



NDA 18-031/S-032

Ayerst Laboratories
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 Inderide (propranolol hydrochloride and hydrochlorothiazide) 40/25 and 80/25 mg Tablets.

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/Propranolol hydrochloride (Inderal®)** 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/Propranolol hydrochloride (Inderal®)** 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/Propranolol hydrochloride (Inderal®)/Allergic** subsection has been changed from :

Laryngospasm and respiratory distress; pharyngitis and agranulocytosis; fever combined with aching and sore throat; erythematous rash.

To:

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

4. The following subsection was added at the end of the **ADVERSE REACTIONS/Propranolol hydrochloride (Inderal®)** section:

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

We have completed our review of this application. The 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).

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

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/s/

Norman Stockbridge
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