DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 200175/S-019

SUPPLEMENT APPROVAL

Daiichi Sankyo, Inc.
Attention: Yuko Komokata
Manager, Regulatory Affairs
399 Thornall Street
10th Floor
Edison, NJ 08837

Dear Ms. Komokata:

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 13, 2014, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tribenzor (olmesartan medoxomil/amlodipine/HCTZ) 20/5/12.5 mg, 40/5/ 12.5 mg, 40/5/25 mg, 40/10/12.5, and 40/10/25 mg Tablets.

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/DRUG INTERACTIONS**, the following text was added/deleted:

   - Lithium: Increases in serum lithium concentrations and lithium toxicity.

   - ~~Lithium: Reduced renal clearance and high risk of lithium toxicity when used with diuretics. Should not be given with diuretics.~~

2. Under **WARNINGS AND PRECAUTIONS**, the following text was deleted:

   ~~**5.13 Lithium Interaction**~~
   ~~***Hydrochlorothiazide.*** Lithium generally should not be given with thiazides *[see Drug Interactions (7.4)].*~~

3. Under **DRUG INTERACTIONS/Drug Interactions with Olmesartan Medoxomil**, the following text was added:

   Lithium

   Increases in serum lithium concentrations and lithium toxicity have been reported with concomitant use of olmesartan or thiazide diuretics. Monitor lithium levels in patients receiving Tribenzor and lithium.

4. Under **DRUG INTERACTIONS/Drug Interactions with hydrochlorothiazide**, the following text was added/deleted:

   Lithium: ~~Should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with hydrochlorothiazide.~~ Monitor lithium levels *[see Drug Interactions (7.2)].*

5. There are several editorial changes noted, (i.e. the sections in **WARNINGS AND PRECAUTIONS** were updated to reflect the deletion of one section; the table of contents was updated to reflect the deletion of a section)

6. The revision date was 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).

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
06/27/2014