mg solution for injection in pre-filled pen is available in a pack containing 1 pre-filled pen and in multipacks containing 3 (3 packs of 1) pre-filled pens.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
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Vista Building
Elm Park, Merrion Road
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Manufacturer
Novartis Pharma GmbH
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90429 Nuremberg
Germany

Sandoz GmbH
Biochemiestrasse 10
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Austria

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Novartis Pharma N.V.
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Slovenská republika
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Suomi/Finland
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United Kingdom
Novartis Pharmaceuticals UK Ltd.
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This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx UnoReady pen 300 mg

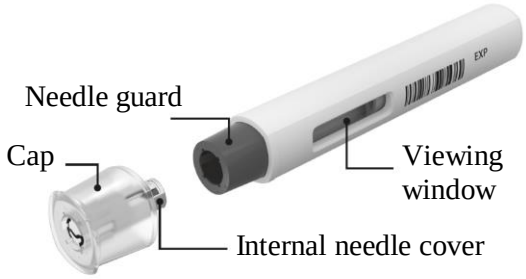
secukinumab

Read ALL the way through these instructions before injecting.

These instructions are to help you to inject correctly using the Cosentyx UnoReady pen.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist.

Your Cosentyx UnoReady pen 300 mg:



Cosentyx UnoReady pen 300 mg is shown above with the cap removed. **Do not** remove the cap until you are ready to inject.

Do not use the Cosentyx UnoReady pen if the seal on the outer carton is broken.

Keep the Cosentyx UnoReady pen in the sealed outer carton until you are ready to use it to protect it from light.

Store your Cosentyx UnoReady pen in a **refrigerator** between 2°C and 8°C and **out of the reach of children**.

- **Do not freeze** the pen.
- **Do not shake** the pen.
- Do not use the pen if it has been **dropped** with the cap removed.

The needle is covered by the needle guard and the needle will not be seen. Do not touch or push the needle guard because you could get a needle stick injury.

What you need for your injection:

Included in the carton:

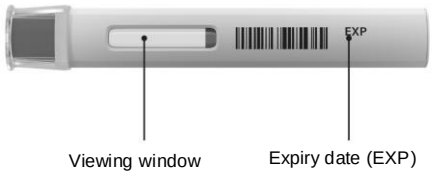
A new and unused Cosentyx UnoReady pen 300 mg.

Not included in the carton:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Before your injection:

Take the Cosentyx UnoReady pen 300 mg out of the refrigerator **30 to 45 minutes before injecting** to allow it to reach room temperature.



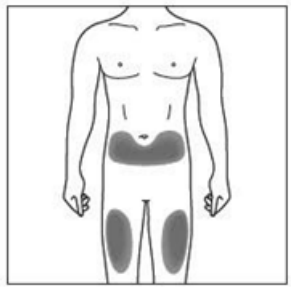
1. Important safety checks before you inject:

For the "Viewing window":
The liquid should be clear. Its colour may vary from colourless to slightly yellow.
Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. You may see a small air bubble, which is normal.

For the "Expiry date":
Look at the expiry date (EXP) on your Cosentyx UnoReady pen. **Do not use** the pen if the **expiry date** has passed.

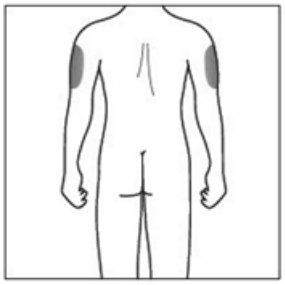
Check that your pen contains the correct medicine and dose.

Contact your pharmacist if the pen fails any of these checks.



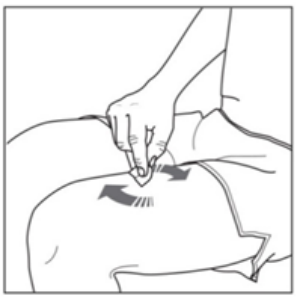
2a. Choose your injection site:

- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



2b. Caregivers and healthcare professionals only:

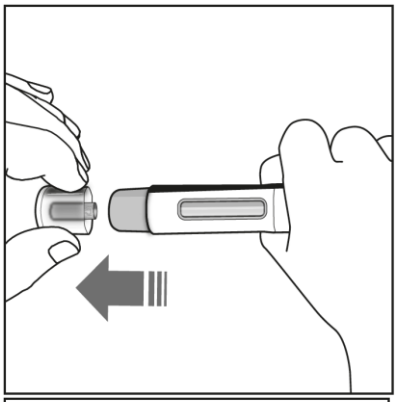
- If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your outer upper arm.



3. Cleaning your injection site:

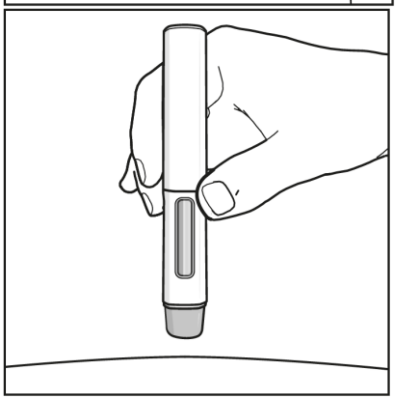
- Wash your hands with soap and hot water.
- Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting.
- Do not touch the cleaned area again before injecting.

Your injection:



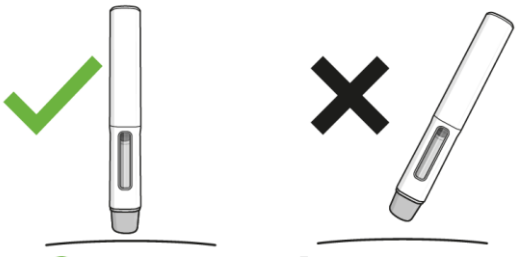
4. Removing the cap:

- Only remove the cap when you are ready to use the pen.
- Pull the cap straight off in the direction of the arrow that is shown in the figure on the left.
- Once removed, throw away the cap. Do not try to re-attach the cap.
- Use the pen within 5 minutes of removing the cap.



5. Holding your pen:

- Hold the pen at 90 degrees to the cleaned injection site.



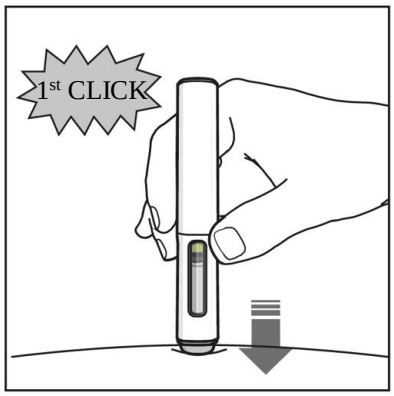
Correct **Incorrect**

YOU MUST READ THIS BEFORE INJECTING.

During the injection you will hear **2 clicks**.

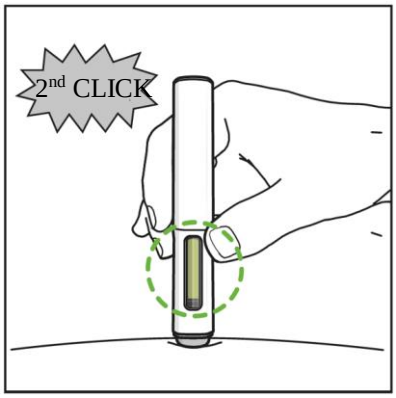
The **1st click** indicates that the injection has started. Several seconds later a **2nd click** will indicate that the injection is **almost** finished.

You must keep holding the pen firmly against your skin until you see a **green indicator with a grey tip** fill the window and stop moving.



6. Starting your injection:

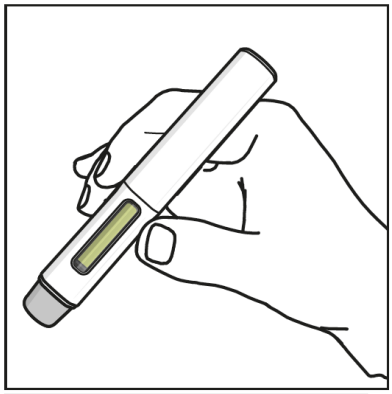
- Press the pen firmly against the skin to start the injection.
- The **1st click** indicates the injection has started.
- **Keep holding** the pen firmly against your skin.
  The **green indicator with the grey tip** shows the progress of the injection.



7. Completing your injection:

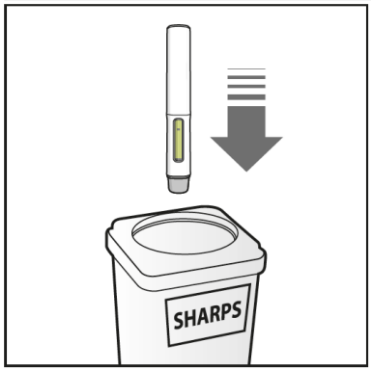
- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator with the grey tip** fills the window and has stopped moving.
- The pen can now be removed.

After your injection:



8. Check the green indicator fills the window:

- This means the medicine has been delivered. Contact your doctor if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.



9. Disposing of your Cosentyx UnoReady pen 300 mg:

- Dispose of the used pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar).
- Never try to reuse your pen.

