DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020033/S-046

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Yifeng Jia, Ph.D.
Drug Regulatory Manager
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Jia:

Please refer to your Supplemental New Drug Application (sNDA) dated and received May 10, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lotensin HCT (benazapril/hydrochlorothiazide) 5/6.25 mg, 10/12.5 mg, 20/12.5 mg, and 25/25/mg Tablets (NDA 020033).

This "Prior Approval" supplemental new drug application provides for labeling revised as follows (additions are marked as underlined text and deletions are marked as ~~strikethrough text~~):

1. Under **CLINICAL STUDIES**, *Benazapril-Hydrochlorothiazide*, the following text was added:

> *Benazapril-Hydrochlorothiazide*
> In 15 controlled clinical trials, 1453 healthy or hypertensive patients were exposed to benazepril and hydrochlorothiazide of which 459 were exposed for at least 6 months, 214 for at least 12 months and 25 for at least 24 months.
> The combination of benazepril-hydrochlorothiazide resulted in mean placebo-adjusted decreases in sitting systolic and diastolic blood pressures of 10/6 mm Hg with 5-6.25 mg and 10-12.5 mg doses, and 20/10 mm Hg with 20-25 mg dose. The combination of benazepril and hydrochlorothiazide 20-25 mg resulted in a mean placebo-adjusted decrease in sitting systolic and diastolic blood pressures of 20/10 mm Hg.
>
> In clinical trials of **benazepril/hydrochlorothiazide** using benazepril doses of 5-20 mg and hydrochlorothiazide doses of 6.25-25 mg, the antihypertensive effects were sustained for at least 24 hours, and they increased with increasing dose of either component. Although benazepril monotherapy is somewhat less effective in blacks than in nonblacks, the efficacy of combination therapy appears to be independent of race.

There are no other changes from the last approved package insert.

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug

registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.
Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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
07/27/2012