

<안전성.유효성 심사관련 제출자료목록>

○ 관련규정 : 의약품등의 품목허가.신고.심사 규정 제2조제7호 신약, [별표1] 화학구조 또는 본질 조성이 전혀 새로운 신물질 의약품

구분	자료번호		3	4							5			6		7	8		
	1	2	가	나	가	나	다	라	마	바			가	나	다			가	나
										1)	2)	3)							
1. 제출자료	○	○	○ ○	○	○	○	○	△	△	△	△	○	○	○	○	○	○	○	
2. 제출여부	○	○	○ ○	○	○	○	○	○	○	○	X	X	X	X	○	○	○	○	
3. 면제사유	△: 개개 의약품에 따라 판단하여 제출하는 것이 무의미하거나 불가능하여 면제할 수 있는 것 - 효력시험 및 일반약리시험은 기 평가된 경구 팔리페리돈 결과로 같음																		

1. 기원 또는 발견 및 개발경위에 관한 자료, 2. 구조결정.물리화학적 성질에 관한 자료 3. 안정성에 관한 자료(가. 장기보존시험 또는 가속시험자료, 나. 가혹시험자료), 4. 독성에 관한 자료(가. 단회투여독성시험자료, 나. 반복투여독성시험자료, 다. 유전독성시험자료, 라. 생식.발생독성시험자료, 마. 발암성시험자료 바. 기타독성시험자료 1)국소독성시험 2)의존성 3)항원성 및 면역독성 5. 약리작용에 관한 자료(가. 효력시험자료, 나. 일반약리시험자료 또는 안전성약리시험자료, 다. 흡수, 분포, 대사 및 배설시험자료), 6. 임상시험성적에 관한 자료(가. 임상시험자료집, 나. 가교자료), 7. 외국의 사용현황 등에 관한 자료, 8. 국내 유사제품과의 비교검토 및 당해 의약품 등의 특성에 관한 자료

○ 제출자료목록

1. 기원 또는 발견 및 개발경위에 관한 자료

2. 구조결정.물리화학적 성질 및 생물학적 성질에 관한 자료

3. 안정성에 관한 자료

가. 장기보존시험 및 가속시험자료

나. 가혹시험자료

4. 독성에 관한 자료

가. 단회투여독성시험자료

① Single Dose Toxicity Study in Minipigs by Intramuscular Route with Various Recovery Periods(R092670)

② Single dose intramuscular toxicity study in the beagle dog(5296)

③ Single dose intramuscular toxicity study in beagle dog(4472)

④ Single dose intramuscular toxicity study in pig(4788)

나. 반복투여독성시험자료

① 1-week Intermittent Dose Intramuscular Toxicity Study in the Dog(TOX6832)

② 3-month intermittent dose intramuscular toxicity study in the rat(TOX6266)

- ③ 1 week Intermittent Dose Intramuscular Toxicity Study in the Dog(TOX6191)
- ④ Twelve month intermittent repeated dose intramuscular toxicity study in the beagle dog(TOX4692)
- ⑤ Evaluation of the subchronic toxicity potential in SPF Wistar rats(TOX3848)
- ⑥ Evaluation of the subchronic toxicity potential in beagle dogs(TOX3849)

다. 생식.발생독성시험자료

- ① Intramuscular Developmental Toxicity Study of R092670 in the Rat(TOX7170)
- ② Pilot Developmental Toxicity Study in the Sprague -Dawley Rat after Single Intramuscular Dosing with Paliperidone Palmitate(TOX7169)

라. 유전독성시험자료

- ① R092670: Mutation at the thymidine kinase (*tk*) locus of mouse lymphoma L5178Y cells (MLA) using the microtitre^R fluctuation technique(TOX6362)
- ② *In Vitro* Bacterial Reverse Mutation Test with *Salmonella typhimurium*(TOX3985)

마. 발암성시험자료

- ① 24-month intermittent dose intramuscular carcinogenicity study in the rat(TOX6726)

바. 기타독성시험자료

- 1) 국소독성시험자료(국소내성): 12-Week local tolerance study of 2 paliperidone palmitate long acting injectable formulations in the minipig

