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Population Pharmacokinetic (PPK) Modeling of Vilazodone in Adolescent Patients with Major Depressive Disorder (MDD)

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Objectives: To confirm the doses for adolescent patients (12-17 years) with MDD and to recommend doses for younger children (7-11 years) to be used in the forthcoming efficacy and safety study in pediatric patients 7-17 years of age. To determine the additional number of serially sampled subjects, if any, needed to meet FDA requirements for PK parameter precision.

Methods: The vilazodone PPK model previously developed for adult patients was applied to the interim data collected from adolescent patients in an ongoing double-blind placebo-controlled efficacy/safety study in pediatric patients with MDD. To stabilize the parameter estimation, the PK parameter estimates from an adult PPK model and their corresponding uncertainties were used as informative priors.

Results: The PPK model for adolescents was developed using the interim data from 26 patients with rich and 59 patients with sparse sampling. The adult PPK model provided an adequate structural fit for the adolescent data. Pediatric doses of 15 and 30 mg/day for 7-17 year olds were predicted to result in exposures that were within 25% of the adult median exposures following doses of 20 and 40 mg/day. For 40 mg/day, the median adult AUCss was estimated to be 1281 ng*h/L, as compared to 1413 and 1127 ng*h/L for 7-11 and 12-17 year olds, respectively. The power analysis found that the rich PK samples already collected in 12-17 year olds provided adequate precision and that further rich PK sampling in younger patients was not neccessary.

Conclusions: The interim adolescent data was successfully modeled using a parameter prior approach; CL/F and Vc/F were estimated with high precision. Reducting the adult dose by 25% was found to be adequate for 7-17 year olds. The completed study is expected to meet FDA's precision requirement with high power (95% CIs for CL/F and V/F to be within 0.6-1.4 of the geometric mean).