DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200045/S-017 **SUPPLEMENT APPROVAL**

Novartis
Attention: Anne-Marie van der Merwe
Global Program Regulatory Director
1 Health Plaza
East Hanover, NJ 07936

Dear Ms. van der Merwe:

Please refer to your Supplemental New Drug Application (sNDA) dated and received May 5, 2014, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Amturnide (aliskiren/amlodipine besylate/hydrochlorothiazide) 150/5/12.5 mg, 300/5/12.5 mg, 300/5/25 mg, and 300/10/25 mg Tablets.

This 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 **USE IN SPECIFIC POPULATIONS/Pediatric Use**, the following text was added as the second paragraph:

   Preclinical studies indicate a potential for substantial increase in exposure to aliskiren in pediatric patients *[see Nonclinical Toxicology (13.2)]*.

2. Under **USE IN SPECIFIC POPULATIONS/Geriatric Use**, the following text was added to the first paragraph to align with other Tekturna products

   Exposure to aliskiren and amlodipine is increased in ~~elderly~~ patients age 65 years and older. ~~thus~~ Consider starting with the lowest available dose of amlodipine. The lowest strength of Amturnide contains 5 mg of amlodipine *[see Clinical Pharmacology (12.3)]*

3. Under **NONCLINICAL TOXICOLOGY/Animal Toxicity and/or Pharmacology**, the following text was added as the third paragraph:

   Juvenile toxicity studies indicated increased systemic exposure to aliskiren 85- to 385-fold in 14 day and 8 day old rats respectively, compared with adult rats. The *mdr1* gene expression in juvenile rats was also significantly lower when compared to adult rats. The increased aliskiren exposure in juvenile rats appears to be mainly attributed to lack of maturation of P-gp. The overexposure in juvenile rats was associated with high mortality *[see Use in Specific Populations (8.4)]*.

4. Under **Who Should Not Take Amturnide?**, in the Medication Guide (MG), the following text was added/deleted:

   Do not take Amturnide if ~~you~~:
   - you get pregnant. Stop taking Amturnide and call your doctor right away. If you plan to become pregnant, talk to your doctor about other treatment options for your high blood pressure.
   - you have diabetes and are taking a kind of medicine called an angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEI).
   - you have low or no urine output

- you are allergic to aliskiren, hydrochlorothiazide, amlodipine or other medicines that contain sulfonamide. See the end of this leaflet for a complete list of ingredients in Amturnide.

5. 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).

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
12/22/2015