SHP465 Mixed Amphetamine Salts in the Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents: Results of a Randomized, Double-Blind Placebo-Controlled Study

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ABSTRACT

Objective:
The aim of this study was to evaluate the efficacy, safety, and tolerability of SHP465 mixed amphetamine salts (MAS) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods:
This randomized, double-blind dose-optimization study enrolled children and adolescents (6–17 years) meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision ADHD criteria and having baseline ADHD Rating Scale IV (ADHD-RS-IV) total scores ≥28. Participants were randomized 1:1 to placebo or dose-optimized SHP465 MAS (12.5–25 mg) for 4 weeks. Total score change (baseline to week 4) on the ADHD-RS-IV (primary endpoint) and the Clinical Global Impressions-Improvement (CGI-I) scale score at week 4 (key secondary endpoint) were assessed using linear mixed-effects models for repeated measures. Safety and tolerability assessments (secondary endpoints) included treatment-emergent adverse events (TEAEs) and vital sign changes.

Results:
Of 264 randomized participants (placebo, n = 132; SHP465 MAS, n = 132), 234 (placebo, n = 118; SHP465 MAS, n = 116) completed the study. The least squares mean (95% confidence interval) treatment difference significantly favored SHP465 MAS over placebo for ADHD-RS-IV total score change from baseline to week 4 (−9.9 [−13.0, −6.8]; p < 0.001; effect size = 0.80) and CGI-I score at week 4 (−0.8 [−1.1, −0.5]; p < 0.001; effect size = 0.65). TEAE frequency was 46.6% (61/131) with placebo and 67.4% (89/132) with SHP465 MAS; no serious TEAEs were reported. TEAEs reported at a frequency of ≥5% and ≥2 times the placebo rate were decreased appetite, insomnia, irritability, nausea, and decreased weight. Mean ± standard deviation increases (baseline to final on-treatment assessment) were higher with SHP465 MAS than placebo for pulse (5.7 ± 11.78 vs. 0.7 ± 10.79), systolic blood pressure (3.8 ± 9.15 vs. 2.1 ± 8.72), and diastolic blood pressure (4.0 ± 8.23 vs. 0.5 ± 7.45).

Conclusions:
SHP465 MAS demonstrated superiority over placebo in improving ADHD symptoms and global functioning in children and adolescents with ADHD. The safety and tolerability profile of SHP465 MAS was consistent with that of SHP465 MAS in adults and other long-acting psychostimulants in children and adolescents.