DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-553/S-036

Wyeth Pharmaceuticals
Attention: Brian D. Schlag, M.A., M.S.
Manager, Global Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Mr. Schlag:

Please refer to your supplemental new drug application (NDA) dated April 24, 2007, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Inderal LA 60, 80, 120, and 160 mg Capsules.

We also refer to your amendment dated July 31, 2007.

In addition to the labeling changes described in your submissions dated April 24 and July 31, 2007, in which you propose to add and delete text for consistency with the Inderal and Innopran XL labeling, this supplemental new drug application also provides for the following modifications to the labeling of Inderal LA:

1) In the **PHARMACOKINETICS AND DRUG METABOLISM** section, **Absorption** subsection of the labeling, change the following statement

From

"Administration of a standardized meal increases the bioavailability of propranolol by about 50% with no change in time to peak concentration or half-life."

To

"The effect of food on Inderal LA bioavailability has not been investigated."

2) In the **PHARMACOKINETICS AND DRUG METABOLISM** section, **Special Population Renal Insufficiency** subsection of the labeling, add the following statement after the fourth paragraph:

"Propranolol is not significantly dialyzable."

3) In the **WARNINGS** section, **Skin Reactions** subsection of the labeling, delete the following duplicative statement which comprises the paragraph before the **PRECAUTIONS** 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").

4) In the **PRECAUTIONS** section, **Drug Interactions** subsection of the labeling, delete the following statement:

"Disopyramide is a Type I antiarrhythmic drug with potent negative inotropic and chronotropic effects and has been associated with severe bradycardia, asystole and heart failure when administered with propranolol."

5) In the **PRECAUTIONS** section, **Drug Interactions** subsection of the labeling, delete the following statement:

"Certain ACE inhibitors have been reported to increase bronchial hyper-reactivity when administered with propranolol."

6) In the **PRECAUTIONS** section, **Drug Interactions** subsection of the labeling, delete the following statement:

"Administration of reserpine with propranolol may also potentiate depression."

7) In the **PRECAUTIONS** section, **Drug Interactions** subsection of the labeling, change the following statement

From

"Amiodarone is an antiarrhythmic agent with negative chronotropic properties that may be additive to those seen with propranolol."

To

"Amiodarone is an antiarrhythmic agent with negative chronotropic properties that may be additive to those seen with β-blockers such as propranolol."

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

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination.

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
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100

Rockville, MD 20852

Marketing the product with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 Dan Brum, Pharm.D., MBA, Regulatory Health Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal 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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