

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, シエリング・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：非臨床試驗報告書

4.1 第4部（モジュール4）目次

4.2 試驗報告書

4.2.1 藥理試驗

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] | |
| 4.2.1.1.2 | 公表文献 | 試験期間 : 20 [REDACTED] 年 [REDACTED] 月 ~ 20 [REDACTED] 年 [REDACTED] 月 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 <i>in vitro</i> 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 <i>in vitro</i> におけるヒト腫瘍由来細胞株の増殖に対する作用 [REDACTED] | 参考資料 |
| 4.2.1.1.6 | 公表文献 | 試験期間 : 20 [REDACTED] 年 [REDACTED] 月 ~ 20 [REDACTED] 年 [REDACTED] 月 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] [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] [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] [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]
[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]
[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]
[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]
[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]
[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]
[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 吸收

- 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
XXXXXXXXXXXXXX
試験期間：19 [] 年 [] 月～19 [] 年 [] 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
XXXXXXXXXXXXXX
試験期間：19 [] 年 [] 月～19 [] 年 [] 月

4.2.2.6 藥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 毒性試驗

4.2.3.1 单回投与毒性試験

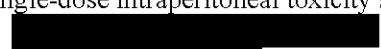
- 4.2.3.1.1 *T001 Single-dose oral toxicity study of SCH 52365 in mice
[REDACTED]
試験期間：19 [REDACTED] 年 [REDACTED] 月～19 [REDACTED] 年 [REDACTED] 月

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

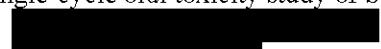
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- 4.2.3.1.4 *T004 Single-dose oral toxicity study with lower doses of SCH 52365 in rats

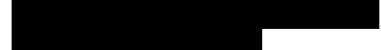
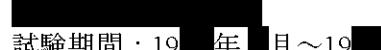
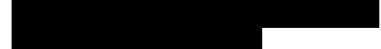
 試験期間：19[年][月]～19[年][月]
- 4.2.3.1.5 *T005 Single-dose intraperitoneal toxicity study of SCH 52365 in rats

 試験期間：19[年][月]～19[年][月]
- 4.2.3.1.6 *T006 Single-dose oral toxicity study of SCH 52365 in beagle dogs

 試験期間：19[年][月]～19[年][月]
- 4.2.3.1.7 *T007 Single-dose oral toxicity study with lower doses of SCH 52365 in beagle dogs

 試験期間：19[年][月]～19[年][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

 試験期間：19[年][月]～19[年][月]
- 4.2.3.2.2 *T009 Single-cycle oral toxicity study with lower doses of SCH 52365 in rats

 試験期間：19[年][月]～19[年][月]
- 4.2.3.2.3 *T010 Three-cycle oral toxicity study of SCH 52365 in rats

 試験期間：19[年][月]～19[年][月]
- 4.2.3.2.4 *T011 Six-cycle oral (gavage) toxicity study of SCH 52365 in rats

 試験期間：19[年][月]～19[年][月]
- 4.2.3.2.5 *T012 Single-cycle oral toxicity study of SCH 52365 in dogs

 試験期間：19[年][月]～19[年][月]

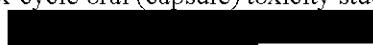
*新薬承認情報提供時に置き換えた

4.2.3.2.6 *T013 Single-cycle oral toxicity study with lower doses of SCH 52365 in dogs

 試験期間：19[年][月]～19[年][月]

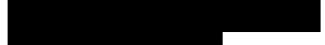
4.2.3.2.7 *T014 Three-cycle oral toxicity study of SCH 52365 in dogs

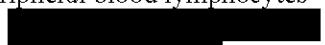
 試験期間：19[年][月]～19[年][月]

4.2.3.2.8 *T015 Six-cycle oral (capsule) toxicity study of SCH 52365 in dogs

 試験期間：19[年][月]～19[年][月]

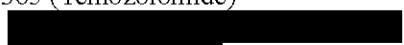
4.2.3.3 遺伝毒性試験

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)*

 試験期間：19[年][月]～19[年][月]

4.2.3.3.1.2 *T017 Chromosome aberration study of SCH 52365 in human peripheral blood lymphocytes

 試験期間：19[年][月]～19[年][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)

 試験期間：20[年][月]～20[年][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 生殖發生毒性試驗

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

試験期間：20 年 月～20 年 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 參考資料

試験期間：19 年 月～19 年 月

- 4.2.3.5.2.2 *T021 Rat developmental toxicity study with SCH 52365

試験期間：19 年 月～19 年 月

- 4.2.3.5.2.3 *T022 Dose range-finding developmental toxicity study in rabbits with 參考資料
SCH 52365

試験期間：19 年 月～19 年 月

- 4.2.3.5.2.4 *T023 Embryo-fetal developmental toxicity and toxicokinetic study of SCH 52365 administered orally by gavage in rabbits

