



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 022275/S-009

**SUPPLEMENT APPROVAL**

Otsuka Pharmaceutical Company, Ltd.  
Attention: Craig Ostroff, PharmD., R.Ph.  
Senior Director Regulatory Affairs  
1 University Square Drive  
Suite 500  
Princeton, NJ 08540

Dear Dr. Ostroff:

Please refer to your Supplemental New Drug Application (sNDA) dated April 18, 2013, received April 19, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Samsca (tolvaptan) 15 mg, and 30 mg Tablets.

This "Changes Being Effected" supplemental new drug application provides for labeling revisions as shown below (additions are marked as underlined text and deletions are marked as ~~striketrough text~~):

1. In **HIGHLIGHTS/RECENT MAJOR CHANGES**, the following text was added/~~deleted~~:

Warnings and Precautions

Liver Injury~~Hepatotoxicity~~ (5.2) \_\_\_\_\_ 04/2013

2. In the **MEDICATION GUIDE**, the following text was deleted from the **What is SAMSCA?** section:

SAMSCA is a prescription medicine used to help increase low sodium levels in the blood, in adults with conditions such as heart failure, ~~liver disease~~, and certain hormone imbalances. SAMSCA helps raise salt levels in your blood by removing extra body water as urine.

It is not known if SAMSCA is safe or works in children.

3. The version number was updated.

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, 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 includes 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(1)(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, RAC  
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 I  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
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  
05/02/2013