Pediatric Extrapolation of Efficacy in Partial Seizures
Regulatory Perspective

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- The views expressed in this presentation do not necessarily represent the policies of the Food and Drug Administration or the Department of Health and Human Services.
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Extrapolation of Efficacy from Adults to Children

FDA may extrapolate pediatric effectiveness from adults if the following is established:

- Similar pathophysiology and disease course in children and adults
- Evidence that adults and children have a sufficiently similar exposure-response relationship

PEACE initiative

- Extrapolation of efficacy from adults to pediatric patients for adjunctive therapy of partial onset seizures (POS) in patients 4 years and older is justifiable based upon our understanding of the disease process and upon exposure-response analysis.
- Office of Clinical Pharmacology (OCP), in consultation with the Division of Neurology Products (DNP), performed careful exposure-response analyses that compared pediatric patients to adult patients.

Pediatric Extrapolation

Efficacy might be extrapolated from adults to children but not pharmacokinetics (PK) and safety

With the understanding of similar pathophysiology and exposure-response, the following is still required for a pediatric indication for treatment of POS :

- Approved indication for the treatment of POS in adults.
- A pharmacokinetic analysis to determine the dosing regimen that provides similar drug exposure (at levels demonstrated to be effective in adults) in pediatric patients 4 years of age and older compared to adult patients with POS. This analysis will require pharmacokinetic data from both the adult and pediatric (4 years of age and older) populations.
- Long-term open-label safety study(ies) in pediatric patients 4 years of age and older.

Pediatric Safety Studies

- Safety from adults may provide some information, but it is not definitive for pediatric population
- Safety should be assessed in pediatric population with condition of interest

Short-term Safety from Placebo- Controlled Study

- If efficacy extrapolation is accepted, there will be no pediatric placebo-controlled efficacy and safety trial
- A placebo comparator arm helps to distinguish AEs attributable to the test drug from AEs attributable to background rate, concomitant drugs, or the underlying seizure disorder.
- Safety from adult studies may provide some information
- Experience to date suggests that short-term AEs in the pediatric patient population are generally similar to those detected in the adult studies

Long-term Safety from Adult and Pediatric Open Label Studies

We require an adequate amount of long- term open label safety experience in both adult and pediatric patients (age 4 years and older) with partial seizures.