



NDA 21894/S-007

**SUPPLEMENT APPROVAL
REMOVE REMS ELEMENT**

Valeant Pharmaceuticals North America LLC
Attention: James H. Medley, Ph.D.
Vice President, Regulatory Affairs
700 Route 202/206 North
Bridgewater, NJ 08807

Dear Dr. Medley:

Please refer to your Supplemental New Drug Application (sNDA) dated February 21, 2012, received February 21, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xenazine (tetrabenazine) Tablets.

We acknowledge receipt of your amendments dated April 16, May 25, June 22, and June 28, 2012, and your risk evaluation and mitigation strategy (REMS) assessment dated April 16, 2012.

This Prior Approval supplemental new drug application proposes to modify the approved REMS and to eliminate the requirement for the Medication Guide as an element of the approved Xenazine (tetrabenazine) REMS.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Xenazine (tetrabenazine) was originally approved on August 15, 2008, and the most recent REMS modification was approved on May 4, 2011. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the REMS consist of the following:

- Revisions to the REMS to reflect Valeant as the Sponsor for Xenazine (tetrabenazine)
- Revisions to the REMS to specify a date for both the annual and final distribution of Communication Plan materials

- Revisions to the REMS to clarify that Xenazine (tetrabenazine) educational materials for pharmacists will only be sent to pharmacists who are authorized to dispense Xenazine (tetrabenazine)
- Revisions to the Patient/Caregiver counseling guide to align the recommendations regarding monoamine oxidase inhibitors and reserpine-containing products and concomitant use of Xenazine (tetrabenazine) with the prescribing information.
- Revisions to the timetable for submission of assessments to include a REMS assessment at year four post-REMS approval

Your proposed modifications to the REMS also consist of 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 Xenazine (tetrabenazine) outweigh the risks.

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

Your proposed modified REMS, submitted on June 28, 2012, 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.

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

1. Surveys designed to monitor the effectiveness of the interventions in educating prescribers on the proper use of tetrabenazine therapy, compliance with the titration and dosing guidelines contained in the labeling, and occurrence of targeted adverse events and their management by the prescriber.
2. For the Ongoing Healthcare Professional Education section, the number of unique healthcare professionals who participated in thought leader symposia, by calendar quarter, since the inception of the REMS program.
3. For the Distribution of Materials section:
 - a. The source(s) of the list of physician addresses
 - b. The source(s) of the list of pharmacist addresses
 - c. The date(s) of each mailing
 - d. The number of recipients at each mailing date
 - e. The number of returned mailings for each mailing date
 - f. A list of the documents included in each mailing

4. Based on the results of the surveys and any other relevant information, an assessment and conclusion whether the REMS is meeting its goals and whether modifications to the REMS are needed.
5. 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 the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 21894 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT
METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

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 021894 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 021894
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021894
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

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

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
Office of Prescription Drug Promotion (OPDP)
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 Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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, call Nicole Bradley, PharmD, Regulatory Project Manager, at (301) 796-1930.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Package Insert
REMS

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

/s/

RUSSELL G KATZ
08/17/2012