Optimization of Methylphenidate Extended-Release Chewable Tablet Dose in Children with ADHD: Open-Label Dose Optimization in a Laboratory Classroom Study

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Abstract

Objective:
To examine methylphenidate extended-release chewable tablets (MPH ERCT) dose patterns, attention-deficit/hyperactivity disorder (ADHD) symptom scores, and safety during the 6-week, open-label (OL) dose-optimization period of a phase 3, laboratory classroom study.

Methods:
Boys and girls (6–12 years) diagnosed with ADHD were enrolled. MPH ERCT was initiated at 20 mg/day; participants were titrated in 10–20 mg/day increments weekly based on efficacy and tolerability (maximum dose, 60 mg/day). Dose-optimization period efficacy assessments included the ADHD Rating Scale (ADHD-RS-IV), analyzed by week in a post hoc analysis using a mixed-effects model for repeated measures with final optimized dose (20, 30/40, or 50/60 mg), visit, final optimized dose and visit interaction, and baseline score as terms. Adverse events (AEs) and concomitant medications were collected throughout the study.

Results:
Mean MPH ERCT daily dose increased weekly from 29.4 mg/day after the first dose adjustment at week 1 (n = 90) to 42.8 mg/day after the final adjustment at week 5 (n = 86). Final optimized MPH ERCT dose ranged from 20 to 60 mg/day. Mean final optimized MPH ERCT dose ranged from 40.0 mg/day in 6–8 year-old participants to 44.8 mg/day for 11–12 year-old participants. There was a progressive decrease in mean (standard deviation) ADHD-RS-IV total score from 40.1 (8.72) at baseline to 12.4 (7.88) at OL week 5, with similar improvement patterns for hyperactivity/impulsivity and inattentiveness subscale scores. Participants optimized to MPH ERCT 50/60 mg/day had a significantly higher mean (standard error) ADHD-RS-IV score at baseline compared with participants optimized to MPH ERCT 20 mg/day (42.4 [1.34] vs. 35.1 [2.55]; p = 0.013). Treatment-emergent AEs were reported by 65/90 (72.2%) participants in the dose-optimization period.

Conclusions:
Dose-optimization period results describing relationships between change in ADHD symptom scores and final optimized MPH ERCT dose will be valuable for clinicians optimizing MPH ERCT dose.