1.7 同種同効品一覧表

本承認申請時点で，効能・効果，用法・用量，化学構造，薬理作用からみて本剤に類似していると考えられる同種同効品は存在しない。

1.8.1　添付文書（案）

最新の添付文書を参照する。

2020年XX月改訂（第1版、効能効果、用法用量変更）

ヒト型抗ヒトIL-17Aモノクローナル抗体製剤
セクキヌマブ(遺伝子組換え)注射剤

日本標準商品分類番号
8 7 3 9 9 9

貯法：2～8℃に保存
有効期間：24ヵ月

コセンティクス®皮下注 150mg ペン
コセンティクス®皮下注 75mg シリンジ
コセンティクス®皮下注 150mg シリンジ

Cosentyx® for s.c. injection 150mg pen
Cosentyx® for s.c. injection 75mg syringe
Cosentyx® for s.c. injection 150mg syringe

	ペン	シリンジ
承認番号	22800AMX 00672000	22600AMX 01396000
販売開始	2016年11月	2015年2月

生物由来製品、劇薬、処方箋医薬品
（注意－医師等の処方箋により使用すること）

NOVARTIS

1. 警告
1.1 本剤は結核等の感染症を含む緊急時に十分に対応できる医療施設において、本剤についての十分な知識と適応疾患の治療に十分な知識・経験をもつ医師のもとで、本剤による治療の有益性が危険性を上回ると判断される症例のみに使用すること。
本剤は感染のリスクを増大させる可能性があり、また結核の既往歴を有する患者では結核を活動化させる可能性がある。また、本剤との関連性は明らかではないが、悪性腫瘍の発現が報告されている。治療開始に先立ち、本剤が疾病を完治させる薬剤でないことも含め、本剤の有効性及び危険性を患者に十分説明し、患者が理解したことを確認した上で治療を開始すること。［8.1-8.3、9.1.1、9.1.2、15.1.3参照］
1.2 重篤な感染症
ウイルス、細菌及び真菌等による重篤な感染症が報告されているため、十分な観察を行うなど感染症の発症に注意し、本剤投与後に感染の徴候又は症状があらわれた場合には、直ちに主治医に連絡するよう患者を指導すること。［8.1、8.2、9.1.1、9.1.2、11.1.1参照］
1.3 本剤の治療を開始する前に、適応疾患の既存治療の適用を十分に勘案すること。［5.1-5.3参照］

2. 禁忌（次の患者には投与しないこと）
2.1 重篤な感染症の患者［症状を悪化させるおそれがある。］［9.1.1参照］
2.2 活動性結核の患者［症状を悪化させるおそれがある。］［9.1.2参照］
2.3 本剤の成分に対し過敏症の既往歴のある患者

3. 組成・性状
3.1 組成

販売名	コセンティクス皮下注150mgペン コセンティクス皮下注150mgシリンジ	コセンティクス皮下注75mgシリンジ
有効成分（1シリンジ中）	セクキヌマブ（遺伝子組換え）150.0mg	セクキヌマブ（遺伝子組換え）75.0mg
添加剤（1シリンジ中）	トレハロース水和物 75.67mg L-ヒスチジン・L-ヒスチジン塩酸塩水和物 3.103mg注) L-メチオニン 0.746mg ポリソルベート80 0.200mg	トレハロース水和物 37.83mg L-ヒスチジン・L-ヒスチジン塩酸塩水和物 1.552mg注) L-メチオニン 0.373mg ポリソルベート80 0.100mg

本剤の有効成分であるセクキヌマブ(遺伝子組換え)は、チャイニーズハムスター卵巣細胞から産生されるヒト型モノクローナル抗体である。
注）L-ヒスチジンとL-ヒスチジン塩酸塩水和物の合計量を、L-ヒスチジンの量として示す。

3.2 製剤の性状

販売名	コセンティクス皮下注150mgペン	コセンティクス皮下注150mgシリンジ	コセンティクス皮下注75mgシリンジ
性状	無色～微黄色の澄明又は混濁した液		
pH	5.5～6.1		
浸透圧	300～400mOsm/kg		

4. 効能又は効果
既存治療で効果不十分な下記疾患
尋常性乾癬、関節症性乾癬、膿疱性乾癬、強直性脊椎炎、X線基準を満たさない体軸性脊椎関節炎

5. 効能又は効果に関連する注意
〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉
5.1 以下のいずれかを満たす患者に投与すること。［1.3参照］
・ 紫外線療法を含む既存の全身療法（生物製剤を除く）で十分な効果が得られず、皮疹が体表面積の10%以上に及ぶ患者。
・難治性の皮疹、関節症状又は膿疱を有する患者。
〈強直性脊椎炎〉
5.2 過去の治療において、既存治療薬（非ステロイド性抗炎症薬等）による適切な治療を行っても、疾患に起因する明らかな臨床症状が残る場合に投与すること。［1.3参照］
〈X線基準を満たさない体軸性脊椎関節炎〉
5.3 過去の治療において、既存治療薬（非ステロイド性抗炎症薬等）による適切な治療を行っても、疾患に起因する明らかな臨床症状及び炎症の客観的徴候が認められる場合に投与すること。［1.3参照］

6. 用法及び用量
〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉
通常、成人にはセクキヌマブ(遺伝子組換え)として、1回300mgを、初回、1週後、2週後、3週後、4週後に皮下投与し、以降、4週間の間隔で皮下投与する。また、体重により、1回150mgを投与することができる。
通常、6歳以上の小児にはセクキヌマブ（遺伝子組換え）として、体重50kg未満の患者には1回75mgを、体重50kg以上の患者には1回150mgを、初回、1週後、2週後、3週後、4週後に皮下投与し、以降、4週間の間隔で皮下投与する。なお、体重50kg以上の患者では、状態に応じて1回300mgを投与することができる。

〈強直性脊椎炎、X線基準を満たさない体軸性脊椎関節炎〉
通常、成人にはセクキヌマブ（遺伝子組換え）として、1回150mgを、初回、1週後、2週後、3週後、4週後に皮下投与し、以降、4週間の間隔で皮下投与する。

7. 用法及び用量に関連する注意

〈効能共通〉

7.1 本剤と他の生物製剤の併用について安全性及び有効性は確立していないので併用を避けること。

7.2 本剤による治療反応は、通常投与開始から16週以内に得られる。16週以内に治療反応が得られない場合は、本剤の治療計画の継続を慎重に再考すること。

〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉

7.3 体重60kg以下の成人患者では1回150mgの投与を考慮すること。［17.1.2参照］

8. 重要な基本的注意

8.1 本剤は、感染のリスクを増大させる可能性がある。そのため本剤の投与に際しては、十分な観察を行い、感染症の発症や増悪に注意すること。感染の徴候又は症状があらわれた場合には、速やかに担当医に連絡するよう患者に指導すること。［1.1、1.2、9.1.1、11.1.1参照］

8.2 本剤投与に先立って結核に関する十分な問診及び胸部X線検査に加えインターフェロンγ遊離試験又はツベルクリン反応検査を行い、適宜胸部CT検査等を行うことにより、結核感染の有無を確認すること。

また、本剤投与中も、胸部X線（レントゲン）検査等の適切な検査を定期的に行うなど結核症の発現には十分に注意し、結核を疑う症状（持続する咳、体重減少、発熱等）が発現した場合には速やかに担当医に連絡するよう患者に指導すること。なお、結核の活動性が確認された場合は結核の治療を優先し、本剤を投与しないこと。［1.1、1.2、9.1.2、11.1.1参照］

8.3 臨床試験において皮膚及び皮膚以外の悪性腫瘍の発現が報告されている。本剤との因果関係は明確ではないが、悪性腫瘍の発現には注意すること。［1.1、15.1.3参照］

8.4 本剤投与中は、生ワクチン接種による感染症発現のリスクを否定できないため、生ワクチン接種は行わないこと。

8.5 他の生物製剤から変更する場合は感染症の徴候について患者の状態を十分に観察すること。

8.6 本剤の投与開始にあたっては、医療施設において、必ず医師によるか、医師の直接の監督のもとで投与を行うこと。自己投与の適用については、医師がその妥当性を慎重に検討し、十分な教育訓練を実施した後、本剤投与による危険性と対処法について患者が理解し、患者自ら確実に投与できることを確認した上で、医師の管理指導の下で実施すること。自己投与の適用後、感染症等の本剤による副作用が疑われる場合や自己投与の継続が困難な状況となる可能性がある場合には、直ちに自己投与を中止させ、医師の管理下で慎重に観察するなど適切な処置を行うこと。また、本剤投与後に副作用の発現が疑われる場合は、医療施設へ連絡するよう患者に指導を行うこと。使用済みの注射器を再使用しないように患者に注意を促し、すべての器具の安全な廃棄方法に関する指導を行うと同時に、使用済みの注射器を廃棄する容器を提供すること。

9. 特定の背景を有する患者に関する注意

9.1 合併症・既往歴等のある患者

9.1.1 感染症（重篤な感染症を除く）の患者又は感染症が疑われる患者

感染症が悪化するおそれがある。［1.1、1.2、2.1、8.1参照］

9.1.2 結核の既往歴を有する患者又は結核感染が疑われる患者

（1）結核の既往歴を有する患者では、結核を活動化させるおそれがある。［2.2、8.2参照］

（2）結核の既往歴を有する場合及び結核感染が疑われる場合には、結核の診療経験がある医師に相談すること。以下のいずれかの患者には、原則として抗結核薬を投与した上で、本剤を投与すること。［1.1、1.2、2.2、8.2参照］

・胸部画像検査で陳旧性結核に合致するか推定される陰影を有する患者

・結核の治療歴（肺外結核を含む）を有する患者

・インターフェロンγ遊離試験やツベルクリン反応検査等の検査により、既感染が強く疑われる患者

・結核患者との濃厚接触歴を有する患者

9.1.3 炎症性腸疾患の患者

炎症性腸疾患の患者に投与する場合は観察を十分に行うこと。症状を悪化させるおそれがある。活動期にあるクローン病の患者を対象とした海外臨床試験において、プラセボ群に比べて本剤群において活動期のクローン病の症状が悪化する傾向がみられている。［11.1.4参照］

9.1.4 ラテックス過敏症の既往歴又は可能性のある患者

アレルギー反応を起こすことがあるので注意すること。注射針部分のカバーは、乾燥天然ゴム（ラテックス類縁物質）を含む。

9.5 妊婦

妊婦又は妊娠している可能性のある女性には、治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。本剤はカニクイザルにおいて胎児への移行が報告されているが、胚・胎児毒性及び催奇形性は認められていない。

9.6 授乳婦

治療上の有益性及び母乳栄養の有益性を考慮し、授乳の継続又は中止を検討すること。本剤のヒトにおける乳汁への移行は不明であるが、本薬を投与した動物実験（マウス）で乳汁中に移行することが報告されている注)。

注）代替抗体を投与した動物実験（マウス）で出生児の血清中への移行を確認した。

9.7 小児等

〈尋常性乾癬、関節症性乾癬〉

9.7.1 低出生体重児、新生児、乳児又は6歳未満の幼児を対象とした臨床試験は実施していない。

〈膿疱性乾癬、強直性脊椎炎、X線基準を満たさない体軸性脊椎関節炎〉

9.7.2 小児等を対象とした臨床試験は実施していない。

9.8 高齢者

感染症等の副作用の発現に留意し、十分な観察を行うこと。一般に生理機能が低下している。

11. 副作用

次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止するなど適切な処置を行うこと。

11.1 重大な副作用

11.1.1 重篤な感染症（1.5%）

ウイルス、細菌あるいは真菌等による重篤な感染症があらわれることがある。［1.2、8.1、8.2参照］

11.1.2 過敏症反応

アナフィラキシー（頻度不明）、蕁麻疹（1.0%）等の過敏症反応があらわれることがある。

11.1.3 好中球数減少（0.5%）

11.1.4 炎症性腸疾患（0.5%）

［9.1.3参照］

11.1.5 紅皮症（剥脱性皮膚炎）（頻度不明）

11.2 その他の副作用

	1%以上	1%未満	頻度不明

感染症	上気道感染（上咽頭炎、上気道感染、鼻炎、咽頭炎、副鼻腔炎、扁桃炎）、カンジダ症	足部白癬、口腔ヘルペス	－
眼障害	－	－	結膜炎
呼吸器、胸郭及び縦隔障害	－	鼻漏	－
胃腸障害	－	下痢	－
皮膚及び皮下組織障害	蕁麻疹	－	－
肝胆道系障害	－	肝機能検査値異常	－
神経系障害	－	－	頭痛
全身障害及び投与部位様態	－	注射部位反応	－

