DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022100/S-010
NDA 022100/S-012

**SUPPLEMENT APPROVAL**

Daiichi Sankyo Inc.
Attention: Manini Patel
Director, Regulatory Affairs
399 Thormall Street
Edison, NJ 08837

Dear Ms. Patel:

Please refer to your Supplemental New Drug Applications (sNDAs) dated February 7, and April 13, 2011, received February 7, and April 13, 2011, respectively, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Azor (amlodipine and olmesartan medoxomil) 5/20 mg, 5/40 mg, 10/20 mg and 10/40 mg Tablets.

These "Changes Being Effected" supplemental new drug applications provide for labeling revised as follows:

The following changes were made for S-010:

1. Under **ADVERSE REACTIONS/Postmarketing Experience,** "anaphylactic reactions, peripheral edema, and diarrhea" were added. The section now reads:

   *Body as a whole:* asthenia, angioedema, anaphylactic reactions, peripheral edema
   *Gastrointestinal:* vomiting, diarrhea
   *Musculoskeletal:* rhabdomyolysis
   *Urogenital System:* acute renal failure
   *Skin and Appendages:* alopecia, pruritus, urticaria

The following changes were made for S-012:

1. Under **HIGHLIGHTS/DRUG INTERACTIONS**, a bullet was added:

   - NSAID use may lead to increased risk of renal impairment and loss of antihypertensive effect (7)

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

*Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors)*
In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors with angiotensin II receptor antagonists, including olmesartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving olmesartan and NSAID therapy.

The antihypertensive effect of angiotensin II receptor antagonists, including olmesartan may be attenuated by NSAIDs including selective COX-2 inhibitors.

3. The version number and revision date were updated.

There are no other changes from the last approved package insert.

We have completed our review of these supplemental applications, and they are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions listed below and indicated in the enclosed labeling.

## 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 via 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 with the revisions listed 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 contact:

Lori Anne Wachter
Regulatory Project Manager for Safety
(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:
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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MARY R SOUTHWORTH
05/19/2011