テモダールカプセル 20 mg
テモダールカプセル 100 mg

第 1 部　申請書等行政情報及び添付文書に関する情報

(12) 添付資料一覧

シェリング・プラウ株式会社

第 3 部：品質に関する文書

3.1 第 3 部（モジュール 3）目次

3.2 データ又は報告書

3.2.S 原薬（テモゾロミド[redacted]）

3.2.S.1 一般情報（テモゾロミド[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.2 製造（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.3 特性（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.4 原薬の管理（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.5 標準品又は標準物質（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.6 容器及び施栓系（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～20[redacted]年[redacted]月

3.2.S.7 安定性（テモゾロミド，[redacted]）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

3.2.P 製剤（テモダールカプセル，硬カプセル剤）

3.2.P.1 製剤及び処方（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

3.2.P.2 製剤開発の経緯（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute，シェリング・プラウ株式会社

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.3 製造（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute，[redacted]

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.4 添加剤の管理（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.5 製剤の管理（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.6 標準品又は標準物質（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.7 容器及び施栓系（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年 [redacted]月～20[redacted]年 [redacted]月

3.2.P.8 安定性（テモダールカプセル，硬カプセル剤）

Schering-Plough Research Institute

[redacted]

試験期間：19[redacted]年 [redacted]月～19[redacted]年 [redacted]月

3.2.A その他

3.2.A.1 製造施設及び設備（テモゾロミド，[redacted]）
製造施設及び設備（テモダールカプセル，[redacted]）

該当なし

3.2.A.2 外来性感染性物質の安全性評価（テモダールカプセル，硬カプセル剤[redacted]）

3.2.A.3 添加剤

該当なし

3.2.R 各極の要求資料

該当なし

3.3 参考文献

該当なし

第 4 部：非臨床試験報告書

4.1 第 4 部（モジュール 4）目次

4.2 試験報告書

4.2.1 薬理試験

4.2.1.1 効力を裏付ける試験

4.2.1.1.1	*P001	Temozolomide のヒト脳腫瘍由来細胞の増殖に対する作用 [redacted] 試験期間：20[redacted]年 [redacted]月～20[redacted]年 [redacted]月	
4.2.1.1.2	公表文献	Antitumour imidazotetrazines-XV. Role of guanine O^6 alkylation in the mechanism of cytotoxicity of imidazotetrazinones Aston University Tisdale MJ Biochem Pharmacol 1987;36:457-62	参考資料
4.2.1.1.3	公表文献	Potentiation of temozolomide and BCNU cytotoxicity by *O*^{6}-benzylguanine: a comparative study *in vitro* Charing Cross Hospital Wedge SR, et al. Br J Cancer 1996;73:482-90	参考資料
4.2.1.1.4	公表文献	Survival of human glioma cells treated with various combination of temozolomide and X-rays Academic Hospital Vrije Universiteit van Rijn J, et al. Int J Radiat Oncol Biol Phys 2000;47:779-84	参考資料
4.2.1.1.5		Temozolomide の *in vitro* におけるヒト腫瘍由来細胞株の増殖に対する作用 [redacted] 試験期間：20[redacted]年 [redacted]月～20[redacted]年 [redacted]月	参考資料
4.2.1.1.6	公表文献	Preclinical antitumor activity of temozolomide in mice: efficacy against human brain tumor xenografts and synergism with 1,3-bis(2-chloroethyl)-1-nitrosourea National Cancer Institute Plowman J, et al. Cancer Res 1994;54:3793-9	参考資料
4.2.1.1.7	公表文献	Activity of temozolomide in the treatment of central nervous system tumor xenografts Duke University Medical Center Friedman HS, et al. Cancer Res 1995;55:2853-7	参考資料

