Population Pharmacokinetic-Pharmacodynamic Modeling of a Novel Methylphenidate Extended-Release Orally Disintegrating Tablet in Pediatric Patients With Attention-Deficit/Hyperactivity Disorder

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Abstract

PURPOSE/BACKGROUND:
A methylphenidate (MPH) extended-release orally disintegrating tablet (MPH XR-ODT) formulation was recently approved for attention-deficit/hyperactivity disorder treatment in children 6 to 17 years of age. This analysis sought to develop a population pharmacokinetic (PK)/pharmacodynamic (PD) model to describe MPH XR-ODT PD-response data in a classroom study and use the model to simulate PD responses for a range of body weights and doses.

METHODS/PROCEDURES:
The MPH XR-ODT PK/PD model was developed with pediatric and adult PK data from prior studies and efficacy data from a laboratory classroom study in children with attention-deficit/hyperactivity disorder. In these studies, the safety profile of MPH XR-ODT was consistent with other extended-release MPH formulations. The PK/PD model efficacy end point was the Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale Combined score. Body weight effects on MPH clearance and volume of distribution were included in the resulting model. Simulations using the PK/PD model were performed for patients with body weights between 7 and 100 kg and MPH XR-ODT doses of 10 to 60 mg MPH hydrochloride equivalents.

FINDINGS/RESULTS:
In the PK/PD model, the maximal reduction in the Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale Combined score was approximately 38 units, and the MPH concentration required to achieve 50% of the maximal reduction was 14.24 ng/mL, suggesting favorable efficacy for MPH XR-ODT. Simulations showed a direct correlation between the effective MPH XR-ODT dose and body weight, with heavier participants requiring higher doses for symptom control.

IMPLICATIONS/CONCLUSION:
This model may help facilitate the dose-titration process by identifying an effective MPH XR-ODT target dose.