

구연 9

## Multiple-Dose Applications of Rotigotine Transdermal Patch to Evaluate the Pharmacokinetics, Safety, and Tolerability In Healthy Subjects

김보형, 임경수, 김재우, 김민걸, 김태은, 정용주, 유경상, 신상구, 장인진

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**Background:** Rotigotine, a non-ergolinic D3/D2/D1 dopamine receptor agonist is developed as a once-daily transdermal patch for the treatment of Parkinson's disease and Restless Legs Syndrome. The objective was to determine the pharmacokinetic characteristics, safety and tolerability of repeated-dose applications of the rotigotine transdermal patch in healthy young male and female Korean subjects.

**Methods:** This was a randomized, double-blind, placebo-controlled, multiple-dose study. Forty-eight healthy Korean subjects (24 male and 24 female) were randomized to either rotigotine or placebo treatment (20 rotigotine and 4 placebo per gender). All subjects were hospitalized from Day -1 until Day 9 at the Clinical Trials Center. Rotigotine patches were applied daily with a dose of 2 mg/24 h from Days 1 to 3 followed by 4 mg/24 h from Days 4 to 6. Serial blood and urine samples were collected for determination of rotigotine and its metabolites from Days 1 to 9. Safety and tolerability were evaluated by adverse events (AE), ECG, vital signs including orthostatic measurements, and clinical laboratory results.

**Results:** Approximately 50% of the total drug content was delivered to the skin within 24 h. For rotigotine, the geometric mean AUC<sub>0-24h,ss</sub> were 5.88 and 13.74 ng\*h/mL and C<sub>max,ss</sub> were 0.35 and 0.84 ng/mL during treatment with rotigotine 2 mg/24 h and 4 mg/24 h, respectively. The mean terminal elimination half-life of rotigotine was 5h and total body clearance of rotigotine was about 12 L/h/kg. Common AEs reported in rotigotine-treated subjects included nausea, headache and dizziness, which are typical dopaminergic side effects. No clinically significant mean changes were observed in systolic blood pressure (BP) or diastolic BP, ECG and laboratory assessments.

**Conclusion:** Rotigotine PK parameters AUC<sub>0-24h,ss</sub> and C<sub>max,ss</sub> values increased with dose. Repeated daily application of rotigotine transdermal patch was safe and well tolerated in healthy subjects.