A Single-Dose, Single-Period Pharmacokinetic Assessment of an Extended-Release Orally Disintegrating Tablet of Methylphenidate in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder


ABSTRACT

Objective:
To determine the pharmacokinetic (PK) profile of a proprietary formulation of methylphenidate (MPH) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) in a phase 1 study. Methylphenidate extended-release orally disintegrating tablets (MPH XR-ODTs) combine two technologies in a single-tablet formulation—an extended-release profile that was designed for once-daily dosing in an ODT that does not require water or chewing for ingestion.

Methods:
This was a single-dose, open-label, single-period, single-treatment study, in which 32 children with ADHD who were receiving MPH in doses of 40 or 60 mg before beginning the study each received a 60-mg dose (2 × 30 mg) of MPH XR-ODT. The following plasma PK parameters of MPH were determined for participants grouped by age (6–7, 8–9, 10–12, and 13–17 years old): maximum concentration (Cmax), time to maximum concentration (Tmax), elimination half-life (T½), area under the curve from 0 hours to infinity (AUCinf), oral clearance (CL/F), and volume of distribution in the terminal phase (Vz/F). Safety and tolerability were also assessed.

Results:
A total of 32 participants received the study drug. For all participants, plasma concentration–time profiles of MPH exhibited a broad peak after administration of MPH XR-ODT through ~8 hours, indicating extended release from the formulation, followed by an apparent first-order elimination phase. As age increased, MPH exposure decreased and mean estimates of CL/F increased; however, weight-normalized CL/F values were comparable across age groups. Similarly, mean estimates of Vz/F increased with age, but weight-normalization decreased differences across age groups, with the exception of the youngest age group, which had higher values. All adverse events (AEs) were mild.

Conclusion:
This XR-ODT formulation of MPH demonstrated weight-normalized clearance rates that were consistent across all age groups, a PK profile consistent with once-daily dosing, and an AE profile consistent with this class of medication in children and adolescents with ADHD.