14. 適用上の注意

14.1 薬剤投与前の注意

14.1.1 冷蔵庫から取り出し室温に戻しておくこと。

14.1.2 投与直前まで本剤の注射針のキャップを外さないこと。キャップを外したら直ちに投与すること。

14.2 薬剤投与時の注意

14.2.1 皮膚が敏感な部位、皮膚に異常のある部位（傷、発赤、鱗屑、硬結、瘢痕、皮膚線条等の部位）、乾癬の部位には注射しないこと。

14.2.2 投与部位は、大腿部、腹部又は上腕部が望ましい。同一箇所へ繰り返し注射することは避けること。

14.2.3 本剤は、1回使用の製剤であり、再使用しないこと。

15. その他の注意

15.1 臨床使用に基づく情報

〈効能共通〉

15.1.1 尋常性乾癬及び関節症性乾癬を対象とした国際共同及び海外第III相臨床試験で、52週までに19/3,364例（0.6%）の患者に抗セクキヌマブ抗体が認められ、うち3/3,364例（0.1%）の抗セクキヌマブ抗体は中和抗体であった（日本人では、1/148例（0.7%）に抗セクキヌマブ抗体が認められ、その1例の抗セクキヌマブ抗体は中和抗体であった）。日本人膿疱性乾癬患者を対象とした国内第III相試験においては、12例中抗セクキヌマブ抗体が認められた患者はいなかった。強直性脊椎炎患者を対象として日本で実施した非盲検試験及び海外第III相試験において、最長156週までに12/1,192例（1.0%）の患者に抗セクキヌマブ抗体が認められたが、中和抗体ではなかった。X線基準を満たさない体軸性脊椎関節炎を対象とした国際共同試験で、543例中抗セクキヌマブ抗体が認められた患者はいなかった。なお、抗体の発現と効果又は有害事象との関連は明らかではない。

15.1.2 本剤との因果関係は明確ではないが、国内の市販後において自殺既遂の死亡例が報告されている。

〈尋常性乾癬、関節症性乾癬〉

15.1.3 国際共同試験及び海外第III相臨床試験で、本剤300mgが投与された患者1,410例（52週時）について、悪性腫瘍（非黒色腫皮膚癌を除く、以下同様）の発現頻度は、0.34/100人年（4/1,410例）であり、その内容は表皮内悪性黒色腫、悪性黒色腫、腎癌、新生物であった。悪性腫瘍の発現頻度は、一般人口で予測される発現頻度と同様であった（標準化発生比：0.64［95%信頼区間：0.17，1.63］）。非黒色腫皮膚癌の発現頻度は、0.43/100人年（5/1,410例）であった。［1.1、8.3参照］

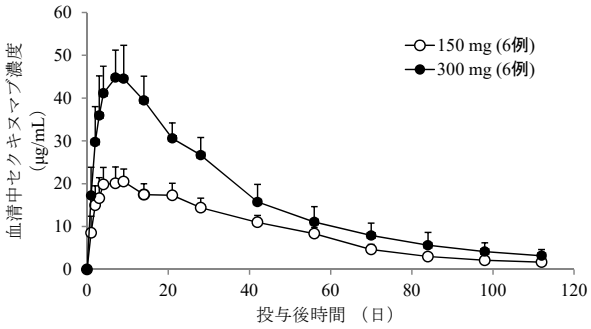
〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉

15.1.4 免疫抑制剤又は光線療法と併用した場合の安全性及び有効性は確立していない。

16. 薬物動態

16.1 血中濃度

日本人健康成人男子にセクキヌマブ（遺伝子組換え）150mg又は300mgを単回皮下投与したとき、血清中セクキヌマブ濃度は投与後8日目にCmaxを示し、消失半減期は26～30日であった。また、絶対バイオアベイラビリティは77%であった。



（平均値+標準偏差）

日本人健康成人男子にセクキヌマブ（遺伝子組換え）150mg又は300mgを単回皮下投与したときの血清中濃度推移

日本人健康成人男子にセクキヌマブ（遺伝子組換え）150mg又は300mgを単回皮下投与したときの薬物動態パラメータ（6例）

	150mg	300mg
Cmax（μg/mL）	21.1 ± 2.90	46.3 ± 7.63
AUC_{0-inf}（μg·day/mL）	1,070 ± 153	1,930 ± 408
Tmax（日）	8（4～21）	8（7～14）
T1/2（日）	30.0 ± 6.93	25.9 ± 5.09

平均値±標準偏差、Tmaxについては中央値（最小～最大）

日本人健康成人男子にセクキヌマブ（遺伝子組換え）1～10mg/kgを単回静脈内投与したときのクリアランスは0.114～0.121L/日、分布容積は4.23～5.34Lであった。

日本人乾癬患者にセクキヌマブ（遺伝子組換え）150mg又は300mgを週1回の頻度で4週間5回投与後、4週間隔で投与後48週目まで皮下投与した。投与後24週目及び52週目のセクキヌマブ（遺伝子組換え）投与前の血清中濃度（平均値±標準偏差）は、150mg群では16.7 ±6.18μg/mL（26例）及び17.3 ±7.65μg/mL（24例）、300mg群では30.9 ±12.4μg/mL（28例）及び31.9 ±9.53μg/mL（27例）であった。

母集団薬物動態解析より推定した日本人尋常性乾癬患者（平均体重：73.3kg）のクリアランスは0.181L/日、中央コンパートメントの分布容積は3.25L、末梢コンパートメントの分布容積は2.53Lであった[1)]。

日本人強直性脊椎炎患者にセクキヌマブ（遺伝子組換え）150mgを週1回の頻度で4週間5回投与後、4週間隔で投与後48週目まで皮下投与した。投与後24週目及び52週目のセクキヌマブ（遺伝子組換え）投与前の血清中濃度（平均値±標準偏差）は、20.9±7.07μg/mL（25例）及び19.9±5.25μg/mL（21例）であった。

日本人のX線基準を満たさない体軸性脊椎関節炎患者にセクキヌマブ（遺伝子組換え）150mgを週1回の頻度で4週間5回投与後、4

週間隔で投与後48週目まで皮下投与した。投与後52週目のセクキヌマブ（遺伝子組換え）投与前の血清中濃度は、12.5及び16.5μg/mL（2例）であった。

重症の小児尋常性乾癬及び関節症性乾癬患者（日本人及び外国人）にセクキヌマブ（遺伝子組換え）を体重に応じて週1回の頻度で4週間5回投与後、4週間隔で皮下投与した時の定常状態における投与前の血清中濃度を下表に示す。なお、日本人患者1例（体重25 kg以上 50 kg未満、150mg皮下投与）の24週目及び52週目における投与前の血清中濃度は、66.1 及び56.0μg/mLであった。

体重	投与量	24週	52週
25kg未満	75mg	24.1，34.6（2）	22.2（1）
25 kg以上50 kg未満	75mg	20.4±7.44（14）	18.7±8.18（14）
	150mg	30.6±16.4（10）	41.9±15.4（5）
50 kg以上	150mg	24.7±8.04（7）	26.1±8.87（8）
	300mg	71.8±24.6（6）	47.7±18.6（9）

μg/mL、平均値±標準偏差（例数）

中等症又は重症の小児尋常性乾癬及び関節症性乾癬患者（外国人）にセクキヌマブ（遺伝子組換え）を体重に応じて週1回の頻度で4週間5回投与後、4週間隔で皮下投与した時の定常状態における投与前の血清中濃度を下表に示す。

体重	投与量	24週	52週
25kg未満	75mg	33.6±12.2（6）	32.7±7.10（4）
25 kg以上50 kg未満	75mg	18.9±6.51（10）	22.0±7.05（10）
	150mg	32.9±19.1（9）	28.4±16.7（8）
50 kg以上	150mg	28.0±10.6（29）	25.6±9.52（24）
	300mg	52.7±22.2（27）	48.9±15.8（24）

μg/mL、平均値±標準偏差（例数）

17. 臨床成績

17.1 有効性及び安全性に関する試験

＜尋常性乾癬及び関節症性乾癬＞

17.1.1 国際共同第III相試験（A2302試験）

中等症又は重症の局面型皮疹を有する尋常性乾癬及び関節症性乾癬患者737例（日本人87例含む）（局面型皮疹の病変が体表面積（BSA）の10%以上、かつPASI[注1)]スコアが12以上）を対象とした52週間プラセボ対照ランダム化二重盲検並行群間比較試験を実施した。

プラセボ又はセクキヌマブ(遺伝子組換え)150mg又は300mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。12週後のPASIスコアがベースラインから75%以上又は90%以上改善した患者の割合（以下、それぞれPASI75反応率又はPASI90反応率）を次表に示す。本剤投与群における12週後のPASI75反応率は、プラセボ群に比べて有意に高かった。その後、52週目までほぼ一定の値で推移した[2)]。

注1）Psoriasis Area and Severity Index

		300mg	150mg	プラセボ	群間差［95%信頼区間］、p値※	
					300mg	150mg
全体集団	PASI 75	81.6%（200/245例）	71.6%（174/243例）	4.5%（11/246例）	77.2［70.9，82.4］p<0.0001	67.1［60.1，73.3］p<0.0001
	PASI 90	59.2%（145/245例）	39.1%（95/243例）	1.2%（3/246例）	58.0［50.3，64.7］p<0.0001	37.9［29.4，46.0］p<0.0001
日本人集団	PASI 75	82.8%（24/29例）	86.2%（25/29例）	6.9%（2/29例）	75.9［53.4，90.0］	79.3［57.7，92.2］
	PASI 90	62.1%（18/29例）	55.2%（16/29例）	0%（0/29例）	62.1［37.2，80.3］	55.2［29.5，75.0］

