NDA 18-303/S-033

Novartis Pharmaceuticals Corporation
Attention: Ms. Donna Vivelo
One Health Plaza
East Hanover, NJ 07936-1080

SUPPLEMENT APPROVAL

Dear Ms. Vivelo:

Please refer to your supplemental new drug application (NDA) dated February 29, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lopressor HCT (metoprolol tartrate and hydrochlorothiazide) 50/25, 100/25, and 100/50 mg Tablets.

This supplemental new drug application provides for the following revisions to the package insert:

1. To change the following section of the **WARNINGS/Lopressor/*Bronchospastic Diseases*** section:

    FROM

    ***Bronchospastic Diseases:* PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS.**

    TO

    ***Bronchospastic Diseases:* PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD, IN GENERAL, NOT RECEIVE BETA BLOCKERS, including Lopressor HCT.**

2. To change the following section of the **WARNINGS/Lopressor/*Major Surgery*** section of the PI:

    FROM

    Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy, prior to major surgery is controversial; the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

    TO

    Major Surgery: The necessity or desirability of withdrawing beta-blocking therapy, including Lopressor HCT prior to major surgery is controversial; the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

3. To change the following section of the **WARNINGS/Lopressor/*Diabetes and Hypoglycemia*** section of the PI:

FROM

Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.

TO

Beta blockers, including Lopressor HCT, may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.

4. To add the following labeling text to the **ADVERSE REACTIONS** section of the labeling:

    Post-Marketing Experience
    The following adverse reactions have been reported during post-approval use of Lopressor: confusional state, an increase in blood triglycerides and a decrease in High Density Lipoprotein (HDL). Because these reports are from a population of uncertain size and are subject to confounding factors, it is not possible to reliably estimate their frequency.

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 electronic labeling text. We will transmit the SPL version of the labeling submitted on February 29, 2008 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., Regulatory 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

cc: Enclosed electronic labeling text