5. 약리작용에 관한 자료

다. 흡수, 분포, 대사 및 배설시험자료

- ① FK5339: Pharmacokinetics of paliperidone (R076477) following single intramuscular administration of a paliperidone palmitate (R092670) long acting injectable (LAI) suspension at 5 mg paliperidone eq./kg in the Göttingen Minipig
- ② FK3539: Plasma concentrations of 9-hydroxy-risperidone (R076477) in pigs in a single dose intramuscular toxicity study (Exp. No. 5187) at 5 mg R076477-eq./kg with aqueous suspensions of 9-hydroxyrisperidone palmitate (R092670) manufactured with the High Pressure Homogenizer at mean specific surface areas of 8.1, 9.6 and 11.4 m²/g in comparison with the F4 formulation (9.5 m²/g)
- ③ FK3538: Plasma concentrations of 9-hydroxy-risperidone (R076477) in dogs in a single dose intramuscular toxicity study (Exp. No. 5187) at 5 mg R076477-eq./kg with aqueous suspensions of 9-hydroxyrisperidone palmitate (R092670) manufactured with the High Pressure Homogenizer at mean specific surface areas of 8.1, 9.6 and 11.4 m²/g in comparison with the F4 formulation (9.5 m²/g)
- ④ FK3028: 9-hydroxy-risperidone, R076477) in the SPF Wistar rat in a six-month intermittent repeated dose intramuscular toxicity study (Exp. No. 4696) on an aqueous depot suspension of

paliperidone palmitate (R092670) at 20, 80 and 160 mg paliperidone-eq./kg/month

- ⑤ FK4736: Pharmacokinetics of paliperidone(R076477) following single IM administration of paliperidone palmitate(R092670) suspension at 5mg paliperidone eq./kg and an aqueous paliperidone solution at 0.31mg/kg to the Gottingen Mini-pig
- ⑥ N130772: Toxicokinetics of 9-hydroxy-risperidone(R076477) in SPF Wistar rats in a 6-month intramuscular chronic toxicity study(Exp. No. 3848) on an aqueous depot suspension formulation of R092670 at 20, 80 and 160mg (R076477-eq.)/kg/month
- ⑦ R092760/FK5747: Injection site and tissue distribution of ³H radioactivity and ¹⁴C radioactivity in male Sprague Dawley rats following single intramuscular injection of an aqueous suspension of ¹⁴Cpaliperidone palmitate (¹⁴C-R092670) and paliperidone ³H-palmitate(³H-R092670) at 10 mg paliperidone equivalents
- ⑧ FK3024: Toxicokinetics and tissue distribution of paliperidone (9-hydroxyrisperidone, R076477) in the beagle dog in a twelve-month intermittent repeated dose intramuscular toxicity study (Exp. No. 4692) on an aqueous depot suspension formulation of paliperidone palmitate (R092670) at 5, 20 and 80 mg paliperidone-eq./kg/month for the first dose and 5, 10 and 40 mg paliperidone-eq./kg/month for the 2nd until the 12th administration
- ⑨ N130773: Toxicokinetics and tissue distribution of 9-hydroxy-risperidone(R076477) in beagle dogs in a 6-month intramuscular toxicity study(Exp. No. 3849) on an aqueous depot suspension formulation of the prodrug R092670 at 2.5, 10 and 40mg(R076477-eq.)/kg/month for the first dose and 5, 20 and 80mg(R076477-eq.)/kg/month from the 2nd until the 6th administration
- ⑩ FK5302: The *in-vitro* hydrolysis of R092670 in selected tissue fractions of human and the identification of esterase(s) involved in the hydrolysis
- ⑪ FK29989: The *in vitro* hydrolysis of Paliperidone palmitate ester (R092670) and the chiral inversion of Paliperidone enantiomers in hepatocytes, liver subcellular fractions, blood and plasma of the male and female rat, male dog and human, and in lymphatic fluid and muscle of dog