評価対象例数は脱落例及び中止例を含み、非反応として集計。

※地域及び体重（90kg未満又は90kg以上）を層としたCochran-Mantel-Haenszel検定

60週時点での副作用発現頻度は、本剤150mg投与群で32.2%（79/245例）及び本剤300mg投与群で27.3%（67/245例）であった。主な副作用は、本剤150mg投与群では鼻咽頭炎4.1%（10/245例）、上気道感染3.7%（9/245例）、本剤300mg投与群では上気道感染2.9%（7/245例）、そう痒症2.9%（7/245例）であった。

17.1.2 国際共同第 III 相試験（体重別：A2302、A2303、A2308 及び A2309 試験の併合）

中等症又は重症の局面型皮疹を有する尋常性乾癬及び関節症性乾癬患者を対象とした臨床試験の体重別の12週後のPASI75反応率又はPASI90反応率を次表に示す。［7.3参照］

	体重	全体集団			
		300mg		150mg	
PASI 75	80 kg 超	75.7 %（289/382例）		66.3 %（258/389例）	
	70～80 kg	84.9 %（107/126例）		73.3 %（96/131例）	
	60～70 kg	87.9 %（102/116例）		69.2 %（63/91例）	
	60 kg 以下	75.8 %（47/62例）		76.9 %（60/78例）	
PASI 90	80 kg 超	45.8 %（175/382例）		35.7 %（139/389例）	
	70～80 kg	69.0 %（87/126例）		42.0 %（55/131例）	
	60～70 kg	75.9 %（88/116例）		48.4 %（44/91例）	
	60 kg 以下	61.3 %（38/62例）		57.7 %（45/78例）	

評価対象例数は脱落例及び中止例を含み、非反応として集計。

17.1.3 国際共同第III相試験（小児：A2310試験）

重症の局面型皮疹を有する6歳以上18歳未満の小児の尋常性乾癬及び関節症性乾癬患者162例（日本人5例含む）（局面型皮疹の病変が体表面積（BSA）の10%以上、かつPASIスコアが20以上）を対象としたプラセボ及び実薬対照ランダム化二重盲検並行群間比較試験を実施した。

プラセボ又はセクキヌマブ(遺伝子組換え)を体重25kg未満の場合は低用量群及び高用量群ともに75mg、25kg以上50kg未満の場合は低用量群は75mg、高用量群は150mg、体重50kg以上の場合は低用量群は150mg、高用量群は300mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。12週後のPASI75反応率、IGAスコアの0又は1への改善率及びPASI90反応率を次表に示す。本剤投与群における12週後のPASI75反応率及びIGAスコアの0又は1への改善率は、いずれもプラセボ群に比べて有意に高かった。その後、PASI75反応率、IGAスコアの0又は1への改善率及びPASI90反応率は、52週目までほぼ一定の値で推移した。

		低用量群	高用量群	プラセボ	プラセボに対するオッズ比[95%信頼区間]、p値※	
					低用量群	高用量群
全体集団	PASI 75	80.1%	80.2%	14.9%	25.97 [7.31,92.22] p<0.0001	26.55 [7.57,93.09] p<0.0001
	PASI 90	71.1%	69.3%	2.5%	121.86 [14.23,1043.28]	110.14 [12.98,934.72]
	IGA0/1	69.8%	62.6%	6.3%	40.39 [8.37, 194.87] p<0.0001	28.35 [6.00, 133.92] p<0.0001

欠測値の取り扱いとして多重補完法を用いたため、反応が得られた被験者数は提示していない。

※投与群、ベースライン時の体重（25kg未満、25kg以上50kg未満、50kg以上）及び年齢（12歳未満、12歳以上）を説明変数とした正確なロジスティック回帰モデル

有意水準片側1.25%、試験全体の有意水準は片側2.5%とし、Bonferroniの方法を用いて低用量群とプラセボ群の比較、高用量群とプラセボ群の比較にそれぞれ1.25%ずつ配分することで、仮説検定の多重性を調整した。

52週時点での副作用発現頻度は、低用量群で27.5%（11/40例）及び高用量群で32.5%（13/40例）であった。主な副作用は、低用量群では上咽頭炎7.5%（3/40例）、上気道感染5.0%（2/40例）、扁桃炎5.0%（2/40例）、注射部位疼痛5.0%（2/40例）、高用量群では上咽頭炎7.5%（3/40例）、咽頭炎5.0%（2/40例）、注射部位紅斑5.0%（2/40例）、咳嗽5.0%（2/40例）であった[3)]。

17.1.4 海外第III相試験（小児：A2311試験）

中等症又は重症の局面型皮疹を有する6歳以上18歳未満の小児の尋常性乾癬及び関節症性乾癬患者84例（局面型皮疹の病変が体表面積（BSA）の10%以上、かつPASIスコアが12以上）を対象としたランダム化非盲検試験を実施した。

セクキヌマブ（遺伝子組換え）を体重25kg未満の場合は低用量群及び高用量群ともに75mg、25kg以上50kg未満の場合は低用量群は75mg、高用量群は150mg、体重50kg以上の場合は低用量群は150mg、高用量群は300mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。本剤投与12週後のPASI75反応率は、低用量群、高用量群のいずれも92.9%（39/42名）であり、IGAスコアの0又は1への改善率は、低用量群で78.6%（33/42例）、高用量群で83.3%（35/42例）であった。また、12週後のPASI90反応率は、低用量群で69.0%（29/42例）、高用量群で76.2%（32/42例）であった。その後、PASI75反応率、IGAスコアの0又は1への改善率及びPASI90反応率は、52週目までほぼ一定の値で推移した。

本剤投与52週時点での副作用発現頻度は、低用量群で14.3%（6/42例）及び高用量群で23.8%（10/42例）であった。主な副作用は、低用量群では白血球減少症7.1%（3/42例）、好中球減少症4.8%（2/42例）、高用量群では上気道感染4.8%（2/42例）であった[4)]。

＜膿疱性乾癬＞

17.1.5 国内第III相試験（A1302試験）

日本人汎発型膿疱性乾癬患者12例（膿疱を伴う紅斑面積が総体表面積の10%以上を占める患者）を対象とした非盲検試験を実施した。

セクキヌマブ（遺伝子組換え）150mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。8週目以降はあらかじめ規定された基準に応じて300mgへの増量を可とした。16週後において、83.3%（10/12例）で奏功[注2)]が認められた（著明改善9例、中等度改善1例）[5)]。

注2）著明改善、中等度改善、又は軽度改善と判断された被験者と定義

52週時点での副作用発現頻度は、本剤投与群で33.3%（4/12例）であった。副作用は、薬物性肝障害、肝機能異常、上室性不整脈、紅色陰癬、灼熱感、腎機能障害が各8.3%(1/12例)であった。

<関節症性乾癬>

17.1.6 海外第III相試験（F2312試験）

非ステロイド性抗炎症薬、疾患修飾性抗リウマチ薬（DMARD）又は抗TNFα製剤による治療で効果不十分もしくは忍容性不良の活動性関節症性乾癬患者397例（腫脹関節及び圧痛関節数がそれぞれ3関節以上）を対象としたプラセボ対照ランダム化二重盲検並行群間比較試験を実施した。プラセボ又はセクキヌマブ(遺伝子組換え)75mg*、150mg又は300mgを0、1、2、3、4週に皮下投与し、その後4週間隔でプラセボ又は75mg、150mg又は300mgを皮下投与した。患者の約35%（139/397例）は抗TNFα製剤治療による効果不十分例であり、約45%（185/397例）はメトトレキサートを併用していた。本剤（75mg群、150mg群、300mg群）の24週後のACR20反応率はプラセボ群に比較して有意に高かった。

300mg	150mg	75mg	プラセボ	群間差[95%信頼区間]、p値※		
				300mg	150mg	75mg
54.0% (54/100例)	51.0% (51/100例)	29.3% (29/99例)	15.3% (15/98例)	38.7% [26.6, 50.8] p<0.0001	35.7% [23.6, 47.8] p<0.0001	14.0% [2.5, 25.4] p=0.0200

※投与群、抗TNFα製剤による治療経験の有無及び体重を説明変数としたlogistic回帰モデル

24週時点での副作用発現頻度は、本剤75mg投与群で24.2%（24/99例）、本剤150mg投与群で17.5%（25/143例）及び本剤300mg投与群で29.0%（42/145例）であった。主な副作用は、本剤75mg投与群では上気道感染7.1%（7/99例）、本剤150mg投与群では鼻咽頭炎2.8%（4/143例）、上気道感染2.1%（3/143例）、本剤300mg投与群では上気道感染4.8%（7/145例）、鼻咽頭炎3.4%（5/145例）であった。

17.1.7 海外第III相試験（F2306試験）

非ステロイド性抗炎症薬、DMARD又は抗TNFα製剤による治療で効果不十分もしくは忍容性不良の活動性関節症性乾癬患者606例（腫脹関節及び圧痛関節数がそれぞれ3関節以上）を対象としたプラセボ対照ランダム化二重盲検並行群間比較試験を実施した。プラセボ又はセクキヌマブ(遺伝子組換え)10mg/kgを0、2、4週に静脈内投与し、その後4週間隔で75mg（IV-75mg群）*、150mg（IV-150mg群）又はプラセボを皮下投与した。患者の約30%（178/606例）は抗TNFα製剤治療による効果不十分例であり、約60%（368/606例）はメトトレキサートを併用していた。本剤（IV-75mg群及びIV-150mg群）の24週後のACR20反応率はプラセボ群に比較して有意に高かった。

150mg	75mg	プラセボ	群間差[95%信頼区間]、p値※	
			150mg	75mg
50.0% (101/202例)	50.5% (102/202例)	17.3% (35/202例)	32.7[24.0, 41.3] p<0.0001	33.2 [24.5, 41.8] p<0.0001

※投与群、抗TNFα製剤による治療経験の有無及び体重を説明変数としたlogistic回帰モデル

また、24週後の関節破壊進展を手及び足のX線スコア（modified Total Sharp Score：mTSS）で評価した結果、セクキヌマブ(遺伝子組換え)投与群（IV-75mg群及びIV-150mg群）のベースラインからの変化量はプラセボ群に比べて有意に小さかった。

	150mg	75mg	プラセボ
ベースライン	22.3±48.0 (185)	20.4±39.4 (181)	28.5±63.5 (179)
投与24週後	22.40± 48.01(185)	20.42±39.63 (181)	29.03±63.90 (179)
変化量	0.13±1.18 (185)	0.02±1.60 (181)	0.57±2.48 (179)
プラセボ群との差[95%信頼区間]、p値※	-0.47 [-0.87, -0.07] p=0.0212	-0.54 [-0.96, -0.11] p=0.0132	
併合群のプラセボ群との差[95%信頼区間]、p値※	-0.50 [-0.89, -0.11] p=0.0113		

