CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS BPCA SUMMARY

NDA:	21-014/SE5-013	**SUBMISSION DATES:** December 13, 2004
	21-285/SE5-008	March 17, 2005
DRUG NAME:	Trileptal® (Oxcarbazepine)	March 29, 2005
DOSAGE STRENGTH:	Tablets (150, 300, 600 mg), oral suspension (60mg/mL)	
APPLICANT:	Novartis	
REVIEWER:	John Duan, Ph.D.	
TEAM LEADERS:	Ramana Uppoor, Ph.D., Jogarao Gobburu, Ph.D. (Pharmacometrics)	
TYPE OF SUBMISSION:	Pediatric supplement in response to pediatric written request	

EXECUTIVE SUMMARY

Trileptal is indicated as monotherapy and adjunctive therapy for the treatment of partial seizures in adults and in children 4-16 years of age. The current submission is in response to the Agency's formal Written Request of February 28, 2000, which requested the sponsor to conduct studies with oxcarbazepine in pediatric patients between the ages of 1 month to 16 years of age. The sponsor conducted one monotherapy trial (study 2339) and one adjunct therapy trial (study 2340) in pediatric patients with ages between 1 month and 16 years. While the monotherapy trial failed the primary endpoint, the adjunct therapy trial was successful. Comparison of results across trials indicated strongly that the monotherapy study 2339 was not adequately designed and conducted. The major deficiencies include the short duration of the study and lack of documentation of seizure rate at baseline. These deficiencies render the study results uninterpretable. However, this study did provide information for comparison of PK between children and adults. Adjunctive therapy study 2340 was a positive trial. Comparison between the current and previous studies indicates that similar concentrations are achieved among different studies. The dosing utilized in the pediatric adjunctive therapy study is considered adequate. Given the higher body weight adjusted clearance in 1 month to <4 years old children, a higher mg/kg dose should be considered in children with body weight under 20 kg. Considering the difficulties and ethical issues in conducting monotherapy in children, coupled with clinical experience in adjunctive therapy in children 1 month to <4 years old, a PK/PD bridging approach is recommended for monotherapy in this pediatric population.

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