6. 임상시험성적에 관한 자료

가. 임상시험자료집

1) 임상약리시험

- ① PSY-1004: Open-Label, Parallel, Randomized, Dose Proportionality Pharmacokinetic Study of Paliperidone After Intramuscular Injection of Paliperidone Palmitate in the Deltoid or Gluteal Muscle in Subjects With Schizophrenia
- ② BEL-1: A single intramuscular injection of 9-hydroxy-risperidone palmitate depot preparation to schizophrenic subjects: a pilot trial for pharmacokinetic and safety evaluation
- ③ BEL-2: Single-dose pharmacokinetics, tolerability and safety of two intramuscular depot formulations of 9-hydroxy-risperidone palmitate (R092670) in schizophrenic subjects
- ④ BEL-4: An open, multiple-dose trial in chronic schizophrenic subjects to explore the pharmacokinetics, tolerability and safety following 4-6 consecutive monthly intramuscular

injections of a depot formulation of 9-hydroxy-risperidone palmitate

- ⑤ BEL-7: Open, multiple dose trial in 60 schizophrenic subjects exploring the pharmacokinetics, tolerability and safety following various dosing regimens of 9-hydroxy-risperidone palmitate (R092670) i.m.
- ⑥ INT-11: Double-blind, multiple-dose study in schizophrenic volunteers exploring the comparative pharmacokinetics, tolerability and safety following i.m. injections of paliperidone palmitate (R092670) originating from 2 different production methods
- ⑦ INT-12: Pharmacokinetics, tolerability and safety of 9-hydroxy-risperidone after a single intramuscular injection of the depot formulation of 9-hydroxy-risperidone in schizophrenic volunteers
- ⑧ PSY-1001: Open-Label, Parallel, Randomized, Multiple-Dose Pharmacokinetic Study of Paliperidone After Intramuscular Injection of Paliperidone Palmitate in the Deltoid or Gluteal Muscle in Subjects With Schizophrenia
- ⑨ PSY-1002: Open-Label, Parallel, Randomized Study to Explore the In Vitro/In Vivo Correlation of Paliperidone Palmitate Long-Acting Formulations and the Comparability of the F011 and F013 Formulations in Subjects With Schizophrenia
- ⑩ USA-3: Pharmacokinetics, Tolerability, and Safety of Paliperidone After Repeated Intramuscular Injection of Paliperidone Palmitate (R092670) in the Arm or the Buttock of Subjects With Schizophrenia
- ⑪ PALM-JPN-1: A single dose study of JNS010 in patients with schizophrenia

2) 치료적 탐색 임상시험

- ① SCH-201(2/3상): A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of 50 and 100 mg eq. of Paliperidone Palmitate in Subjects With Schizophrenia
- ② PALM-JPN-2(1/2상): A repeated dose study of JNS010 in patients with schizophrenia

3) 치료적 확증 임상시험

- ① PSY-3001: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Evaluating Paliperidone Palmitate in the Prevention of Recurrence in Subjects With Schizophrenia
- ② PSY-3002: A Randomized, Double Blind, Parallel-Group Comparative Study of Flexibly Dosed Paliperidone Palmitate (25, 50, 75, or 100 mg eq.) Administered Every 4 Weeks and Flexibly Dosed RISPERDAL® CONSTA® (25, 37.5, or 50 mg) Administered Every 2 Weeks in Subjects With Schizophrenia
- ③ PSY-3003: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (50 mg eq., 100 mg eq., and 150 mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia
- ④ PSY-3004: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (25 mg eq., 50 mg eq., and 100 mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia
- ⑤ PSY-3005: A Randomized, Crossover Study to Evaluate the Overall Safety and Tolerability of Paliperidone Palmitate Injected in the Deltoid or Gluteus Muscle in Subjects With Schizophrenia
- ⑥ PSY-3007: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Response

Study to Evaluate the Efficacy and Safety of 3 Fixed Doses (25 mg eq., 100 mg eq., and 150 mg eq.) of Paliperidone Palmitate in Subjects With Schizophrenia

나. 가교자료 : 가교임상보고서(PSY-3003, PSY-3007, PSY-3001), 가교자료설명서

7. 외국의 사용현황 등에 관한 자료

8. 국내 유사제품과의 비교검토 및 당해 의약품등의 특성에 관한 자료