

## Statistical Review Memo for NDA Submission

NDA/Ser: 20406/S067  
Drug: Lansoprazole Oral Suspension (Prevacid)  
Sponsor: TAP Pharmaceutical Products  
Indication: Treatment of symptomatic GERD in infants  
Statistical Reviewer: Mike Welch, PhD, DBIII  
Medical Team: Ali Niak, MD, Ruyi He, MD, TL, DGP  
Project Manager: Matthew Scherer, DGP  
Documents reviewed: Study report and supporting documents for Clinical Study  
P-GI05-109, Efficacy and Safety Evaluation of Pediatric Patients  
1 to 11 Months of Age (\\Cdsesub1\evsprod\NDA020406\0042)  
Letter date: April 25, 2008  
PDUFA date: October 28, 2008

### Background

TAP Pharmaceutical Products is requesting Pediatric Exclusivity for lansoprazole (NDA's 20-406, 21-281 and 21-428) under Section 505A of the Food Drug and Cosmetic Act. As required by the Agency's Written Request (Amendment #4) dated September 6, 2005, TAP claims to have completed all required clinical studies, formulation requirements, non clinical studies and literature reviews. This current submission provides additional clinical and non clinical study reports, literature reviews, drug information and proposed labeling.

Part C of the Written Request (WR) directed the sponsor to conduct an efficacy and safety evaluation of lansoprazole in infants, 1 to 11 months of age for the treatment of symptomatic GERD. According to the WR, the study design was to be either a multi-center, randomized withdrawal study or a parallel group, placebo controlled study. The study was to be adequately powered to provide clinically meaningful comparisons of GERD symptoms and other related parameters between treatment regimens.

### Study Overview

To comply with the WR, the sponsor conducted Study P-GI05-109 to assess the safety and efficacy of once-daily administration of lansoprazole pediatric suspension in infants with symptomatic GERD. This was a double-blind, multi-center, randomized, placebo-controlled study at 16 investigative sites in the U.S. and Poland. The study enrolled 162 subjects; efficacy was assessed using data from daily symptom diaries and global symptom assessments made by the parent or primary caregiver. The primary efficacy analysis was a comparison of proportions of treatment responders, where responders were required to have at least 50% reduction from baseline in number or duration of feedings with crying/fussing/irritability episodes.

The clinical trial study report concludes that there was no difference between the lansoprazole pediatric suspension and placebo groups in improvement of GERD symptoms. For the primary endpoint, 44/81 (54.32%) was observed for both lansoprazole and placebo groups ( $p = 1.0$ ). No significant differences were observed for any secondary endpoints, and several sensitivity and subgroup analyses performed by the sponsor were likewise inconclusive. With regard to labeling for this study population, the sponsor intends to add the following statement: *PREVACID was not effective in patients less than 1 year of age in a multi-center, double-blind, placebo controlled study.*

### Reviewer Summary

I reviewed the clinical trial report, protocol and amendments, and the statistical analysis plan and concur that the study design and statistical methods were adequate and met the requirements of the WR. The sponsor did not provide electronic data sets, but since the sponsor is not claiming efficacy based on this study, an independent analysis of study data is not warranted. Reasons for failure of the study to show efficacy are not clear but are likely related to lack of assay sensitivity of the endpoint. I concur with the sponsor's proposed labeling statement.

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Mike Welch  
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