DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200045/S-007

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Lori Ann Kneafsey
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936

Dear Ms. Kneafsey:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 16, 2011, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Amturnide (amlodipine/aliskiren/hydrochlorothiazide) 150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, 300/10/12.5 mg and 300/10/25 mg Tablets.

We acknowledge receipt of your submissions dated August 31, October 26, and November 18, 2011.

This "Prior Approval" supplemental new drug application provides for labeling revised as follows:

1. In **HIGHLIGHTS/DRUG INTERACTIONS/Aliskiren**, a third bullet was added:

    - NSAIDS use may lead to increased risk of renal impairment and loss of antihypertensive effect (7)

2. Under **ADVERSE REACTIONS/Post-Marketing Experience/***Aliskiren***,** "severe cutaneous adverse reactions, including Stevens Johnson syndrome and toxic epidermal necrolysis" was added.

3. Under **DRUG INTERACTIONS,** a new section was added:

    Non-Steroidal Anti-Inflammatory Agents(NSAIDS) including Selective Cyclooxygenase Inhibitors (COX-2 inhibitors): Non-steroidal anti-inflammatory drugs (NSAIDs): In patients who are elderly, volume depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs with agents acting on the renin-angiotensin system, including COX-2 inhibitors with agents acting on the renin-angiotensin system, including aliskiren, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving aliskiren and NSAID therapy.

    The antihypertensive effect of agents acting on the renin-angiotensin system, including aliskiren, may be attenuated by NSAIDs.

4. Under **OVERDOSAGE,** the following text was added:

Aliskiren is poorly dialyzed. Therefore, hemodialysis is not adequate to treat aliskiren overexposure *[see Clinical Pharmacology (12.3)]*.

5. Under **CLINICAL PHARMACOLOGY/Pharmacokinetics/Renal Impairment,** the following text was added as the second paragraph:

   The pharmacokinetics of aliskiren following administration of a single oral dose of 300 mg was evaluated in patients with End Stage Renal Disease (ESRD) undergoing hemodialysis. When compared to matched healthy subjects, changes in the rate and extent of aliskiren exposure (Cmax and AUC) in ESRD patients undergoing hemodialysis was not clinically significant.

   Timing of hemodialysis did not significantly alter the pharmacokinetics of aliskiren in ESRD patients. Therefore, no dose adjustment is warranted in ESRD patients receiving hemodialysis.

6. The revision date and version number were updated.

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).

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, Pharm.D.
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
01/25/2012