DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-553/S-030

Wyeth Pharmaceuticals
Attention: Ms. Diane Mitrione
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Mitrione:

Please refer to your supplemental new drug application dated December 23, 2003 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Inderal (propranolol hydrochloride) 60, 80, 120 and 160 mg LA Capsules.

This "Changes Being Effected" supplemental new drug application provides for draft labeling revised as follows:

1. The following sentence was added at the beginning of the **WARNINGS** section:

   Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, have been associated with the administration of propranolol (see "**ADVERSE REACTIONS**").

2. The following subsection was added at the end of the **WARNINGS** section:

   Skin Reactions: Cutaneous reactions, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, and urticaria, have been reported with use of propranolol (see "**ADVERSE REACTIONS**").

3. The **ADVERSE REACTIONS/Allergic** subsection has been changed from:

   Pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm, and respiratory distress.

   To:

   Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm, and respiratory distress.

4. The following subsection was added at the end of the **ADVERSE REACTIONS** section:

   Skin: Stevens-Johnson Syndrome; toxic epidermal necrolysis; exfoliative dermatitis; erythema multiforme; urticaria.

In addition, the following changes were noted in a review of the submitted labeling:

1. In the first sentence of the fourth paragraph of the **DESCRIPTION** section, hydroxypropyl methylcellulose was changed to hypromellose.

2. The first sentence of the **DOSAGE AND ADMINISTRATION** section was changed from:

   Inderal® LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily.

   To:

   Inderal® LA (propranolol hydrochloride) provides propranolol hydrochloride in a sustained-release capsule for administration once daily.

3. In the **HOW SUPPLIED** section, mention of the bottles of 1,000 and the corresponding NDC numbers have been deleted for all dosages. In addition, mention of the Unit Dose package of 100 and the corresponding NDC numbers have been deleted for the 80, 120 and 160 mg capsules.

4. In the **HOW SUPPLIED** section, the sixth paragraph has been changed from:

   The appearance of these capsules is a registered trademark of Wyeth-Ayerst Laboratories.

   To:

   The appearance of these capsules is a registered trademark of Wyeth Pharmaceuticals.

5. In the **HOW SUPPLIED** section, the storage statement has been changed from:

   Store at room temperature (approximately 25°C).

   To:

   Store at controlled room temperature 20° to 25°C (68° to 77°F).

6. The following sentence was deleted from the end of the **HOW SUPPLIED** section:

   Use carton to protect contents from light.

We have completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted December 23, 2003) with the following exceptions agreed upon by Ms. Roberta Acchione of Wyeth and Dr. Stuart Zimmerman on June 3, 2004:

1. In the **HOW SUPPLIED** section, the storage statement should read:

Store at 20-25°C (68° to 77°F)
[see USP Controlled Room Temperature]

2. The following sentence should remain at the end of the **HOW SUPPLIED** section:

   Use carton to protect contents from light.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (February 2004). The guidances specify that labeling is to be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Ms. Melissa Robb
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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