

**ADDENDUM
CLINICAL REVIEW**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 19, 2009

SUBJECT: Update on clinical review of sNDA 22-020/S001, 002 and NDA 20-987/S036, 037 due to [REDACTED] (b) (4)

DRUG: Protonix (Pantoprazole Sodium) For Delayed Release Oral Suspension and Delayed Release Tablets

Background

On November 21, 2008, Wyeth submitted an efficacy supplement (S-001) for Protonix (pantoprazole sodium) For Delayed-Release Oral Suspension and Protonix (pantoprazole sodium) Delayed-Release Tablets. This SE-5 supplement was submitted in response to a Pediatric Written Request dated December 31, 2001, and finally amended on May 17, 2007. The efficacy supplement was for the short-term treatment of GERD in pediatric patients 1 to 16 years of age.

On August 10, 2009, my clinical review of this submission was entered into DARRTS. In this review, I recommended approval of Protonix for Delayed-Release Oral Suspension for the short-term treatment (up to eight weeks) of erosive esophagitis (EE) associated with gastroesophageal reflux disease (GERD) for pediatric patients age 1 year through 5 years. I also recommended approval of Protonix Delayed-Release Tablets for the short-term treatment of EE associated with GERD for pediatric patients age 5 years through 16 years. This recommendation was based on extrapolation of efficacy from the adult indication as the pathophysiology of EE associated with GERD is believed to be the same in adults and pediatric patients older than one year. There were also sufficient pharmacokinetic (PK) and pharmacodynamic (PD) studies and evidence of safety provided by three clinical trials to support this indication and to provide adequate directions for use.

As outlined in my original review, Wyeth currently markets a 40 mg granule formulation referred to as the Nycomed granules for adult patients unable to take the tablet form. Although the pediatric studies used a different granule formulation, referred to as the Wyeth granules, [REDACTED] (b) (4)

(b) (4)

Revised Recommendation on Regulatory Action

My review of the submitted data concludes that the safety and effectiveness of PROTONIX for short-term treatment (up to eight weeks) of erosive esophagitis (EE) associated with GERD have been established in pediatric patients 1 year through 16 years of age. However, for patients 1 year to 5 years of age, there is no appropriate dosage strength in an age-appropriate formulation available (b) (4). As I am unable to create dosing instructions for EE patients 1 year to 5 years of age if a product does not exist, I recommend that PROTONIX be indicated for the short-term treatment (up to 8 weeks) in the healing and symptomatic relief of erosive esophagitis only in adults and pediatric patients five years of age and older. I recommend that we continue to use the 15 kg minimum weight cut-off as a reference with the weight-based dosing as this is the lowest 5% weight range for five year-old females. In the labeling, patients and practitioners should be cautioned that the 40 mg PROTONIX For Delayed-Release Oral Suspension packet should not be divided to create a 20 mg dosage form, as the granules are small and the total volume of drug in a 40 mg packet is too little to divide accurately.

Revised Post-Marketing Commitments

(b) (4)

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|-------------------------|------------------------|----------------------------------|---------------------------------------------|
| NDA-20987 | SUPPL-36 | WYETH PHARMACEUTICA LS INC | PROTONIX (PANTOPRAZOLE SODIUM) 40MG ENTE |
| NDA-20987 | SUPPL-37 | WYETH PHARMACEUTICA LS INC | PROTONIX (PANTOPRAZOLE SODIUM) 40MG ENTE |
| NDA-22020 | SUPPL-1 | WYETH PHARMACEUTICA LS INC | PROTONIX DELAYED RELEASE GRANULES |
| NDA-22020 | SUPPL-2 | WYETH PHARMACEUTICA LS INC | PROTONIX DELAYED RELEASE GRANULES |

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/s/

II-LUN CHEN
10/19/2009

JOHN E HYDE
10/20/2009