*新薬承認情報提供時に置き換えた

4.2.1.1.8	公表文献	Systemic administration of GPI 15427, a novel poly(ADP-ribose) polymerase-1 inhibitor, increases the antitumor activity of temozolomide against intracranial melanoma, glioma, lymphoma University of Rome Tor Vergata Tentori L, et al. Clin Cancer Res 2003;9:5370-9	参考資料
4.2.1.1.9	公表文献	Comparison of the cytotoxicity in vitro of temozolomide and dacarbazine, prodrugs of 3-methyl-(triazen-1-yl)imidazole-4-carboxamide Aston University Tsang LL, et al. Cancer Chemother Pharmacol 1991;27:342-6	参考資料
4.2.1.1.10	公表文献	Inhibition of O^6-alkylguanine DNA-alkyltransferase or poly(ADP-ribose) polymerase increases susceptibility of leukemic cells to apoptosis induced by temozolomide University of Rome Tor Vergata Tentori L, et al. Mol Pharmacol 1997;52:249-58	参考資料
4.2.1.1.11	公表文献	Mismatch repair mutations override alkyltransferase in conferring resistance to temozolomide but not to 1,3-bis(2-chloroethyl)nitrosourea Case Western Reserve University School of Medicine Liu L, et al. Cancer Res 1996;56:5375-9	参考資料
4.2.1.1.12	公表文献	Sensitization of pancreatic tumor xenografts to carmustine and temozolomide by inactivation of their O^6-methylguanine-DNA methyltransferase with O^6-benzylguanine or O^6-benzyl-2'-deoxyguanosine The University of Pittsburgh Kokkinakis DM, et al. Clin Cancer Res 2003;9:3801-7	参考資料
4.2.1.1.13	公表文献	Involvement of the mismatch repair system in temozolomide-induced apoptosis Istituto Dermopatico dell'Immacolata D'Atri S, et al. Mol Pharmacol 1998;54:334-41	参考資料

4.2.1.2 副次的薬理試験

該当なし

4.2.1.3 安全性薬理試験

4.2.1.3.1	*P002	Single-cycle oral toxicity study with lower doses of SCH 52365 in rats（4.2.3.2.2に添付）
4.2.1.3.2	*P003	Single-cycle oral toxicity study of SCH 52365 in rats（4.2.3.2.1に添付）
4.2.1.3.3	*P004	Single-cycle oral toxicity study with lower doses of SCH 52365 in dogs（4.2.3.2.6 に添付）*新薬承認情報提供時に置き換えた

4.2.1.3.4	*P005	Single-cycle oral toxicity study of SCH 52365 in dogs （4.2.3.2.5 に添付）	
4.2.1.3.5	*P006	Effect of temozolomide on gastrointestinal function in rats Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月	
4.2.1.3.6	公表文献	O^6-benzylguanine increases the sensitivity of human primary bone marrow cells to the cytotoxic effects of temozolomide Christie Hospital NHS Trust Fairbairn LJ, et al. Exp Hematol 1995;23:112-6	参考資料
4.2.1.3.7	公表文献	DNA repair enzymes and cytotoxic effects of temozolomide: comparative studies between tumor cells and normal cells of the immune system Istituto Dermopatico dell'Immacolata Pagani E, et al. J Chemother 2003;15:173-83	参考資料

4.2.1.4 薬力学的薬物相互作用試験

該当なし

4.2.2 薬物動態試験

4.2.2.1 分析法及びバリデーション報告書

4.2.2.1.1	*A001	SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in rat plasma [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日	
4.2.2.1.2	*A002	Determination of SCH 52365 in rat plasma by high-performance liquid chromatography [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日	
4.2.2.1.3	*A003	SCH 52365: An LC/MS/MS method for quantitation of MTIC (a bioconversion product of temozolomide) in rat plasma Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	
4.2.2.1.4	*A004	Determination of SCH 52365 in rat urine by high-performance liquid chromatography [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日	

*新薬承認情報提供時に置き換えた

4.2.2.1.5	*A005	SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in rat brain [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.6	*A006	SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in dog plasma [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.7	*A007	Determination of SCH 52365 in dog plasma by high-performance liquid chromatography [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.8	*A008	SCH 52365: An LC/MS/MS method for quantitation of MTIC (metabolite of temozolomide) in dog plasma Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.1.9	*A009	Determination of SCH 52365 in dog urine by high-performance liquid chromatography [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.10	*A010	SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in dog urine [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.11	*A011	SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in rat urine [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日
4.2.2.1.12	*A012	SCH 52365: Analysis of SCH 52365 (temozolomide) in beagle dog plasma using HPLC with UV detection Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.1.13	*A013	SCH 52365: Analysis of SCH 52365 (temozolomide) in rat plasma using HPLC with UV detection Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

