



NDA 019901/S-067

SUPPLEMENT APPROVAL

Pfizer Inc.
Attention: Marcio De Godoy, PhD
Senior Manager, Pfizer Essential Health Global Regulatory Affairs R&D
500 Arcola Road, G4347
Collegeville, PA 19426

Dear Dr. Godoy:

Please refer to your Supplemental New Drug Application (sNDA) dated December 5, 2016, received, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Altace (ramipril) 1.25 mg, 2.5 mg, 5 mg, and 10 mg Capsules.

This Prior Approval supplemental new drug application provides for the following changes to the approved labeling for Altace (additions are shown as underlined text and deletions are shown as strikethrough text):

1. Under **CONTRAINDICATIONS**, the following text was added:

ALTACE is contraindicated in patients who are hypersensitive to this product or any other ACE inhibitor (e.g., a patient who has experienced angioedema during therapy with any other ACE inhibitor).

ALTACE is contraindicated in combination with a neprilysin inhibitor (e.g., sacubitril). Do not administer ALTACE within 36 hours of switching to or from sacubitril/valsartan, a neprilysin inhibitor [see Warnings and Precautions (5.1)].

Do not co-administer ALTACE with aliskiren:

- in patients with diabetes

2. Under **WARNINGS AND PRECAUTIONS**, the following text was added to the 6th paragraph under section 5.1:

Patients taking concomitant mammalian target of rapamycin (mTOR) inhibitor (e.g. temsirolimus) therapy or a neprilysin inhibitor may be at increased risk for angioedema. *[see Drug Interactions (7.7)]*

3. Under **DRUG INTERACTIONS**, the following section was updated:

7.7 mTOR Inhibitors or Other Drugs Known to Cause Angioedema

Patients taking concomitant mTOR inhibitor (e.g. temsirolimus) therapy or a neprilysin inhibitor may be at increased risk for angioedema. *[see Warnings and Precautions (5.1)]*

4. The **HIGHLIGHTS and CONTENTS** sections were updated to reflect the above label revisions.

The revision date and version number were updated.

APPROVAL & LABELING

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, Medication Guide), 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 that include labeling changes 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:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), 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, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

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
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
04/26/2017