※投与群及び抗TNFα製剤による治療経験の有無、体重、ベースライン値を説明変数としたノンパラメトリック共分散分析モデル

52週時点での副作用発現頻度は、本剤75mg投与群で30.5%（89/292例）及び本剤150mg投与群で38.6%（114/295例）であった。主な副作用は、本剤75mg投与群では上気道感染6.5%（19/292例）、鼻咽頭炎3.8%（11/292例）、本剤150mg投与群では上気道感染7.8%（23/295例）、鼻咽頭炎3.7%（11/295例）であった。

〈強直性脊椎炎〉

17.1.8 海外第III相試験（F2310試験）

非ステロイド性抗炎症薬による治療で効果不十分又は忍容不良な強直性脊椎炎患者219例（BASDAI[注4)]総スコアが4以上かつBASDAIの脊椎痛VAS[注5)]が4cm以上）を対象としたプラセボ対照ランダム化二重盲検並行群間比較試験を実施した。プラセボ又はセクキヌマブ（遺伝子組換え）75mg*又は150mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。150mg群の16週後のASAS[注6)]20反応率はプラセボ群に比べて有意に高かった。

注4）Bath Ankylosing Spondylitis Disease Activity Index

注5）Visual Analogue Scale

注6）Assessment of SpondyloArthritis international Society

	150mg	プラセボ	オッズ比 [95%信頼区間] p値※
ASAS 20	61.1% (44/72例)	28.4% (21/74例)	4.38 [2.14,8.96] p<0.0001
ASAS 40	36.1% (26/72例)	10.8% (8/74例)	5.07 [2.06,12.44]

※ 投与群、抗TNFα製剤による治療経験の有無（全体集団のみ）及び体重を説明変数としたlogistic回帰モデル

156週での副作用発現頻度は、本剤75mg投与群で41.0%（43/105例）、本剤150mg投与群で45.9%（51/111例）であった。主な副作用は、本剤75mg投与群では上気道感染7.6%（8/105例）、鼻咽頭炎4.8%（5/105例）、下痢、気管支炎及びインフルエンザ3.8%（4/105例）、本剤150mg投与群では上気道感染及び鼻咽頭炎6.3%（7/111例）、インフルエンザ4.5%（5/111例）であった。

17.1.9 国内第III相試験（H1301試験）

非ステロイド性抗炎症薬による治療で効果不十分又は忍容不良な強直性脊椎炎患者30例（BASDAI総スコアが4以上かつBASDAIの脊椎痛VASが4cm以上）を対象とした非盲検試験を実施した。セクキヌマブ（遺伝子組換え）150mgを0、1、2、3及び4週、その後4週間隔で皮下投与した。16週後のASAS20反応率は70.0%（21/30例）、ASAS40反応率は46.7%（14/30例）であり、52週目までほぼ一定の値で推移した。

52週での副作用発現頻度は、本剤投与群で46.7%（14/30例）であった。主な副作用は、上咽頭炎7例（23.3%）、口内炎4例（13.3%）等であった[6)]。

〈X線基準を満たさない体軸性脊椎関節炎〉

17.1.10 国際共同第III相試験（H2315試験）

非ステロイド性抗炎症薬による治療で効果不十分又は忍容不良なX線基準を満たさない体軸性脊椎関節炎患者555例（BASDAI総スコアが4以上、BASDAIの脊椎痛VASが4cm以上、かつCRP高値（基準値超）又はMRI画像所見上の仙腸関節炎が認められる）を対象としたプラセボ対照ランダム化二重盲検比較試験を実施した。プラセボ又はセクキヌマブ（遺伝子組換え）150mgを0、1、2、3及び4週、その後4週間隔で皮下投与（プラセボ、導入投与）又は150mgを4週間隔[注7)]で皮下投与（非導入投与*）した。主要な解析対象集団である抗TNFα製剤未治療患者において、主要評価項目である16週後のASAS40反応率は、本剤導入投与群でプラセボ群に比べて有意に高かった。

注7）1、2及び3週後にプラセボを皮下投与

	150 mg 導入投与あり	プラセボ	オッズ比 [95%信頼区間] p値※
抗TNFα製剤未治療患者集団 ASAS 40	41.5% (68/164例)	29.2% (50/171例)	1.72 [1.09,2.70] p=0.0197
全体集団 ASAS 40	40.0% (74/185例)	28.0% (52/186例)	1.77 [1.14,2.74] p=0.0197

※ 投与群、CRP基準値超又は以下（CRP+/-）及びMRI画像所見による仙腸関節炎の有無（MRI+/-）に基づく層別因子（CRP+かつMRI+、CRP+かつMRI-、CRP-かつMRI+）、抗TNFα製剤による治療経験の有無（全体集団での解析のみ）及び体重を説明変数としたlogistic回帰モデル

52週での副作用発現頻度は、本剤導入投与群で44.9%（83/185例）であった。主な副作用は、本剤導入投与群で上咽頭炎9.2%（17/185例）、上気道感染及び尿路感染4.9%（9/185例）、頭痛3.2%（6/185例）であった[7)]。

#本剤の尋常性乾癬、関節症性乾癬、膿疱性乾癬における承認用法及び用量は、「通常、成人にはセクキヌマブ（遺伝子組換え）として、1回300mgを、初回、1週後、2週後、3週後、4週後に皮下投与し、以降、4週間の間隔で皮下投与する。また、体重により、1回150mgを投与することができる。」である。
また、本剤の強直性脊椎炎、X線基準を満たさない体軸性脊椎関節炎における承認用法及び用量は、「通常、成人にはセクキヌマブ（遺伝子組換え）として、1回150mgを、初回、1週後、2週後、3週後、4週後に皮下投与し、以降、4週間の間隔で皮下投与する。」である。

18. 薬効薬理

18.1 作用機序

セクキヌマブは、ヒト抗ヒトIL-17Aモノクローナル抗体であり、炎症性サイトカインであるIL-17Aと結合し、IL-17AのIL-17受容体への結合を阻害することにより、その活性を中和する。

18.2 *In vitro*における薬理活性

セクキヌマブは、選択的にヒトIL-17Aに結合し（解離定数：約200pM）、ヒト線維芽細胞様滑膜細胞[8]及びヒト皮膚線維芽細胞[9]において、ヒトIL-17Aにより誘導したIL-6産生作用を中和した。

18.3 *In vivo*における薬理活性

セクキヌマブは、ヒト遺伝子組換えIL-17Aにより誘発した関節炎モデルマウスにおいて、関節炎を誘発する24時間前及び2時間前にセクキヌマブを腹腔内投与することにより、関節の腫脹及び軟骨に対する作用を完全に抑制した[10]。また、ヒト遺伝子組換えIL-17Aで誘発されるマウス空気嚢への好中球浸潤を、好中球浸潤誘発前にセクキヌマブを単回腹腔内投与することにより、用量依存的に抑制した[11]。

19. 有効成分に関する理化学的知見

一般的名称：セクキヌマブ（遺伝子組換え）（Secukinumab（Genetical Recombination））

分子量：約151,000

本　質：ヒトインターロイキン-17Aに対する遺伝子組換えヒトIgG1モノクローナル抗体であり、チャイニーズハムスター卵巣細胞により産生される457個のアミノ酸残基からなる重鎖（$C_{2268}H_{3477}N_{597}O_{686}S_{16}$：分子量：50,595.50）2分子及び215個のアミノ酸残基からなる軽鎖（$C_{1024}H_{1594}N_{280}O_{335}S_{6}$：23,379.68）2分子で構成される糖タンパク質

20. 取扱い上の注意

20.1 室温で保存する場合は、30℃を超えない場所で保存し、4日以内に使用すること。

20.2 外箱開封後は遮光して保存すること。

21. 承認条件

21.1 医薬品リスク管理計画を策定の上、適切に実施すること。

21.2 感染症等の発現を含めた長期投与時の安全性及び有効性について十分な検討が必要であることから、適切な製造販売後調査を実施すること。

22. 包装

〈コセンティクス皮下注150mgペン〉

1本

〈コセンティクス皮下注75mgシリンジ〉

1シリンジ

〈コセンティクス皮下注150mgシリンジ〉

1シリンジ

23. 主要文献

1） 社内資料：乾癬患者を対象とした母集団薬物動態解析（2014年12月26日承認、CTD2.7.2-2.4）[20145119]

2） Ohtsuki, M. et al.: J. Dermatol. 2014; 41 (12), 1039-1046 [20145357]

3） 社内資料：重症の局面型皮疹を有する小児乾癬患者を対象とした国際共同第Ⅲ相試験（A2310試験）（CTD2.7.3-3.3.3, CTD2.7.6-4.1） [XXXXXXXX]

4） 社内資料：中等症又は重症の局面型皮疹を有する小児乾癬患者を対象とした海外第Ⅲ相試験（A2311試験）（CTD2.7.6-4.1）[XXXXXXXX]

5） Imafuku, S. et al.: J. Dermatol. 2016; 43(9), 1011-1017 [20160759]

6） 社内資料：活動性強直性脊椎炎患者を対象としたセクキヌマブ国内第Ⅲ相試験（H1301試験）（2018年12月21日承認、CTD2.7.6-4.2.1） [20180629]

7） 社内資料：X線基準を満たさない体軸性脊椎関節炎患者を対象としたセクキヌマブ国際共同第Ⅲ相試験（H2315試験）（CTD2.7.6-4.1.1） [20200390]

8） 社内資料：ヒト線維芽細胞様滑膜細胞におけるIL-6産生に対するセクキヌマブの中和作用（2014年12月26日承認、CTD2.6.2-2.3.1）[20145120]

9） 社内資料：ヒト皮膚線維芽細胞におけるIL-6産生に対するセクキヌマブの中和作用（2014年12月26日承認、CTD2.6.2-2.3.3）[20145121]

10） 社内資料：ヒトIL-17A産生細胞の注入によるマウス膝関節腫脹に対するセクキヌマブの抑制作用（2014年12月26日承認、CTD2.6.2-2.4.1）[20145122]

11） 社内資料：ヒトIL-17A産生細胞誘発によるマウス空気嚢への好中球遊走に対するセクキヌマブの抑制作用（2014年12月26日承認、CTD2.6.2-2.4.2）[20145123]

