DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200175/S-001

SUPPLEMENT APPROVAL

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

Dear Ms. Patel:

Please refer to your Supplemental New Drug Application (sNDA) dated February 4, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TRIBENZOR (olmesartan medoxomil / amlodipine / hydrochlorothiazide) Tablets.

This "Prior Approval" supplemental new drug application provides for labeling revised as follows:

HIGHLIGHTS OF PRESCRIBING INFORMATION

1. Under Recent Major Changes, a reference to the addition of Acute Myopia and Secondary Angle-Closure Glaucoma to the WARNINGS AND PRECAUTIONS section has been added.

2. Under WARNINGS AND PRECAUTIONS, the following has been added as the last bullet:

   Thiazides have been associated with acute angle-closure glaucoma (5.9).

3. Under DRUG INTERACTIONS, the following has been added as the first item:

   Olmesartan medoxomil (7.2):
   - Nonsteroidal anti-inflammatory drugs (NSAIDS): Increased risk of renal impairment and loss of antihypertensive effect

FULL PRESCRIBING INFORMATION: CONTENTS

4. Under WARNINGS AND PRECAUTIONS, Acute Myopia and Secondary Angle-Closure Glaucoma has been added as the new section 5.9. Subsequent sections have been renumbered accordingly.

FULL PRESCRIBING INFORMATION

5. Under WARNINGS AND PRECAUTIONS, the following has been added as the new section 5.13 (subsequent sections have been renumbered accordingly):

   5.13 Acute Myopia and Secondary Angle-Closure Glaucoma
   Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-

closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

6. Under ADVERSE REACTIONS/Post-Marketing Experience, the following reactions have been added: "anaphylactic reactions, peripheral edema, diarrhea."

7. Under DRUG INTERACTIONS/Drug Interactions with Olmesartan Medoxomil, the following has been 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.

PATIENT LABELING

8. The following information has been added to the Patient Labeling section under the heading "What are the possible side effects of Tribenzor?"

- **Eye problems.** One of the medicines in Tribenzor can cause eye problems that may lead to vision loss. Symptoms of eye problems can happen within hours to weeks of starting Tribenzor. Tell your doctor right away if you have:
    - decrease in vision
    - eye pain

We have completed our review of this supplemental application. 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, 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 (text for the package insert, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements and any 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.

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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to 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, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

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

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
03/25/2011