4.2.2.2 吸収

4.2.2.2.1	*A014	SCH 52365: Absorption, metabolism, excretion, and pharmacokinetics of ^{14}C-SCH 52365 following a single oral or intravenous dose in the male rat [redacted] 試験期間：19[redacted]月～19[redacted]年[redacted]月
4.2.2.2.2	*A015	SCH 52365: Pharmacokinetics of SCH 52365 and its metabolite MTIC following a single oral suspension administration of SCH 52365 to male and female rats Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.2.3	*A016	SCH 52365: Absorption, metabolism, excretion, and pharmacokinetics of ^{14}C-SCH 52365 following a single oral or intravenous dose in the male dog [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.2.4	*A017	SCH 52365: Pharmacokinetics of SCH 52365 and its metabolite MTIC following a single oral suspension administration of SCH 52365 to male and female beagle dogs Schering-Plough Research Institute [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.2.5	*A018	SCH 52365: Pharmacokinetics of SCH 52365 in rats following a single oral gavage or intravenous dose [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.2.6	*A019	SCH 52365: Pharmacokinetics of SCH 52365 in beagle dogs following a single oral gavage or a single intravenous cross-over dose [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.2.2.7	*A020	SCH 52365: Single-dose two-way crossover comparative bioavailability study of formulated versus unformulated SCH 52365 capsules in dogs [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.2.3 分布

4.2.2.3.1	*A021	SCH 52365: Absorption, distribution, and metabolism of ^{14}C-SCH 52365 following a single oral dose in the male rat [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

4.2.2.3.2 *A022 SCH 52365: Tissue distribution of ^{14}C-SCH 52365 following a single oral dose in the female pigmented rat
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.2.3.3 *A023 SCH 52365: Tissue distribution of radioactivity by whole body autoradiography following a single oral administration of ^{14}C-SCH 52365 suspension to male rats
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.2.4 代謝

該当なし

4.2.2.5 排泄

4.2.2.5.1 *A024 SCH 52365: Mass balance and excretion of ^{14}C-SCH 52365 following a single intravenous or oral dose in the male rat
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.2.5.2 *A025 SCH 52365: Biliary excretion and enterohepatic circulation of radioactivity following administration of a single oral dose of ^{14}C-SCH 52365 suspension to male rats
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.2.6 薬物動態学的薬物相互作用（非臨床）

該当なし

4.2.2.7 その他の薬物動態試験

該当なし

4.2.3 毒性試験

4.2.3.1 単回投与毒性試験

4.2.3.1.1 *T001 Single-dose oral toxicity study of SCH 52365 in mice
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.1.2 *T002 Single-dose intraperitoneal toxicity study of SCH 52365 in mice
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

4.2.3.1.3	*T003	Single-dose oral toxicity study of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.1.4	*T004	Single-dose oral toxicity study with lower doses of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.1.5	*T005	Single-dose intraperitoneal toxicity study of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.1.6	*T006	Single-dose oral toxicity study of SCH 52365 in beagle dogs [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.1.7	*T007	Single-dose oral toxicity study with lower doses of SCH 52365 in beagle dogs [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.2 反復投与毒性試験

4.2.3.2.1	*T008	Single-cycle oral toxicity study of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.2.2	*T009	Single-cycle oral toxicity study with lower doses of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.2.3	*T010	Three-cycle oral toxicity study of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.2.4	*T011	Six-cycle oral (gavage) toxicity study of SCH 52365 in rats [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月
4.2.3.2.5	*T012	Single-cycle oral toxicity study of SCH 52365 in dogs [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

4.2.3.2.6 *T013 Single-cycle oral toxicity study with lower doses of SCH 52365 in dogs
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.2.7 *T014 Three-cycle oral toxicity study of SCH 52365 in dogs
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.2.8 *T015 Six-cycle oral (capsule) toxicity study of SCH 52365 in dogs
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.3 遺伝毒性試験

4.2.3.3.1 *In vitro* 試験

4.2.3.3.1.1 *T016 *Salmonella-Escherichia coli*/mammalian-microsome reverse mutation assay of SCH 52365 (Temozolomide)
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.3.1.2 *T017 Chromosome aberration study of SCH 52365 in human peripheral blood lymphocytes
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.3.2 *In vivo* 試験

