



NDA 16-320/S-060

Wyeth Pharmaceuticals, Inc.
Attention: Mary Ellen Menz, R.N., MBA, JD
Manager
Worldwide Regulatory Affairs
Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Menz:

Please refer to your supplemental new drug application dated April 30, 2003, received May 1, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Myambutol[®] (ethambutol hydrochloride) Tablets, 100 mg and 400 mg.

Your submission of December 9, 2003 constituted a complete response to our October 27, 2003 letter.

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the package insert (additions are double underlined and deletions are ~~striketrough~~):

1. The following sentence was added at the end of the **CONTRAINDICATIONS** section:

MYAMBUTOL is contraindicated in patients who are known to be hypersensitive to this drug. It is also contraindicated in patients with known optic neuritis unless clinical judgment determines that it may be used. MYAMBUTOL is contraindicated in patients who are unable to appreciate and report visual side effects or changes in vision (e.g., young children, unconscious patients).

2. A new **Drug Interactions** subsection was added to the **PRECAUTIONS** section:

DRUG INTERACTIONS

The results of a study of coadministration of ethambutol (50 mg/kg) with an aluminum hydroxide containing antacid to 13 patients with tuberculosis showed a reduction of mean serum concentrations and urinary excretion of ethambutol of approximately 20% and 13%, respectively, suggesting that the oral absorption of ethambutol may be reduced by these antacid products. It is recommended to avoid concurrent administration of ethambutol with aluminum hydroxide containing antacids for at least 4 hours following ethambutol administration.

3. A new **Nursing Mothers** subsection was added to the **PRECAUTIONS** section:

Nursing Mothers

MYAMBUTOL is excreted into breast milk. The use of MYAMBUTOL should be considered only if the expected benefit to the mother outweighs the potential risk to the infant.

4. A new **Pediatric Use** subsection was added to the **PRECAUTIONS** section:

Pediatric Use

MYAMBUTOL ethambutol hydrochloride is not recommended for use in pediatric patients under thirteen years of age since safe conditions for use have not been established.

5. The **ADVERSE REACTIONS** section, was revised as follows:

ADVERSE REACTIONS

Other adverse reactions reported include: hypersensitivity, anaphylactic/anaphylactoid reactions, dermatitis, pruritus, and joint pain; anorexia, nausea, vomiting, gastrointestinal upset, and abdominal pain; fever, malaise, headache, and dizziness; mental confusion, disorientation, and possible hallucinations; thrombocytopenia, leukopenia, and neutropenia. Numbness and tingling of the extremities due to peripheral neuritis have been reported.

Elevated serum uric acid levels occur and precipitation of acute gout has been reported. Pulmonary infiltrates, ~~and~~ with or without eosinophilia, also have been reported during MYAMBUTOL therapy. Liver toxicities, including fatalities, have been reported. (See **WARNINGS**.) Since MYAMBUTOL is recommended for therapy in conjunction with one or more other antituberculous drugs, these changes may be related to the concurrent therapy.

Hypersensitivity syndrome consisting of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following: hepatitis, pneumonitis, nephritis, myocarditis, pericarditis. Fever and lymphadenopathy may be present.

We have completed the review of this application, 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 labeling text (enclosed). Accordingly, this application is 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 submitted December 9, 2003).

If a letter communicating important information about this drug product (i.e., a “Dear Health Care Practitioner” 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, please call Christine Lincoln, RN, MS, MBA, Labeling Reviewer, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Renata Albrecht
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