



NDA 21-894/S-001 and 002

**SUPPLEMENT APPROVAL
REMS MODIFICATION**

Biovail Americas Corporation
Attention: Robert W. Ashworth, Ph.D.
Vice President, Regulatory Affairs
700 Route 202/206 North
Bridgewater, NJ 08807

Dear Dr. Ashworth:

Please refer to your supplemental new drug applications (sNDA) dated February 24, 2009, received February 25, 2009 (NDA 21-894/S-001), and dated June 18, 2009, received June 19, 2009 (NDA 21-894/S-002), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xenazine (tetrabenazine) Tablets.

We acknowledge receipt of your submission dated August 19, 2009, to both NDA 21-894/S-001 and NDA 21-894/S-002 that stated that it is too early to provide a meaningful REMS assessment at this time. We also acknowledge receipt of your submission dated November 13, 2009 to both NDA 21-894/S-001 and NDA 21-894/S-002.

These supplemental new drug applications provide for modifications to the communication plan element and timetable for submission of assessments of your Risk Evaluation and Mitigation Strategy (REMS), originally approved on August 15, 2008.

The modifications to the communication plan component of your REMS include the distribution of introductory materials to pharmacists in specialty pharmacies and deletion of the requirement to have speaker materials cleared through the Division of Drug Marketing, Advertising, and Communications (DDMAC). The modifications to the timetable for submission of assessments are changing the submission dates to FDA to no less frequently than at 18 months, 3 years, and 7 years after approval from August 15, 2008.

The proposed modified REMS contains the same Medication Guide, communication plan, and timetable for submission of assessments as the original REMS, with the exception of the modifications to the communication plan and timetable for submission of assessments listed above.

Your proposed modified REMS is approved and is appended to this letter.

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

- a. an evaluation of patients' understanding of the serious risks of tetrabenazine, the importance of titration, and monitoring for targeted adverse events
- b. a report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
- c. a report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance
- d. 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

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. 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 updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that 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.

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

NDA 21-894 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 21-894
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 21-894
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, call Beverly Connor, Regulatory Project Manager, at (301) 796-1171.

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: REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21894	SUPPL-1	BIOVAIL AMERICAS CORP	XENAZINE
NDA-21894	SUPPL-2	BIOVAIL AMERICAS CORP	XENAZINE

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/s/

RUSSELL G KATZ
12/01/2009