24. 文献請求先及び問い合わせ先

ノバルティスファーマ株式会社　ノバルティスダイレクト

〒105-6333　東京都港区虎ノ門1-23-1

マルホ株式会社　製品情報センター

〒531-0071 大阪市北区中津1-11-1

26. 製造販売業者等

26.1 製造販売（輸入）

ノバルティスファーマ株式会社

東京都港区虎ノ門1-23-1

26.2 販売

マルホ株式会社

大阪市北区中津1-5-22

1.8.2 効能・効果（案），用法・用量（案）及び その設定根拠

目　　次

略号一覧

略号	略していない表現（英）	略していない表現（日）
CDLQI	Children's Dermatology Life Quality Index	―
CHAQ	Childhood Health Assessment Questionnaire	―
GPP	generalized pustular psoriasis	膿疱性乾癬
IGA	Investigator’s Global Assessment	治験責任医師の総合評価
PASI	psoriasis area and severity index	―
PK	pharmacokinetics	薬物動態（学）
PsA	psoriatic arthritis	関節症性乾癬
PsO	psoriasis vulgaris	尋常性乾癬
QOL	quality of life	生活の質

用語の定義一覧

用語	定義
投与群の表記	投与群名を，本文中では以下のように表記した。 • AIN 低用量群（AIN457 Low dose）：ランダム化時にセクキヌマブ低用量群に割り付けられた被験者 • AIN 高用量群（AIN457 High dose）：ランダム化時にセクキヌマブ高用量群に割り付けられた被験者 • エタネルセプト群（Etanercept）：エタネルセプト群に割り付けられた被験者 • プラセボ群（Placebo）：プラセボ群に割り付けられた被験者
試験の表記	各臨床試験は治験実施計画書番号の下 5 字で示した。 • 例）CAIN457A2310 試験→A2310 試験

1 用法及び用量及びその設定根拠

1.1 用法及び用量

〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉
通常、成人にはセクキヌマブ（遺伝子組換え）として、1回300 mgを、初回、1週後、2週後、3 週後、4 週後に皮下投与し、以降、4 週間の間隔で皮下投与する。また、体重により、1 回 150 mg を投与することができる。
通常、6歳以上の小児にはセクキヌマブ（遺伝子組換え）として、体重50 kg未満の患者には1回 75 mg を、体重 50 kg 以上の患者には 1 回 150 mg を、初回、1 週後、2 週後、3 週後、4 週後に皮下投与し、以降、4週間の間隔で皮下投与する。なお、体重50 kg以上の患者では、状態に応じて 1 回 300 mg を投与することができる。
〈強直性脊椎炎、X 線基準を満たさない体軸性脊椎関節炎〉
通常、成人にはセクキヌマブ（遺伝子組換え）として、1回150 mgを、初回、1週後、2週後、3 週後、4 週後に皮下投与し、以降、4 週間の間隔で皮下投与する。
（下線部：追記箇所）

1.2 用法及び用量の設定根拠

本剤は小児に対する尋常性乾癬（PsO），関節症性乾癬（PsA）及び膿疱性乾癬（GPP）の用法及び用量を追加する予定である。小児の用法・用量は，局面型皮疹を有する小児乾癬患者を対象とした国際共同第 III 相試験 A2310 試験及び A2311 試験の結果を主な根拠として設定した。GPP の用法及び用量の設定については，成人と小児の GPP の病態が大きく異ならないと考えられることから，局面型皮疹を有する小児乾癬患者を対象とした臨床試験成績の他，成人 GPP の臨床試験成績も踏まえて設定した。

A2310 試験，A2311 試験で，主要評価項目（co-primary）とした PASI 75 反応率及び IGA スコアの 0 又は 1 への改善率は，プラセボ及びヒストリカルプラセボと比較して，AIN 低用量及び AIN 高用量で有意に高く，また，AIN 群はエタネルセプト群に比べて反応率及び改善率が高かった。セクキヌマブの優れた皮膚症状改善効果が示された。A2310 試験で，セクキヌマブ投与後早期（Week 2）から効果発現が認められ，PASI 反応率及び IGA スコアの 0 又は 1 への改善率は，その後 Week 24 まで経時的に上昇し，Week 52 まで長期にわたり持続した。A2311 試験でも同様にセクキヌマブの投与開始後早期（Week 2）から効果発現が認められ，Week 52 まで持続した。

また，A2310 試験では，CDLQI 総スコアの 0 又は 1 への改善率は，12 週間の導入投与期を通してプラセボ群及びエタネルセプト群と比べて AIN 低用量群，AIN 高用量群で高かった。Week 52 まで，CDLQI 総スコアの 0 又は 1 への改善率はエタネルセプト群と比べて AIN 低用量群，AIN 高用量群で高く，QOL の改善は長期にわたり維持された。A2311 試験では，CDLQI 総スコアの 0 又

は 1 への改善率は，AIN 低用量群，AIN 高用量群ともに投与後経時的に上昇し，Week 52 では両群で同程度であった。

さらに，A2310 試験に組み入れられた PsA 患者を対象に，CHAQ スコアを用いて関節症状を含む全身状態を評価した結果，AIN 低用量群の被験者で CHAQ スコアのベースラインから低下（改善）がみられ，Week 52 まで維持された。[2.5-6.2 項] 。

それから，膿疱性乾癬（汎発型）診療ガイドライン（Fujita et al. 2018）では小児汎発性 GPP を GPP（汎発型）に包括し得る疾患としており，成人と小児での病態は大きく異ならないと考えられる。成人の GPP 患者の用法・用量は，成人の PsO と同じ用法・用量で承認されている。日本人の成人 GPP 患者と日本人及び外国人の成人 PsO 患者の患者間で PK に違いはないと考えられ，また，小児及び成人の PsO 及び PsA 患者において曝露量と PASI 反応率の関係は概ね同様であった。さらに，セクキヌマブの曝露が高いほど PASI を指標とした皮疹の改善効果が高いことは GPP でも PsO と同様であると考えられる。これらのことから，上記の推奨用量を投与した時の小児 GPP 患者での有効性は，小児の PsO 及び PsA 患者と同様となると期待できる [2.5-6.4 項] 。

一方，中等症又は重症の小児 PsO 及び PsA 患者の安全性プロファイルは，成人患者と同様であり，セクキヌマブの新たなリスクは特定されなかった。小児併合集団の有害事象発現率は，試験期間を通してエタネルセプト群と比べて Any AIN 群で低かった。主にみられた有害事象の上咽頭炎，頭痛，咽頭炎は，用量依存的な発現率の増加はみられなかった。有害事象の重症度はほとんどが軽度又は中等度であり，重篤又は投与中止を要する事象は少なく，本剤投与の忍容性は良好であった。また，投与期間の延長に伴い発現率が上昇する事象はみられなかった。Week 52 までを通して，小児併合集団と成人併合集団の有害事象及び重篤な有害事象の発現率は，中等症小児で中等症成人に比べて低く，重症小児と重症成人と同程度であった [2.5-6.3 項] 。

以上より，セクキヌマブの低用量と高用量を投与したときの有効性及び安全性は同様であり，セクキヌマブ低用量は中等症又は重症の小児乾癬患者に対し臨床的なベネフィットを示すと考えられる。ただし，体重 25 kg 以上の患者では低用量（75 mg 又は 150 mg）で治療を開始し，個々の患者で十分な臨床的改善が認められない場合は，高用量（150 mg 又は 300 mg）に増量することが推奨される。

機構の審査内容に基づき，以下の理由から，体重 50 kg 以上の小児患者のみ，本剤の 1 回 300 mg 投与を設定することは可能とする。

- 体重 50 kg 以上の小児患者への本剤 1 回 300 mg 投与について，本剤の有効性が認められるとともに，安全性について用量間で明らかな違いは認められなかった。
- 上限が設定されていない体重 50 kg 以上の小児患者において，曝露量が低くなることが想定される場合には，本剤 1 回 300 mg 投与を患者の状態に応じて選択可能とすることは意義があると考えられる。

1.3 用法及び用量に関連する注意の案

〈効能共通〉

7.1 本剤と他の生物製剤の併用について安全性及び有効性は確立していないので併用を避けること。

7.2 本剤による治療反応は、通常投与開始から 16 週以内に得られる。16 週以内に治療反応が得られない場合は、本剤の治療計画の継続を慎重に再考すること。

〈尋常性乾癬、関節症性乾癬、膿疱性乾癬〉

7.3 体重 60kg 以下の成人患者では 1 回 150 mg の投与を考慮すること。［17.1.2 参照］

7.4 体重 25kg 以上 50kg 未満の小児患者で、効果不十分な場合は、1 回 150 mg まで増量できる。体重 50kg 以上の小児患者で、効果不十分な場合は、1 回 300 mg まで増量できる。

（下線部：追記箇所）

1.4 用法及び用量に関連する注意の案の設定根拠

7.3 は成人患者に対する注意であることを明記した。

曝露-反応関係の解析から，曝露が最も低いカテゴリー（25 パーセンタイル未満）の患者では，曝露がより高いカテゴリー（25 以上 50 未満，50 以上 75 未満，又は 75 パーセンタイル以上）の患者と比較して有効性反応（PASI スコアの改善）が低い傾向であった。セクキヌマブの曝露が高いほど PASI を指標とした皮疹の改善効果が高いことから，体重 25kg 以上の患者では低用量（75 mg 又は 150 mg）で治療を開始し，個々の患者で十分な臨床的改善が認められない場合は，高用量（150 mg 又は 300 mg）に増量できるように設定した。

機構の審査内容に基づき，7.4 項を削除とする。

1.8.3 使用上の注意（案）及びその設定根拠

目　　次

1 使用上の注意（案）及びその設定根拠

今回の用法及び用量の追加申請では，重症の局面型皮疹を有する 6 歳以上 18 歳未満の小児の尋常性乾癬及び関節症性乾癬を対象とした国際共同第 III 相試験（A2310 試験）及び中等症から重症の局面型皮疹を有する 6 歳以上 18 歳未満の小児の尋常性乾癬及び関節症性乾癬を対象とした海外第 III 相試験（A2311 試験）を基に，小児乾癬患者における本剤の有効性及び安全性を検討した。

使用上の注意（案）については，2020 年 8 月に X 線基準を満たさない体軸性脊椎関節炎の適応追加で改訂となった添付文書を基に，Core Data Sheet (CDS)，A2310 試験及び A2311 試験の結果を総合的に勘案して作成した。

A2310 試験及び A2311 試験では，既承認の適応症に対する使用経験より特定された安全性プロファイルと比較して，新たな安全性の懸念となる事象は認められなかったことから，「9.7 小児等」以外の使用上の注意に関する追記及び変更は不要と判断した。なお，「11.2 その他の副作用」での鼻咽頭炎から上咽頭炎への事象変更は，MedDRA のバージョンアップによるものである。

