DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 019787/S-047

SUPPLEMENT APPROVAL

Pfizer Inc.
Attention: Tricia S. Douglas, MS, RAC
Manager, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Douglas:

Please refer to your Supplemental New Drug Application (sNDA) dated March 26, 2010, received March 26, 2010 submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Norvasc (amlodipine besylate) 2.5 mg, 5 mg, and 10 mg Tablets.

We acknowledge receipt of your amendment dated November 10, 2010.

The November 10, 2010, submission constituted a complete response to our September 23, 2010, action letter.

This "Changes Being Effected" supplemental new drug application provides for changes to the **DRUG INTERACTIONS** section of the package insert and the **How should I take NORVASC?** section of the patient package insert.

1. Under **FULL PRESCRIBING INFORMATION/DRUG INTERACTIONS**, the following headings were added:

   7.10 CYP3A4 Inhibitors
   7.11 CYP3A4 Inducers

2. Under **DRUG INTERACTIONS**, the following text was added:

   7.10 CYP3A4 Inhibitors
   Co-administration of 180 mg daily dose of diltiazem with 5 mg amlodipine in elderly hypertensive patients resulted in a 60% increase in amlodipine systemic exposure. Erythromycin co-administration in healthy volunteers did not significantly change amlodipine systemic exposure. But strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir) may increase the plasma concentrations of amlodipine to a greater extent. Monitor for symptoms of hypotension and edema when co-administered with strong CYP3A4 inhibitors.

7.11 CYP3A4 Inducers

No information is available on the quantitative effects of CYP3A4 inducers on amlodipine. Blood pressure should be closely monitored when Amlodipine is co-administered with CYP3A4 inducers.

3. In the Patient Package Insert, under **How should I take NORVASC?**, the following text has been deleted from the first bullet:

You can take **NORVASC** with most drinks, including grapefruit juice.

We have completed our review of this supplemental application, as amended. 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, text for the patient 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 Michael Monteleone, Regulatory Project Manager, at (301) 796-1952.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
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
05/09/2011