DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021985 / S-012 **SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation
Attention: Lily Chan, PharmD
Associate Director
Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Chan:

Please refer to your supplemental new drug application dated February 5, 2010, received February 5, 2010, submitted under section 505(b)1 of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tekturna (aliskiren) tablets.

This "CBE-0" supplemental new drug application provides for revision to the labeling of Tekturna with the following content changes:

The addition of Section **6.3 Post-marketing Experience**

6.3 Post-marketing Experience

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

In section **7.1 Effects of Other Drugs on Aliskiren**

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.

AND

From

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

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

AND

New Text

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.

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 labeling text.

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 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.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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 Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD
Deputy Director

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-21985	SUPPL-12	NOVARTIS PHARMACEUTICALS CORP	TEKTURNA

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