4.2.3.3.2.1 *T018 Mouse bone marrow erythrocyte micronucleus study of SCH 52365 (Temozolomide)
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

4.2.3.4 がん原性試験

4.2.3.4.1 長期がん原性試験

該当なし

4.2.3.4.2 短期又は中期がん原性試験

該当なし

4.2.3.4.3 その他の試験

該当なし

*新薬承認情報提供時に置き換えた

4.2.3.5 生殖発生毒性試験

4.2.3.5.1 受胎能及び着床までの初期胚発生に関する試験

4.2.3.5.1.1 *T019 Fertility and early embryonic developmental toxicity study of SCH 52365 administered orally by gavage in rats
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

4.2.3.5.2 胚・胎児発生に関する試験

4.2.3.5.2.1 *T020 Dose range-finding developmental toxicity study in rats with SCH 52365 参考資料
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.5.2.2 *T021 Rat developmental toxicity study with SCH 52365
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.5.2.3 *T022 Dose range-finding developmental toxicity study in rabbits with SCH 52365 参考資料
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

4.2.3.5.2.4 *T023 Embryo-fetal developmental toxicity and toxicokinetic study of SCH 52365 administered orally by gavage in rabbits
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

4.2.3.5.3 出生前及び出生後の発生並びに母体の機能に関する試験

4.2.3.5.3.1 *T024 A pre- and postnatal developmental toxicity and maternal function study of SCH 52365 administered orally by gavage in rats
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

4.2.3.5.4 新生児を用いた試験

該当なし

4.2.3.6 局所刺激性試験

該当なし

4.2.3.7 その他の毒性試験

4.2.3.7.1 抗原性試験

該当なし

*新薬承認情報提供時に置き換えた

4.2.3.7.2 免疫毒性試験

該当なし

4.2.3.7.3 毒性発現の機序に関する試験

該当なし

4.2.3.7.4 依存性試験

該当なし

4.2.3.7.5 代謝物の毒性試験

該当なし

4.2.3.7.6 不純物の毒性試験

4.2.3.7.6.1	*T025	A single-cycle (5-day dosing) oral gavage toxicity study of SCH52365 with impurities in rats [redacted] 試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月	
4.2.3.7.6.2	*T026	*Salmonella-Escherichia*/mammalian-microsome reverse mutation assay of SCH 52365 (Temozolomide) with impurities [redacted] 試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月	
4.2.3.7.6.3	*T027	Chromosome aberration study of SCH 52365 (Temozolomide) with impurities in human peripheral blood lymphocytes [redacted] 試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月	

4.2.3.7.7 その他の試験

4.2.3.7.7.1	*T028	Dermal sensitization study in guinea pigs (Buehler's technique modified) of SCH 52365 (Temozolomide) [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	
4.2.3.7.7.2	*T029	A single dose study by intravenous injection in mice of compound CRC 84/07 [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
4.2.3.7.7.3	*T030	A single dose study by intraperitoneal injection in mice of compound CRC 84/07 [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料

*新薬承認情報提供時に置き換えた

4.2.3.7.7.4	*T031	A repeat dose study by intraperitoneal injection in mice of compound CRC 84/07 [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
4.2.3.7.7.5	*T032	A repeat dose study by intraperitoneal injection in rats of compound CRC 84/07 [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料

4.3 参考文献

該当なし

*新薬承認情報提供時に置き換えた

第 5 部：臨床試験報告書

5.1 第 5 部（モジュール 5）目次

5.2 全臨床試験一覧表

5.3 臨床試験報告書

5.3.1 生物薬剤学試験報告書

5.3.1.1 バイオアベイラビリティ（BA）試験報告書

該当なし

5.3.1.2 比較 BA 試験及び生物学的同等性（BE）試験報告書

該当なし

5.3.1.3 In Vitro-In Vivo の関連を検討した試験報告書

5.3.1.3.1 *C001 SCH52365 カプセル 5mg，20mg 及び 100mg における溶出挙動の同等性確認試験
シェリング・プラウ株式会社
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

