Single- and Multiple-dose Pharmacokinetics of KP415, a Novel d-Methylphenidate Product Containing a Prodrug of d-Methylphenidate, in Healthy Adult Volunteers

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BACKGROUND

KP415 is an investigational ADHD product containing a novel prodrug of d-methylphenidate. d-MPH (d-methylphenidate) is a 32-carbon molecule.

KP415 has been designed to provide both a rapid onset of d-MPH as well as sustained d-MPH concentrations throughout the day as sustained d-MPH concentrations throughout the day

METHODS

Study design and subjects

This was a Phase 1, double-blind, single- and multiple-dose, randomized, parallel pharmacokinetic study evaluating oral solutions with different ratios of d-MPH API and prodrug compared with Concerta, in healthy adult volunteers (N=48) under fasted conditions.

Enrolled subjects (12 per treatment group) were randomized to receive oral solutions, or one Concerta tablet each day for 7 days. Oral KP415 solutions were administered containing d-MPH API/prodrug ratios (each component expressed as % of total dose) of approximately 25%, 30%, 35%, and 40%. The total API equivalent dose was 40 mg.

- Treatment A: 5.04 mg d-MPH API/prodrug (25%:75% ratio) - Treatment B: 12.56 mg d-MPH API/prodrug (30%:70% ratio) - Treatment C: 16.48 mg d-MPH API/prodrug (35%:65% ratio) - Treatment D: 54 mg Concerta tablet

RESULTS

Pharmacokinetic Findings for d-MPH

Figure 1-3 show single-dose (Day 1) and multiple-dose (Day 7) pharmacokinetic profiles of KP415-determined d-MPH plasma concentrations. Following administrations of d-MPH API/prodrug, d-MPH plasma concentrations increased rapidly and exhibited a single peak at approximately 1.5 to 2 hours post-dose for Concerta and 4.5 hours post-dose when compared with Concerta.

Figure 4 shows that exposure to intact prodrug peaked at approximately 2 hours post-dose and was highest eliminated by 4 hours post-dose. Accumulation of intact prodrug at steady-state (Dose 7 vs. Dose 1) was 24% for Concerta, 48% for KP415, 80% for KP415, 12/56 mg, and 16/48 mg d-MPH API/KP415 prodrug, and 34 mg Concerta tablet.

Adverse Events

Pharmacokinetic Findings for Intact Prodrug

No marked differences in demographic or baseline characteristics were determined between the four treatment groups. Over the course of the study, 8/64 mg (15.5 ng/mL), 12/56 mg (20.9 ng/mL), and 16/48 mg d-MPH API/KP415 prodrug, and 34 mg Concerta tablet.

Support

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