DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21438/S-012 **SUPPLEMENT APPROVAL**

GlaxoSmithKline
Attention: Chrystal Eve Jackson
Assistant Director, US Regulatory Affairs
One Franklin Plaza
200 North 16th Street
Philadelphia, PA 19102

Dear Ms. Jackson:

Please refer to your supplemental new drug application dated May 29, 2009, received May 29, 2009, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Innopran XL (propranolol hydrochloride) Extended Release Capsules.

This "Changes Being Effected" supplemental new drug application provides for revisions to the **CLINICAL PHARMACOLOGY**, **CONTRAINDICATIONS**, **PRECAUTIONS** and **OVERDOSAGE** sections of the label. The following changes were made:

1. In **CLINICAL PHARMACOLOGY/ Cardiovascular Drugs: Antiarrhythmics**, "Concomitant administration of propranolol with lidocaine, bupivacaine or mepivacaine has been reported to decrease the clearance of these amide anesthetics significantly, resulting in higher serum concentrations of the anesthetic." has been added to the third paragraph.

2. In **CONTRAINDICATIONS,** the first paragraph has been changed from:

   > Propranolol is contraindicated in 1) cardiogenic shock; 2) sinus bradycardia, and greater than first-degree block 3) bronchial asthma; and 4) in patients with known hypersensitivity to propranolol hydrochloride.
   >
   > To:
   >
   > Propranolol is contraindicated in 1) cardiogenic shock; 2) sinus bradycardia, sick sinus syndrome, and greater than first-degree block unless a permanent pacemaker is in place; 3) bronchial asthma; and 4) in patients with known hypersensitivity to propranolol hydrochloride.

3. In **PRECAUTIONS/Antiarrhythmics**, "(see also PRECAUTIONS, Drug Interactions, Non-Cardiovascular Drugs, Anesthetic Agents) has been added to the fifth paragraph.

4. In **PRECAUTIONS/Non-Cardiovascular Drugs: Anesthetic Agents**, "The clearance of local amide anesthetics (e.g., lidocaine, bupivacaine, mepivacaine) is reduced with administration of propranolol. Lidocaine and bupivacaine toxicity has been reported following coadministration

with propranolol. Caution should be exercised when amide anesthetic agents are administered concomitantly with propranolol." has been added to the second paragraph.

5. In **OVERDOSAGE**, "**Decontamination:** Gastric lavage and **Supportive Therapy:**" has been deleted.

6. The revision date has been updated.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text, which is identical to the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format submitted on May 29, 2009.

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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:

Lori Anne Wachter, RN, BSN
Regulatory Project Manager
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm. D.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure:
Content of Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21438	SUPPL-12	SMITHKLINE BEECHAM CORP DBA GLAXOSMITHKLINE	INNOPRAN XL 80/120MG

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

/s/

MARY R SOUTHWORTH
12/30/2009