Human Abuse Potential of Oral Serdexmethylphenidate (SDX), a Novel Prodrug of d-Methylphenidate, Compared to Focalin® XR and Phentermine in Stimulant Abusers

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BACKGROUND

Serdexmethylphenidate (SDX) is a novel prodrug of d-Methylphenidate (d-MPH) that is currently under development as the major active pharmaceutical ingredient (API) in KP415, an investigational product for the treatment of ADHD.

Unlike MPH, SDX is not a Schedule II drug because it is converted to d-MPH, a process which occurs efficiently after oral administration without the need for N-demethylation. SDX does not produce any discernable pharmacodynamic effects until it is converted to d-MPH, a process which occurs efficiently after oral administration without the need for N-demethylation.

METHODS

Study Design and Subjects

This was a Phase I, randomized, double-blind, single-dose, 3-active-drug, 3-placebo treatment, randomized, 2-way crossover study comparing placebo, Focalin® XR (XR, 80 mg), and SDX (120 mg and 240 mg). Subjects were not previously treated with MPH (Schedule II) or SDX (an investigational drug).

Eligible subjects were recreational stimulant users between 18 and 50 years of age who had >10 lifetime experiences with any stimulant (e.g., cocaine, amphetamines, MPH), had used any stimulant for non-prescribed reasons within the last 12 months, had used alcohol within 6 months prior to screening, and had used marijuana within 6 months prior to screening.

24 subjects were randomized to receive Focalin® XR (80 mg), SDX 120 mg (B), and SDX 240 mg (D). Subjects were treated with 6 treatment arms: two doses of SDX and placebo.

Pharmacodynamic Assessments and Statistical Analyses

Primary outcomes included the percentage of subjects with positive cut points on the primary endpoint that showed greater Drug Liking compared to 120 mg SDX and 240 mg SDX at least 10 points higher than placebo.

Safety

Analysis of variance (ANOVA), analysis of covariance (ANCOVA), and mixed-effects models were used to analyze continuous safety data. For discrete adverse events, Fisher’s Exact test was used. For treatment-emergent adverse events occurring in ≥20% of subjects in Treatment D, statistical comparison was made to Focalin® XR and phentermine.

RESULTS

Drug Liking VAS scores that did not exceed 60 at any individual time point assessed by ANOVA with treatment (D, B, A) and time (4, 5, 6, 7, 8, 10, 12, 14, 16, and 24 hours post-dose) as factors. For endpoints that were not normally distributed, treatment differences were analyzed using one-sided hypothesis tests at a significance level of α=0.05 and reported with two-sided 95% CIs. For the absolute abuse potential comparisons, although the difference in mean Emax score between SDX and placebo was <11 points, the differences were not statistically significant in the primary endpoint.

CONCLUSIONS

- Overall SDX produced a gradual onset of abuse-related effects and maximal effects for the primary endpoint and other endpoints were generally significantly lower (Schedule III vs Schedule II stimulant).

- These data suggest that SDX may have lower oral abuse potential (relative to other available stimulant products).

- SDX produced fewer stimulant-like adverse effects compared to Focalin® XR and no new AEIs were identified with subsequent dosing.

Disclosures

PB, SD, TCM, and ASK are employees and shareholders of KemPharm, Inc. BS is an employee of KemPharm, Inc., Celebration, FL. KemPharm, Inc. is a wholly-owned subsidiary of Royalty Pharma, Inc. Rhoads-Tregear, C.G. and Kumpfer, L.K. have received research support from KemPharm, Inc.

References


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