



NDA 021894/S-009

**SUPPLEMENT APPROVAL
REMS MODIFICATION
REMS ASSESSMENT PLAN REVISION**

Valeant International Bermuda
Attention: John B. Dubeck
US Regulatory Agent
1001 G Street NW, Suite 500 W
Washington, DC 20001

Dear Mr. Dubeck:

Please refer to your Supplemental New Drug Application (sNDA) dated May 21, 2013, received May 21, 2013, 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 July 16 and July 19, 2013 and your risk evaluation and mitigation strategy (REMS) assessment dated August 22, 2012.

This supplemental new drug application provides for proposed modifications to the approved 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 Xenazine (tetrabenazine) was originally approved on August 15, 2008, and last modified on August 17, 2012. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of a revised timetable for submission of assessments, which adds an assessment at six years following the original REMS approval, and a one-page Fact Sheet for Healthcare Professionals highlighting potential drug interactions with CYP2D6 inhibitors, testing for CYP2D6 enzyme activity, and recommendations for dosing above 50 mg per day.

Your proposed modified REMS, submitted on July 16, 2013, and appended to this letter, is approved.

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 Xenazine (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; this comprehensive evaluation should be submitted with all of your assessments except for your six-year assessment due by August 15, 2014.
2. A prescriber survey designed to monitor prescriber understanding of the proper use of Xenazine (tetrabenazine) therapy and compliance with the titration and dosing guidelines contained in the labeling; this more targeted survey should be submitted only with your six-year assessment due by August 15, 2014.
3. 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. This should be submitted with all of your assessments except for your six-year assessment due by August 15, 2014.
4. 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

This should be submitted with all of your assessments except for your six-year assessment due by August 15, 2014.

5. An evaluation of healthcare providers understanding of the serious risk of Xenazine (tetrabenazine). This should be submitted with all of your assessments except for your six-year assessment due by August 15, 2014.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

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 the 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 21894 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 21894
PROPOSED REMS MODIFICATION**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 21894
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 L. Bradley, PharmD, Regulatory Project Manager, at (301) 796-1930.

Sincerely,

{See appended electronic signature page}

Alice Hughes, M.D.
Deputy Director for Safety
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
REMS

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

/s/

ALICE HUGHES
08/02/2013