The Efficacy and Safety of Evekeo, Racemic Amphetamine Sulfate, for Treatment of Attention-Deficit/Hyperactivity Disorder Symptoms: A Multicenter, Dose-Optimized, Double-Blind, Randomized, Placebo-Controlled Crossover Laboratory Classroom Study

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Objective: The study goal was to determine the efficacy and safety of an optimal dose of Evekeo, racemic amphetamine sulfate, 1:1 d-amphetamine and l-amphetamine (R-AMPH), compared to placebo in treating children with attention-deficit/hyperactivity disorder (ADHD) in a laboratory classroom setting.

Methods: A total of 107 children ages 6–12 years were enrolled in this multicenter, dose-optimized, randomized, double-blind, placebo-controlled crossover study. After 8 weeks of open-label dose optimization, 97 subjects were randomized to 2 weeks of double-blind treatment in the sequence of R-AMPH followed by placebo (n=47) or placebo followed by R-AMPH (n=50). Efficacy measures included the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) Rating Scale and Permanent Product Measure of Performance (PERMP) administered predose and at 0.75, 2, 4, 6, 8, and 10 hours postdose on 2 laboratory classroom days. Safety assessments included physical examination, chemistry, hematology, vital signs, and treatment-emergent adverse events (TEAEs).

Results: Compared to placebo, a single daily dose of R-AMPH significantly improved SKAMP-Combined scores (p<0.0001) at each time point tested throughout the laboratory classroom days, with effect onset 45 minutes postdose and extending through 10 hours. R-AMPH significantly improved PERMP number of problems attempted and correct (p<0.0001) throughout the laboratory classroom days. During the twice-daily dose-optimization open-label phase, improvements were observed with R-AMPH in scores of the ADHD-Rating Scale IV and Clinical Global Impressions Severity and Improvement Scales. TEAEs and changes in vital signs associated with R-AMPH were generally mild and not unexpected. The most common TEAEs in the open-label phase were decreased appetite (27.6%), upper abdominal pain (14.3%), irritability (14.3%), and headache (13.3%).

Conclusions: Compared to placebo, R-AMPH was effective in treating children aged 6–12 years with ADHD, beginning at 45 minutes and continuing through 10 hours postdose, and was well tolerated.