DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22275/S-003

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENT

Otsuka Pharmaceutical Company, Ltd.
Attention: Ms. Sandra Bihary-Waltz, MSN
Senior Director, Regulatory Affairs
100 Overlook Centre
Princeton, NJ 08540

Dear Ms. Bihary-Waltz:

Please refer to your Supplemental New Drug Application (sNDA) dated May 9, 2011, received May 9, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Samsca (tolvaptan) Tablets.

We acknowledge receipt of your amendments dated May 23, August 26, and September 15, 2011, and your risk evaluation and mitigation strategy (REMS) assessment dated November 20, 2010.

This Prior Approval supplemental new drug application proposes modifications to the approved Samsca (tolvaptan) REMS, consisting of an updated Prescriber Brochure and a Dear Healthcare Professional Letter. It also proposes to eliminate the Medication Guide as an element of the approved Samsca (tolvaptan) REMS.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Samsca (tolvaptan) was originally approved on May 19, 2009. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of revisions to the Prescriber Brochure and Dear Healthcare Professional Letter. You also propose eliminating the requirement for the Medication Guide as an element of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an

element of the approved REMS to ensure that the benefits of Samsca (tolvaptan) outweigh its risks.

Your proposed modified REMS, submitted on September 15, 2011, and appended to this letter, is approved.

The modified REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Samsca (tolvaptan) in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on May 19, 2009.

The revised REMS assessment plan should include, but is not limited to, the following:

a. A survey of prescribers' understanding of the risk of ODS.

b. Narrative summary and analysis of cases of suspected ODS reported with use of Samsca (tolvaptan).

c. Based on the information reported, an assessment of and conclusion as to whether the REMS is meeting its goals, and whether modifications to the REMS are needed.

d. Information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 22275 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 22275
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 22275
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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 Dan Brum, PharmD, BCPS, RAC, Regulatory Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director of Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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
09/23/2011