



NDA 20-987/S-001
NDA 20-987/S-002

Wyeth-Ayerst Laboratories
Attention: Caroline Henesey, Ph.D.
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Henesey,

Please refer to your supplemental new drug application dated June 12, 2000, received June 12, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PROTONIX[®] (pantoprazole sodium) Delayed-Release Tablets, 40 mg.

This supplemental new drug application was administratively split as follows:

- Supplement number-001, proposes the use of PROTONIX[®] (pantoprazole sodium) Delayed-Release Tablets for the following new indication: Maintenance of Healing of Erosive Esophagitis and control of daytime and nighttime heartburn symptoms in patients with gastroesophageal reflux disease (GERD).
- Supplement number-002 proposes to market a 20-mg PROTONIX[®] Delayed-Release Tablet.

We acknowledge receipt of your submissions dated June 16, September 14, October 12, November 17, and December 14, 2000, and January 24, February 9, March 5 and 30, April 6 and 27, May 1, 7, 9, 10, 11, 24, 25, 31 and June 4, 6, 8, and your facsimile dated June 12, 2001.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text and with the minor editorial revisions listed below. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted draft labeling (immediate container and carton labels submitted May 24, 2001) with the following minor editorial revisions to the immediate container labels:

- Per 21 CFR 201.15, enlarge and bold the font of "Delayed Release Tablets" on the 20-mg and 40-mg immediate container labels as exemplified on the carton label. These revisions should be made to the 20-mg label prior to marketing, and to the 40-mg label at the next printing.

These revisions are terms of the approval of these applications.

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 15 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-987/S-001, S-002." Approval of these submissions by FDA is not required before the labeling is used.

Based on the stability data submitted, the 20-mg tablet configurations and expiration dates are as follows:

<i>Immediate Container (20-mg tablets)</i>	<i>Storage Conditions</i>	<i>Expiration</i>
Bottle of 90	Controlled room temperature	24 months
Carton of 10 blister strips of 10	Controlled room temperature	15 months

In addition, we request that you provide a revised stability protocol and stability data for each packaging configuration that is distributed in the next Annual Report for the NDA.

We remind you of your postmarketing study commitment in your submission dated June 8, 2001. This commitment is listed below.

1. Long-Term Prospective Observational Study of the Incidence of Cancer Among Pantoprazole Users Compared to an Appropriate Control Group.

Protocol Submission:	Within 3 months of the date of this letter
Study Start:	Within 6 months of the date of this letter
Progress Report(s):	First report within 1½ years of the date of this letter, then yearly
Final Report Submission:	Within 10½ years of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to this postmarketing study commitment must be prominently labeled "**Postmarketing Study Protocol**", "**Postmarketing Study Final Report**", or "**Postmarketing Study Correspondence**."

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We acknowledge your January 19, 2001 updated proposed pediatric study request to support the issuance of a written request for pediatric studies with pantoprazole sodium in patients 2 to 16 years of age. Your submission is under review.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

{See appended electronic signature page}

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure