

Initial REMS Approval: 08/15/2008
Most Recent Modification: August 2013

NDA 21-894 Xenazine[®] (tetrabenazine)

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL:

The goal of the REMS for Xenazine is:

- To inform healthcare professionals of the increased risk of drug-associated depression and suicidality, proper titration and dosing, and the risk of drug-drug interactions with strong CYP2D6 inhibitors in patients taking Xenazine.

II. REMS ELEMENTS

A. Communication Plan

Valeant will implement a communication plan to healthcare providers to support implementation of this REMS:

- 1 The audience is healthcare professionals (HCPs) – especially neurologists and movement disorder specialists and pharmacists.
- 2 Valeant will provide physicians and pharmacists with the education materials listed below that describe the key risks and benefits of tetrabenazine:
 - a. Prescriber materials:
 - i. Xenazine[®] Package Insert (PI)
 - ii. Dear Healthcare Professional Letter
 - iii. Xenazine[®] Medication Guide
 - iv. Prescribing Xenazine[®] (tetrabenazine) Tablets: A Healthcare Professional Guide
 - v. Patient/Caregiver Counseling Guide
 - vi. Initial Dosing Plan
 - vii. Xenazine Fact Sheet for Healthcare Professionals

- b. Pharmacist materials
 - i. Dear Pharmacist Letter
 - ii. Xenazine[®] Package Insert (PI)
 - iii. Xenazine[®] Medication Guide
 - iv. Prescribing Xenazine[®] (tetrabenazine) Tablets: A Healthcare Professional Guide
 - c. All final communication and educational materials listed above are appended to the REMS.
- 3 Pharmacy Management Systems – Valeant will work with First Data Bank, MediSpan, Facts and Comparisons, Micromedex, major pharmacy benefit managers and other leading providers of point of sale clinical alert data to inform dispensing pharmacists and pharmacy technicians of the significant known risks of tetrabenazine. In working with these data providers, Valeant will seek to include appropriate drug-drug interaction information, dosing guidelines and other clinical alerts available to it through the use of standard NCPDP data formats.
- 4 Ongoing Healthcare Professional Education – The Sponsor will also use several educational vehicles to continue educating and updating Healthcare Professionals about tetrabenazine and the REMS. These include a trained Speaker’s Bureau which will schedule local and regional thought leader symposia. The speaker materials will include information on the tetrabenazine REMS and will be used to reinforce the risk minimization measures after launch. The Sponsor’s clinical team and sales professionals will be present at annual meetings of the major professional societies of neurologists and movement disorder specialists (e.g., American Academy of Neurology, American Neurological Association, Movement Disorder Society) and will use these opportunities to reinforce the REMS messages. Continuing education formats will also be available for physicians and pharmacists on the product web site.
- 5 Distribution of materials:
- a. At the time of tetrabenazine availability, the Dear Healthcare Professional Letter will be sent by mass mailing to targeted medical specialists to announce the availability of tetrabenazine and to educate them on proper patient selection and use of the drug. The mailing will also include a copy of the PI, the *Prescribing Xenazine[®] (tetrabenazine) Tablets: A Healthcare Professional Guide*, the patient Medication Guide, the *Patient/Caregiver Counseling Guide* and the Initial Dosing Plan (as described above). Additional materials will be available via sales and/or clinical representatives, the product website or through the Sponsor toll-free medical information line.
 - b. At the time of tetrabenazine availability, a letter will be sent by mass

mailing to pharmacists who dispense tetrabenazine through specialty pharmacies to announce the availability of tetrabenazine and to educate pharmacists on the tetrabenazine REMS. The mailing will also include a copy of the PI and the *Prescribing Xenazine® (tetrabenazine) Tablets: A Healthcare Professional Guide*. Pharmacists will also be provided with 10 copies of the Medication Guide. The pharmacist can obtain additional educational materials from the Sponsor toll-free medical information line or the product website.

- c. In order to ensure that healthcare professionals remain informed of the tetrabenazine REMS, the Dear Healthcare Professional letter and the Dear Pharmacist letter will be updated and distributed annually from the date of the initial approval of the REMS (August 15, 2008) and sent to all neurologists, movement disorder specialists and pharmacists within the specialty pharmacy networks authorized to dispense Xenazine. These annual mailings will include the most current *Prescribing Xenazine® (tetrabenazine) Tablets: A Healthcare Professional Guide, What You Need to Know About Xenazine® : Patient/Caregiver Counseling Guide*, and Medication Guide. The *Xenazine Fact Sheet for Healthcare Professionals*, which was created in May 2013, will be included with the final distribution of the Dear Healthcare Professional Letter. The final distribution date will be August 15, 2013.

B. Timetable for Submission of Assessments

Valeant will submit REMS Assessments to the FDA at 18 months, 3 years, 4 years, 6 years, and 7 years from the date of initial approval of the REMS (August 15, 2008). The 6 year assessment report will be limited to a prescriber survey designed to monitor prescriber understanding of the proper use of Xenazine therapy and compliance with the titration and dosing guidelines contained in the labeling. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. Valeant will submit each assessment so that it will be received by the FDA on or before the due date.