5.3.1.4 生物学的及び理化学的分析法検討報告書

5.3.1.4.1 *C002 SCH 52365: Stability of temozolomide and MTIC (active metabolite), and HPLC quantitation of MTIC in human plasma
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.2 *C003 SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in human plasma
[redacted]
報告書作成日：19[redacted]年[redacted]月[redacted]日

5.3.1.4.3 *C004 SCH 52365: Analysis of SCH 52365 (temozolomide) in human plasma using HPLC with UV detection
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.4 *C005 SCH 52365: Validation of a high performance liquid chromatographic-tandem mass spectrometric (LC-MS/MS) method for the determination of SCH 52365 concentrations in human plasma
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

5.3.1.4.5 *C006 SCH 52365: Determination of MTIC in human plasma using high performance liquid chromatography with ultraviolet detection : pre-study validation
[redacted]
報告書作成日：19[redacted]年[redacted]月[redacted]日

5.3.1.4.6 *C007 SCH 52365: Validation of the HPLC method for the determination of MTIC in human plasma
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.7 *C008 SCH 52365: An analytical HPLC method for quantitation of MTIC (metabolite of temozolomide) in human plasma
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.8 *C009 SCH 535108: Validation of a high performance liquid chromatographic-tandem mass spectrometric (LC-MS/MS) method for the determination of SCH 535108 concentrations in human plasma
[redacted]
試験期間：20[redacted]年[redacted]月～20[redacted]年[redacted]月

5.3.1.4.9 *C010 SCH 52365: Validation of a high performance liquid chromatographic assay for AIC in human plasma
[redacted]
報告書作成日：19[redacted]年[redacted]月[redacted]日

5.3.1.4.10 *C011 SCH 52365: Analysis of AIC (a metabolite of temozolomide) in human plasma using HPLC with UV detection
Schering-Plough Research Institute
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.11 *C012 SCH 52365: Validation of a high performance liquid chromatography assay for SCH 52365 (temozolomide) in human urine
[redacted]
報告書作成日：19[redacted]年[redacted]月[redacted]日

5.3.1.4.12 *C013 SCH 52365: Validation of the HPLC method for the determination of temozolomide in human urine
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

5.3.1.4.13 *C014 SCH 60387: Validation of the HPLC method for the determination of dacarbazine in human plasma.
[redacted]
試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月

*新薬承認情報提供時に置き換えた

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

5.3.2.1 血漿蛋白結合試験報告書

該当なし

5.3.2.2 肝代謝及び薬物相互作用試験報告書

該当なし

5.3.2.3 他のヒト生体試料を用いた試験報告書

該当なし

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

5.3.3.2.1	*C015	Absorption, metabolism and excretion of ^{14}C-SCH 52365 (temozolomide) in patients with advanced cancer [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.2.2	*C016	SCH 52365 薬物動態試験 神経膠腫の再発患者における SCH 52365 の薬物動態の検討 [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	
5.3.3.2.3	*C017	A phase I study of temozolomide (SCH 52365) in adult patients with advanced cancer [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.2.4	*C018	A phase I study of temozolomide (SCH 52365) using a single oral dose in adult patients with advanced cancer [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.2.5	*C019	A randomized, phase III study of temozolomide (SCH 52365) versus dacarbazine in the treatment of patients with advanced, metastatic malignant melanoma [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.2.6	*C020	SCH 52365: Temozolomide in the treatment of metastatic malignant melanoma with brain metastases Schering-Plough Research Institute [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日	参考資料

*新薬承認情報提供時に置き換えた

5.3.3.3 内因性要因を検討した PK 試験報告書

5.3.3.3.1	*C021	A phase I study of temozolomide (SCH 52365) in pediatric patients with advanced cancer [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.3.2	*C022	A phase II/pharmacokinetic study of temozolomide (SCH 52365) in the treatment of patients with advanced hepatocellular carcinoma [redacted] 報告書作成日：19[redacted]年[redacted]月[redacted]日	参考資料

5.3.3.4 外因性要因を検討した PK 試験報告書

5.3.3.4.1	*C023	Effect of gastric pH on the oral bioavailability of temozolomide (SCH 52365): SCH 52365 - ranitidine pharmacokinetic interaction study in patients with advanced cancer [redacted] 19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料
5.3.3.4.2	*C024	A phase I study of temozolomide (SCH 52365) in adult patients with advanced cancer stratified by extent of prior therapy [redacted] 試験期間：19[redacted]年[redacted]月～19[redacted]年[redacted]月	参考資料