以下に，今回改訂する「9.7 小児等」及び「11.2 その他の副作用」の注意喚起について，設定根拠とともに記載した。

2 小児等欄

9.7 小児等

〈尋常性乾癬、関節症性乾癬〉

9.7.1 低出生体重児、新生児、乳児又は 6 歳未満の幼児を対象とした臨床試験は実施していない。

〈膿疱性乾癬、強直性脊椎炎、X 線基準を満たさない体軸性脊椎関節炎〉

9.7.2 小児等を対象とした臨床試験は実施していない。

9.7 小児等の設定根拠

9.7.1 尋常性乾癬，関節症性乾癬患者で低出生体重児，新生児，乳児又は 6 歳未満の幼児を対象とした臨床試験は実施していないことを明記した。

3 副作用欄

3.1 その他の副作用欄

11.2 その他の副作用

	1%以上	1%未満	頻度不明
感染症	上気道感染（上咽頭炎、上気道感染、鼻炎、咽頭炎、副鼻腔炎、扁桃炎）、カンジダ症	足部白癬、口腔ヘルペス	-
眼障害	-	-	結膜炎
呼吸器、胸郭及び縦隔障害	-	鼻漏	-
胃腸障害	-	下痢	-
皮膚及び皮下組織障害	蕁麻疹	-	-
肝胆道系障害	-	肝機能検査値異常	-
神経系障害	-	-	頭痛
全身障害及び投与部位様態	-	注射部位反応	-

11.2 その他の副作用の設定根拠

現行の添付文書に記載されている内容について，変更を要する追加情報は得られていないことから，現行添付文書に基づき設定した。なお，MedDRA のバージョンアップにより鼻咽頭炎から上咽頭炎へ記載を変更した。

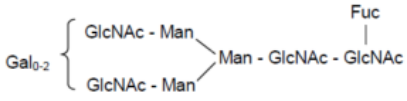
NOVARTIS

1.9 一般的名称に係る文書

既承認医薬品に係る資料を参照

1.10 毒薬・劇薬等の指定審査資料のまとめ

<現行>

化学名・別名	セクキヌマブは，ヒトインターロイキン-17A に対する遺伝子組換えヒト IgG1 モノクローナル抗体である。セクキヌマブは，チャイニーズハムスター卵巣細胞により産生される。セクキヌマブは，457 個のアミノ酸残基からなる H 鎖（γ1 鎖）2 分子及び 215 個のアミノ酸残基からなる L 鎖（κ 鎖）2 分子で構成される糖タンパク質（分子量：約 151,000）である。
構造式	アミノ酸配列及びジスルフィド結合 **L 鎖** EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWYQQK PGQAPRLLIY GASSRATGIP DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ QYGSSPCTFG QGTRLEIKRT VAAPSVFIFP PSDEQLKSGT ASVVCLLNNF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYSLSSTL TLSKADYEKH KVYACEVTHQ GLSSPVTKSF NRGEC **H 鎖** EVQLVESGGG LVQPGGSLRL SCAASGFTFS NYWMNWVRQA PGKGLEWVAA INQDGSEKYY VGSVKGRFTI SRDNAKNSLY LQMNSLRVED TAVYYCVRDY YDILTDYYIH YWYFDLWGRG TLVTVSSAST KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKRVEPKSC DKTHTCPPCP APELLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK H 鎖 E1：部分的ピログルタミン酸；N307：糖鎖結合；H 鎖 K457：部分的プロセシング L 鎖 C215－H 鎖 C230，H 鎖 C236－H 鎖 C236，H 鎖 C239－H 鎖 C239：ジスルフィド結合 主な糖鎖の推定構造  $C_{6584}H_{10134}N_{1754}O_{2042}S_{44}$：147,942.30（タンパク質部分，4本鎖） H鎖：$C_{2268}H_{3477}N_{597}O_{686}S_{16}$：50,595.50 L鎖：$C_{1024}H_{1594}N_{280}O_{335}S_{6}$：23,379.68

<table>
<tr><td>効能・効果</td><td>既存治療で効果不十分な下記疾患
尋常性乾癬，関節症性乾癬，膿疱性乾癬，強直性脊椎炎，X 線基準を満たさない体軸性脊椎関節炎</td></tr>
<tr><td>用法・用量</td><td>尋常性乾癬，関節症性乾癬，膿疱性乾癬
通常，成人にはセクキヌマブ(遺伝子組換え)として，1 回 300 mg を，初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降，4 週間の間隔で皮下投与する。また，体重により，1 回 150 mg を投与することができる。
強直性脊椎炎，X 線基準を満たさない体軸性脊椎関節炎
通常，成人にはセクキヌマブ（遺伝子組換え）として，1 回 150 mg を，初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降，4 週間の間隔で皮下投与する。</td></tr>
<tr><td>劇薬等の指定</td><td>生物由来製品
劇薬：原体・製剤
処方箋医薬品</td></tr>
<tr><td>市販名及び有効成分・分量</td><td>原体：セクキヌマブ(遺伝子組換え)
製剤：コセンティクス皮下注 150 mg シリンジ
［1 シリンジ中の含有量：セクキヌマブ（遺伝子組換え）150.0 mg］
コセンティクス皮下注 150 mg ペン
［1 シリンジ中の含有量：セクキヌマブ（遺伝子組換え）150.0 mg］</td></tr>
<tr><td>毒性</td><td>単回投与毒性試験
<table>
<tr><td>動物種</td><td>静脈内</td><td>皮下</td></tr>
<tr><td>カニクイザル</td><td>150 mg/kg まで死亡はみられず</td><td>150 mg/kg まで死亡はみられず</td></tr>
</table>
静脈内投与の単回投与毒性試験は実施していないため，反復投与毒性試験の結果から記載した。

反復投与毒性試験
<table>
<tr><td>動物種</td><td>投与期間</td><td>投与経路</td><td>投与量 (mg/kg/週)</td><td>無毒性量 (mg/kg/週)</td><td>主な所見</td></tr>
<tr><td>カニクイザル</td><td>13 週間</td><td>皮下</td><td>15, 50, 150</td><td>150</td><td>毒性所見なし</td></tr>
<tr><td>カニクイザル</td><td>26 週間</td><td>静脈内</td><td>15, 50, 150</td><td>150</td><td>毒性所見なし</td></tr>
</table></td></tr>
<tr><td>副作用</td><td>【尋常性乾癬，関節症性乾癬，膿疱性乾癬，強直性脊椎炎患者対象の臨床試験における日本人の副作用発現率】
副作用発現率　62/182=34.1%
副作用の種類　例数
鼻咽頭炎　16 例（8.8%）
口内炎　5 例（2.7%）
好酸球増加症　3 例（1.6%）
毛包炎　3 例（1.6%）
副作用発現率は，初回申請承認時及び一部変更承認申請（膿疱性乾癬）の承認時の副作用発現率に一部変更承認申請（強直性脊椎炎）の評価資料に用いた国内臨床試験の副作用発現率を合算し算出した

【X 線基準を満たさない体軸性脊椎関節炎患者対象の国際共同臨床試験における日本人の副作用発現率】
副作用発現率　4/12=33.3%</td></tr>
</table>

	副作用の種類　例数 毛包炎　1 例（8.3%） 皮下組織膿瘍　1 例（8.3%） 上咽頭炎　1 例（8.3%） 胃腸炎　1 例（8.3%） 口腔ヘルペス　1 例（8.3%） 咽頭炎　1 例（8.3%） （効能又は効果の一変承認時までの集計）
会　　社	ノバルティスファーマ株式会社　製剤：製造販売（輸入）

＜追加・変更＞（下線部）

化学名・別名	
構造式	
効能・効果	
用法・用量	尋常性乾癬，関節症性乾癬，膿疱性乾癬 通常，成人にはセクキヌマブ(遺伝子組換え)として，1 回 300 mg を，初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降，4 週間の間隔で皮下投与する。また，体重により，1 回 150 mg を投与することができる。 通常，6 歳以上の小児にはセクキヌマブ（遺伝子組換え）として，体重 50 kg 未満の患者には 1 回 75 mg を，体重 50 kg 以上の患者には 1 回 150 mg を，初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降，4 週間の間隔で皮下投与する。なお，体重 50 kg 以上の患者では，状態に応じて 1 回 300 mg を投与することができる。 強直性脊椎炎，X 線基準を満たさない体軸性脊椎関節炎 通常，成人にはセクキヌマブ（遺伝子組換え）として，1 回 150 mg を，初回，1 週後，2 週後，3 週後，4 週後に皮下投与し，以降，4 週間の間隔で皮下投与する。
劇薬等の指定	
市販名及び有効成分・分量	原体：セクキヌマブ(遺伝子組換え) 製剤：コセンティクス皮下注 150 mg シリンジ ［1 シリンジ中の含有量：セクキヌマブ（遺伝子組換え）150.0 mg］ コセンティクス皮下注 150 mg ペン ［1 シリンジ中の含有量：セクキヌマブ（遺伝子組換え）150.0 mg］ コセンティクス皮下注 75 mg シリンジ ［1 シリンジ中の含有量：セクキヌマブ（遺伝子組換え）75.0 mg］
毒性	
副作用	【尋常性乾癬，関節症性乾癬，膿疱性乾癬，強直性脊椎炎患者対象の臨床試験における日本人の副作用発現率】 副作用発現率　62/182=34.1% 副作用の種類　例数 鼻咽頭炎　16 例（8.8%） 口内炎　5 例（2.7%） 好酸球増加症　3 例（1.6%） 毛包炎　3 例（1.6%） 副作用発現率は，初回申請承認時及び一部変更承認申請（膿疱性乾癬）の承認時の副作用発現率に一部変更承認申請（強直性脊椎炎）の評価資料に用いた国内臨床試験の副作用発現率を合算し算出した 【X 線基準を満たさない体軸性脊椎関節炎患者対象の国際共同臨床試験における日本人の副作用発現率】 副作用発現率　4/12=33.3% 副作用の種類　例数 毛包炎　1 例（8.3%） 皮下組織膿瘍　1 例（8.3%） 上咽頭炎　1 例（8.3%） 胃腸炎　1 例（8.3%）

	口腔ヘルペス　1 例（8.3%） 咽頭炎　1 例（8.3%） （効能又は効果の一変承認時までの集計） 【重症の尋常性乾癬及び関節症性乾癬小児患者対象の国際共同臨床試験における日本人の副作用発現率】 副作用発現率　1/3=33.3% 副作用の種類　例数 過換気　1 例(33.3%) （用法及び用量の一変承認時までの集計）
会　社	