試験期間：20 年 月～20 年 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

試験期間：20 年 月～20 年 月

4.2.3.5.4 新生児を用いた試験

該当なし

4.2.3.6 局所刺激性試驗

該当なし

4.2.3.7 その他の毒性試験

4.2.3.7.1 抗原性試驗

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otoxic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

該当なし

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

参考資料

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

4.2.3.7.7.3

*T030

A single dose study by intraperitoneal injection in mice of compound CRC 84/07

参考資料

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

*新葉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 | 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 | 参考資料 |

試験期間：19[年][月]～19[年][月]

試験期間：19[年][月]～19[年][月]

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

試験期間：20[]年[]月～20[]年[]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

試験期間：19[]年[]月～19[]年[]月

5.3.1.4.2 *C003 SCH 52365: Validation of a high performance liquid chromatographic assay for SCH 52365 (temozolomide) in human plasma

報告書作成日：19[]年[]月[]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

試験期間：19[]年[]月～19[]年[]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

試験期間：20[]年[]月～20[]年[]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 [] 年 [] 月 [] 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 [] 年 [] 月 ~ 19 [] 年 [] 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 [] 年 [] 月 ~ 19 [] 年 [] 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 [] 年 [] 月 ~ 20 [] 年 [] 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 [] 年 [] 月 [] 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 [] 年 [] 月 ~ 19 [] 年 [] 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 [] 年 [] 月 [] 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 [] 年 [] 月 ~ 19 [] 年 [] 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 [] 年 [] 月 ~ 19 [] 年 [] 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 ¹⁴C-SCH 52365 (temozolomide) in patients with advanced cancer 参考資料

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

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 参考資料

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

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 参考資料

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

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 参考資料

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

5.3.3.2.6 *C020 SCH 52365: Temozolomide in the treatment of metastatic malignant melanoma with brain metastases
Schering-Plough Research Institute 参考資料

[REDACTED]
報告書作成日：19 [REDACTED] 年 [REDACTED] 月 [REDACTED] 日

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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 参考資料

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

- 5.3.3.3.2 *C022 A phase II/pharmacokinetic study of temozolomide (SCH 52365) in the treatment of patients with advanced hepatocellular carcinoma 参考資料

[REDACTED]
報告書作成日：19[REDACTED]年[REDACTED]月[REDACTED]日

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 参考資料

[REDACTED]
19[REDACTED]年[REDACTED]月～19[REDACTED]年[REDACTED]月

- 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 参考資料

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

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 参考資料
報告書作成日：19[REDACTED]年[REDACTED]月[REDACTED]日

- 5.3.3.5.2 *C026 Population pharmacokinetic analysis of SCH 52365 in adult patients Schering-Plough Research Institute 参考資料
報告書作成日：19[REDACTED]年[REDACTED]月[REDACTED]日

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 █ 年 █ 月 █ 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 █ 年 █ 月 █ 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 █ 年 █ 月 █ 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 █ 年 █ 月 █ 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 █ 年 █ 月 █ 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 Capsules, (Schering-Plough Research Institute, January 26, 1999 to July 25, 1999)
- 5.3.6.2 PSUR#2 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research 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 Capsules, (Schering-Plough Research Institute, January 26, 2000 to July 25, 2000)
- 5.3.6.4 PSUR#4 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research Institute, July 26, 2000 to January 25, 2001)
- 5.3.6.5 PSUR#5 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research Institute, January 26, 2001 to January 25, 2002)
- 5.3.6.6 PSUR#6 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research Institute, January 26, 2002 to January 25, 2003)
- 5.3.6.7 PSUR#7 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research Institute, January 26, 2003 to July 12, 2003)
- 5.3.6.8 PSUR#8 Periodic Safety Update Report For: Temozolomide Capsules, (Schering-Plough Research 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[]年 []月 []日
- 5.4.1.2 平成 1[]年 []月 []日

5.4.2 参考文献

- 5.4.2.1 Zürich K.j.: Histological Typing of Tumors of the Central Nervous System. World Health Organization, Geneva, 1979.
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- 5.4.2.3 Cavenee WK. Accumulation of genetic defects during astrocytoma progression. Cancer 1992;70:1788-93.
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- 5.4.2.8 The Committee of Brain Tumor Registry of Japan. Report of Brain Tumor Registry of Japan(1969-1996) 11th Edition. *Neurologia Medical-Chirurgia* 2003; 43 suppl.
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- 5.4.2.15 Newton HB, Junck L, Bromberg J, et al. Procarbazine chemotherapy in the treatment of recurrent malignant astrocytomas after radiation and nitrosourea failure. *Neurology* 1990;40:1743-1746.
- 5.4.2.16 Rodriguez LA, Prados M, Silver P, et al. Reevaluation of procarbazine for the treatment of recurrent malignant central nervous system tumors. *Cancer* 1989;64:2420-2423.
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