DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022217/S-005

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals
Attention: Lily Chan, Pharm.D
Associate Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936

Dear Dr. Chan:

Please refer to your Supplemental New Drug Application (sNDA) dated February 9, 2010, received February 12, 2010, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Valturna (aliskiren/valsartan) 150 mg/160 mg and 300 mg/320 mg Combination Tablets.

This "Changes Being Effected" supplemental new drug application provides for changes to the **FULL PRESCRIBING INFORMATION**, **ADVERSE REACTIONS**, and **DRUG INTERACTIONS** sections of the label.

The following changes were made:

1. Under **FULL PRESCRIBING INFORMATION/ADVERSE REACTIONS**, a section titled 6.3 Post-Marketing Experience was added.

2. Under **ADVERSE REACTIONS/Post-Marketing Experience,** the following text was added:

   The following adverse reactions have been reported in aliskiren post-marketing experience. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

   Hypersensitivity: angioedema requiring airway management and hospitalization

   Peripheral edema

3. Under **DRUG INTERACTIONS**/**Aliskiren**, the fourth paragraph was changed from:

   P-glycoprotein Effects: Pgp (MDR1/Mdr1a/1b) was found to be the major efflux system involved in absorption and disposition of aliskiren in preclinical studies. The potential for drug interactions at the Pgp site will likely depend on the degree of inhibition of this transporter. Coadministration of aliskiren with Pgp substrates or weak to moderate inhibitors such as atenolol, digoxin, and amlodipine did not result in clinically relevant interactions.

   To:

P-glycoprotein Effects: Pgp (MDR1/Mdr1a/1b) was found to be the major efflux system involved in absorption and disposition of aliskiren in preclinical studies. The potential for drug interactions at the Pgp site will likely depend on the degree of inhibition of this transporter.

4. Under **DRUG INTERACTIONS/Aliskiren**, the fifth paragraph was changed from:

   Atorvastatin: Coadministration of atorvastatin, a potent Pgp inhibitor resulted in about a 50% increase in aliskiren C_{max} and AUC after multiple dosing.

   To:

   Atorvastatin: Coadministration of atorvastatin, resulted in about a 50% increase in aliskiren C_{max} and AUC after multiple dosing.

5. Under **DRUG INTERACTIONS/Aliskiren**, the sixth paragraph was changed from:

   Ketoconazole: Coadministration of 200 mg twice-daily ketoconazole, a potent Pgp inhibitor, with aliskiren resulted in an approximate 80% increase in plasma levels of aliskiren. A 400-mg once-daily dose was not studied but would be expected to increase aliskiren blood levels further.

   To:

   Ketoconazole: Coadministration of 200 mg twice-daily ketoconazole, with aliskiren resulted in an approximate 80% increase in plasma levels of aliskiren. A 400-mg once-daily dose was not studied but would be expected to increase aliskiren blood levels further.

6. Under **DRUG INTERACTIONS/Aliskiren**, the seventh paragraph was changed from:

   Cyclosporine: Coadministration of 200 mg and 600 mg cyclosporine, a highly potent Pgp inhibitor, with 75 mg aliskiren resulted in an approximately 2.5-fold increase in C_{max} and 5-fold increase in AUC of aliskiren. Concomitant use of aliskiren with cyclosporine is not recommended.

   To:

   Cyclosporine: Coadministration of 200 mg and 600 mg cyclosporine, with 75 mg aliskiren resulted in an approximately 2.5-fold increase in C_{max} and 5-fold increase in AUC of aliskiren. Concomitant use of aliskiren with cyclosporine is not recommended.

7. Under **DRUG INTERACTIONS/Aliskiren**, the following text was added as the eighth paragraph:

   Verapamil: Coadministration of 240 mg of verapamil, a moderate Pgp inhibitor, with 300 mg aliskiren resulted in an approximately 2-fold increase in Cmax and AUC of aliskiren. However, no dosage adjustment is necessary.

8. The revision date and version number were update

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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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.

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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to 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, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Agreed upon labeling text

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22217	SUPPL-5	NOVARTIS PHARMACEUTICALS CORP	ALISKIREN & VALSARTAN

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
08/04/2010