1.12　添付資料一覧

目　　次

1 第 3 部

添付資料	表　題	試験実施期間	報種類	評価／参考
3.2 データ又は報告書				
	原薬：セクキヌマブ（遺伝子組換え） 製剤：コセンティクス皮下注 75mg シリンジ	―	海外	評価

2 第 4 部

該当資料なし

3 第 5 部

添付資料番号	Report No./Study No.	表　題	試験実施期間	試験実施場所	報種類（国内／海外）	評価／参考	電子データの提出
5.2 全臨床試験一覧表							
5.2	―	全臨床試験一覧表	―	―	国内	評価	―
5.3 臨床試験報告書							
5.3.1 生物薬剤学試験報告書							
		該当資料なし					
5.3.2 ヒト生体試料を用いた薬物動態関連の試験報告書							
		該当資料なし					
5.3.3 臨床薬物動態（PK）試験報告書							
5.3.3.1 健康被験者における PK 及び初期忍容性試験報告書							
		該当資料なし					
5.3.3.2 患者における PK 及び初期忍容性試験報告書							
		該当資料なし					
5.3.3.3 内因性要因を検討した PK 試験報告書							
		該当資料なし					
5.3.3.4 外因性要因を検討した PK 試験報告書							

		該当資料なし					
5.3.3.5 ポピュレーション PK 試験報告書							
5.3.3.5-1	Pooled Studies CAIN457A	Population pharmacokinetic and exposure-response analyses for Cosentyx in pediatric psoriasis patients	2020 年 5 月 26 日	-	海外	参考	あり
5.3.3.5-2	CAIN457A2318	Population PK and exposure-PASI response analyses of secukinumab (AIN457) in Chinese patients with plaque psoriasis	2018 年 6 月 11 日	-	海外	参考	あり
5.3.3.5-3	NPH100100	Population Pharmacokinetics of Secukinumab in Patients with Rheumatoid Arthritis	2015 年 6 月 9 日	-	海外	参考	なし
5.3.4 臨床薬力学(PD)試験報告書							
		該当資料なし					
5.3.5 有効性及び安全性試験報告書							
5.3.5.1 申請する適応症に関する比較対照試験報告書							
5.3.5.1-1	AIN457A2310_Week 24	A randomized, double-blind, placebo- and active controlled multicenter trial to demonstrate efficacy of subcutaneous secukinumab compared to placebo and etanercept (in a single-blinded arm) after twelve weeks of treatment, and to assess the safety, tolerability, and long-term efficacy in subjects from 6 to less than 18 years of age with severe chronic plaque psoriasis (Week 24 Analysis)	2015 年 9 月 29 日～2019 年 3 月 7 日	ベルギー, コロンビア, エジプト, エストニア, フランス, ドイツ, グアテマラ, ハンガリー, イスラエル, イタリア, 日本, ラトビア, ポーランド, ルーマニア, ロシア, スペイン, スイス, イギリス, 米国, 計 47 施設	国際共同	評価	あり
	AIN457A2310_Week 24 Amendment 1	Amendment 1 to CAIN457A2310 (Week 24 Analysis)	2020 年 1 月 31 日(Release date)	-	国際共同	評価	あり
	DMPK RCAIN457A2310-pk	Bioanalytical data report: Determination of AIN457 in human serum	2019 年 8 月 21 日	中国	海外	評価	なし

	DMPK RCAIN457A2310-pk-int	Interim Bioanalytical Data Report: Determination of AIN457 in human serum	2019 年 11 月 20 日	フランス	海外	評価	なし
	DMPK RCAIN457A2310-ig-int	Interim Bioanalytical Data Report: Detection of anti-AIN457 antibodies in human serum	2019 年 11 月 20 日	フランス	海外	評価	なし
	AIN457A2310_Week 52	A randomized, double-blind, placebo- and active controlled multicenter trial to demonstrate efficacy of subcutaneous secukinumab compared to placebo and etanercept (in a single-blinded arm) after twelve weeks of treatment, and to assess the safety, tolerability, and long-term efficacy in subjects from 6 to less than 18 years of age with severe chronic plaque psoriasis (Week 52 Analysis)	2015 年 9 月 29 日～2019 年 9 月 18 日	ベルギー, コロンビア, エジプト, エストニア, フランス, ドイツ, グアテマラ, ハンガリー, イスラエル, イタリア, 日本, ラトビア, ポーランド, ルーマニア, ロシア, スペイン, スイス, イギリス, 米国, 計 47 施設	国際共同	評価	あり
	AIN457A2310_Week 52 Amendment 1	Amendment 1 to CSR CAIN457A2310-Week 52	2020 年 6 月 29 日（Release date）	-	国際共同	評価	あり
	AIN457A2310_Week 52 Amendment 2	Amendment 2 to CSR CAIN457A2310-Week 52	2020 年 8 月 27 日（Release date）	-	国際共同	評価	あり
	DMPK RCAIN457A2310-pka-int2	Second Interim Bioanalytical Data Report: Determination of AIN457 in human serum	2020 年 2 月 17 日	フランス	海外	評価	なし
	DMPK RCAIN457A2310-ig-int2	Second Interim Bioanalytical Data Report: Detection of anti-AIN457 antibodies and of neutralizing anti-AIN457 antibodies in human serum	2020 年 2 月 11 日	フランス	海外	評価	なし

5.3.5.1-2	AIN457A2311_Week 24	A randomized, open-label, multicenter trial to assess the efficacy of subcutaneous secukinumab after twelve weeks of treatment, and to assess the long-term safety, tolerability and efficacy in patients from 6 to less than 18 years of age with moderate to severe chronic plaque psoriasis (Week 24 Analysis)	2018 年 8 月 29 日～2019 年 11 月 14 日	ベルギー, チェコ, エストニア, ドイツ, ペルー, ポーランド, ロシア, スペイン, 米国, 計 23 施設	海外	評価	あり
	AIN457A2311_Week 24 Amendment 1	Amendment 01 to CAIN457A2311 (Week 24 Analysis)	2020 年 9 月 30 日（Release date）	-	海外	評価	あり
	DMPK RCAIN457A2311-pk-int	Interim Bioanalytical Data Report: Determination of AIN457 in human serum	2020 年 2 月 19 日	フランス	海外	評価	なし
	DMPK RCAIN457A2311-ig-int	Interim Bioanalytical Data Report: Detection of anti-AIN457 antibodies and of neutralizing anti-AIN457 antibodies in human serum	2020 年 2 月 25 日	フランス	海外	評価	なし
	AIN457A2311_Week 52	A randomized, open-label, multicenter trial to assess the efficacy of subcutaneous secukinumab after twelve weeks of treatment, and to assess the long-term safety, tolerability and efficacy in patients from 6 to less than 18 years of age with moderate to severe chronic plaque psoriasis (Week 52 Analysis)	2018 年 8 月 29 日～2020 年 5 月 28 日	ベルギー, チェコ, エストニア, ドイツ, ペルー, ポーランド, ロシア, スペイン, 米国, 計 23 施設	海外	評価	あり
	DMPK RCAIN457A2311-pk	Bioanalytical Data Report: Determination of AIN457 in human serum	2020 年 12 月 14 日	フランス	海外	評価	なし
	DMPK RCAIN457A2311-ig	Bioanalytical Data Report: Detection of anti-AIN457 antibodies and of neutralizing anti-AIN457 antibodies in human serum	2021 年 1 月 7 日	フランス	海外	評価	なし
5.3.5.1-3	AIN457F2304	A three-part randomized, double-blind, placebo-controlled study to investigate the efficacy and safety of secukinumab treatment in Juvenile Idiopathic arthritis subtypes of psoriatic and enthesitis-related arthritis	2017 年 5 月 23 日～2020 年 11 月 9 日	ベルギー, ドイツ, イタリア, ポーランド, ロシア, 南アフリカ, スペイン, トル	海外	参考	なし

				コ，英国，米国，計 34 施設			
	DMPK RCAIN457F2304-pk	Bioanalytical Data Report: Determination of AIN457 in human serum	2019 年 3 月 29 日	中国	海外	参考	なし
	DMPK RCAIN457F2304-pka	Bioanalytical Data Report: Determination of AIN457 in human serum	2021 年 4 月 1 日	フランス	海外	参考	なし
	DMPK RCAIN457F2304-ig	Bioanalytical Data Report: Detection of anti-AIN457 antibodies and of neutralizing anti-AIN457 antibodies in human serum	2021 年 4 月 6 日	フランス	海外	参考	なし
5.3.5.2 非対照試験報告書							
		該当資料なし					
5.3.5.3 複数の試験成績を併せて解析した報告書							
5.3.5.3-1	US SCE Appendix 1	Pediatric FDA submission SCE Appendix 1 (Integrated Summary of Efficacy, data analyses)	-	-	海外	ー	あり
5.3.5.3-2	US SCS Appendix 1	Pediatric SCS submission Appendix 1 (Integrated Summary of Safety, data analyses)	-	-	海外	ー	あり
5.3.5.3-3	JP SCE Appendix 1	Pediatric JP SCE Appendix 1 (Integrated Summary of Efficacy, data analyses)	-	-	海外	ー	あり
5.3.5.3-4	JP SCS Appendix 1	Pediatric JP SCS Appendix 1-1 (Integrated Summary of Safety, data analyses)	-	-	海外	ー	あり
	JP SCS Appendix 1	Pediatric JP SCS Appendix 1-2 (Integrated Summary of Safety, data analyses)	-	-	海外	-	あり
5.3.5.4 その他の臨床試験報告書							
		該当資料なし					
5.3.6 市販後の使用経験に関する報告書							
5.3.6-1	PSUR (26 Dec 2018 - 25 Dec 2019)	PERIODIC SAFETY UPDATE REPORT (PSUR)	Period covered: 2018 年 12 月 26 日～ 2019 年 12 月 25 日	ー	海外	参考	ー
5.3.6-2	第 7 回安全性定期報告 (26 Dec 2018 - 25 Dec 2019)	第 7 回安全性定期報告	Period covered: 2018 年 12 月	ー	海外	参考	ー

			26 日～ 2019 年 12 月 25 日				
5.3.7 患者データー覧表及び症例記録							
5.3.7-1	patients-lists	症例一覧表	ー	ー	国内	評価	ー

添付資料番号	著者・表 題・掲載誌	報種類（国内／海外）
5.4 参考文献 （評価／参考の別：参考資料）		
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