Single-Dose Pharmacokinetic Properties and Relative Bioavailability of a Novel Methylphenidate Extended-Release Chewable Tablet Compared With Immediate-Release Methylphenidate Chewable Tablet

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Abstract

Purpose
A novel methylphenidate hydrochloride extended-release chewable tablet (MPH ERCT) was developed to potentially address an unmet need for patients with attention-deficit/hyperactivity disorder, especially children, who cannot or will not swallow tablets or would prefer the convenience of a chewable tablet. This randomized, open-label, crossover trial compared the pharmacokinetic properties and relative bioavailability of MPH ERCT with an MPH chewable immediate-release tablet (IR MPH) formulation in healthy adults.

Methods
Healthy men and women 18 to 55 years of age were randomly assigned to MPH ERCT 40 mg or 40 mg IR MPH administered in 2 equal doses of 20 mg 6 hours apart with a 7-day washout period. Plasma concentrations of MPH at selected time points up to 24 hours were measured, and pharmacokinetic parameters were determined using a noncompartmental approach in the SAS (Version 9.2) PROC general linear model procedure.

Findings
A total of 33 participants were enrolled in the study; 31 participants were included in the pharmacokinetic analysis. The exposure ratios for MPH ERCT and IR MPH (MPH ERCT/IR MPH) for area under the analyte concentration versus time curves (AUC) from time zero to the last measurable analyte concentration (AUC0–last) (87.64%; 95% CI, 84.96–90.41) and AUC0–∞ (89.11%; 95% CI, 86.57–91.73) were within the standard 80% to 125% bioequivalence acceptance criteria. Mean Cmax for MPH ERCT and IR MPH was 12.51 ng/mL and 15.57 ng/mL, respectively; mean time to Cmax was 4.16 hours and 6.43 hours, respectively. The mean Cmax of MPH ERCT was 80% of the Cmax of IR MPH due to a higher peak concentration that occurs after the second dose of IR MPH. All adverse events were mild in severity.

Implications
The relative bioavailability of MPH ERCT 40 mg, based on the exposure (AUC), was comparable to that of IR MPH 40 mg administered in 2 equal doses of 20 mg 6 hours apart. Both formulations were generally well tolerated.