5.3.3.5 ポピュレーション PK 試験報告書

5.3.3.5.1	*C025	Population pharmacokinetic analysis of SCH 52365 in adult patients with anaplastic astrocytoma or glioblastoma multiforme Schering-Plough Research Institute 報告書作成日：19[redacted]年[redacted]月[redacted]日	参考資料
5.3.3.5.2	*C026	Population pharmacokinetic analysis of SCH 52365 in adult patients Schering-Plough Research Institute 報告書作成日：19[redacted]年[redacted]月[redacted]日	参考資料

5.3.4 臨床薬力学（PD）試験報告書

5.3.4.1 健康被験者における PD 試験及び PK/PD 試験報告書

該当なし

5.3.4.2 患者における PD 試験及び PK/PD 試験報告書

該当なし

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

*新薬承認情報提供時に置き換えた

5.3.5.1.1 プラセボ対照試験

該当なし

5.3.5.1.2 実薬対照試験

5.3.5.1.2.1	*C027	A Randomized, Multicenter, Open-Label Phase II Study of Temozolomide (SCH 52365) and Reference Agent (Procarbazine) in the Treatment of Patients with Glioblastoma Multiforme at First Relapse 報告書作成日：19[redacted]年[redacted]月[redacted]日
5.3.5.1.2.2	*C028	Concomitant and Adjuvant Temozolomide (SCH 52365) and Radiotherapy for Newly Diagnosed Glioblastoma Multiforme. A Randomized Phase 3 Study. 報告書作成日：20[redacted]年[redacted]月[redacted]日 (EORTC Trial 26981/22981; NCIC CE3)

5.3.5.2 非対照試験報告書

5.3.5.2.1	*C029	SCH 52365 第Ⅱ相臨床試験 －退形成性星細胞腫の初回再発患者における SCH 52365 単剤投与の有効性及び安全性の検討－ 報告書作成日：20[redacted]年[redacted]月[redacted]日
5.3.5.2.2	*C030	A Multicenter Open-Label Phase II Study of Temozolomide (SCH 52365) in the Treatment of Anaplastic with Anaplastic Astrocytoma at First Relapse 報告書作成日：19[redacted]年[redacted]月[redacted]日
5.3.5.2.3	*C031	A Multicenter Open-Label Phase II Study of Temozolomide (SCH 52365) in the Treatment of Patients with Glioblastoma Multiforme at First Relapse 報告書作成日：19[redacted]年[redacted]月[redacted]日

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	ISE	Integrated Summary of Efficacy
5.3.5.3.2	ISS	Integrated Summary of Safety Information

5.3.5.4 その他の試験報告書

該当なし

5.3.6 市販後の使用経験に関する報告書

5.3.6.1	PSUR#1	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, January 26, 1999 to July 25, 1999)
5.3.6.2	PSUR#2	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, July 26, 1999 to January 25, 2000)

*新薬承認情報提供時に置き換えた

5.3.6.3	PSUR#3	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, January 26, 2000 to July 25, 2000)
5.3.6.4	PSUR#4	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, July 26, 2000 to January 25, 2001)
5.3.6.5	PSUR#5	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, January 26, 2001 to January 25, 2002)
5.3.6.6	PSUR#6	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, January 26, 2002 to January 25, 2003)
5.3.6.7	PSUR#7	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, January 26, 2003 to July 12, 2003)
5.3.6.8	PSUR#8	Periodic Safety Update Report For: Temozolomide Capusles, (Schering-Plough Resach Institute, July 13, 2003 to July 12, 2004)

5.3.7 患者データ一覧表及び症例記録

5.3.7.1 主要な試験の症例一覧表

5.3.7.2 副作用が観察された症例の一覧表

5.3.7.3 重篤な有害事象が観察された症例の一覧表

5.3.7.4 臨床検査異常変動が観察された症例の一覧表

5.3.7.5 臨床検査値の変動を適切に示した図

5.4 参考文献

5.4.1 治験相談記録

5.4.1.1 平成 1[redacted]年 [redacted]月 [redacted]日

5.4.1.2 平成 1[redacted]年 [redacted]月 [redacted]日

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