DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 019901/S-065

SUPPLEMENT APPROVAL

King Pharmaceuticals, LLC
Attention: Marcio De Godoy, PhD
Senior Manager, Worldwide Safety and Regulatory
500 Arcola Road
G-4347
Collegeville, PA 19426

Dear Dr. De Godoy

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 23, 2013, submitted under section 505(b)(1) 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 supplemental new drug application provides for labeling revised as follows (additions are marked as underlined text and deletions are marked as ~~strikethrough text~~):

1. In **HIGHLIGHTS**, the following text was added/deleted:

~~----------RECENT MAJOR CHANGES----------~~
~~Indications and Usage, Hypertension (1.1) 11/2013~~
~~Contraindications 5/2014~~
~~Warnings and Precautions, Anaphylactoid and Possibly Related Reactions (5.1) 9/2013~~
~~Warnings and Precautions, Dual Blockade of the Renin-Angiotensin-Aldosterone System (5.7) 5/2014~~
Warnings and Precautions, Hyperkalemia (5.8) x/2015

2. Under **WARNINGS/Hyperkalemia**, the following text was added/deleted:

In clinical trials with ALTACE, hyperkalemia (serum potassium >5.7 mEq/L) occurred in approximately 1% of hypertensive patients receiving ALTACE. In most cases, these were isolated values, which resolved despite continued therapy. None of these patients were discontinued from the trials because of hyperkalemia. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of ~~potassium-sparing diuretics, potassium supplements, and/or potassium-containing salt substitutes,~~ and/or ~~other drugs that raise serum potassium levels. Monitor serum potassium in such patients.~~ ~~which should be used cautiously, if at all, with ALTACE~~*[see Drug Interactions (7.~~1~~2)]*.

3. Under **DRUG INTERACTIONS/Diuretics**, the following text was added/deleted:

7.1 Diuretics

Patients on diuretics, especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with ALTACE. The possibility of hypotensive effects with ALTACE can be minimized by either decreasing or discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with ALTACE. If this is not possible, reduce the starting dose *[see Dosage and Administration (2)]*.

7.2 Agents Increasing Serum Potassium

(b) (4)

Coadministration of ALTACE with other drugs that raise serum potassium levels may result in hyperkalemia. Monitor serum potassium in such patients.

4. The **DRUG INTERACTIONS** section was re-numbered.

3. Revisions were made to remove the passive voice and the numbered subsections from the Information for Patients section.

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
09/11/2015