

Initial REMS Approved: 09/2010
Last modified/revised: 04/2016

NDA 21-107

**LOTRONEX[®] (alosetron hydrochloride) Tablets
and Authorized Generic (alosetron hydrochloride) Tablets**

Selective 5-HT₃ antagonist

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

The goals and objectives of the LOTRONEX REMS are to mitigate the risks of ischemic colitis (IC) and serious complications of constipation (CoC) associated with LOTRONEX and its authorized generic alosetron hydrochloride by:

- Informing prescribers of LOTRONEX/alosetron hydrochloride about:
 - the serious risks of IC and serious CoC associated with LOTRONEX/alosetron hydrochloride
 - the importance of understanding that LOTRONEX/alosetron hydrochloride should only be used in severely affected diarrhea-predominant irritable bowel syndrome patients for whom the benefits exceed the risks.
 - the importance of counseling patients about the risks of IC and serious CoC
- Informing patients about the risks of IC and CoC and actions to take should they experience early warning signs and symptoms of these risks.

II. REMS ELEMENTS:

A. Elements to Assure Safe Use

1. Training will be provided to healthcare providers who prescribe LOTRONEX and its authorized generic.

- a. Sebela will ensure that training provided to healthcare providers who prescribe LOTRONEX and its authorized generic includes information on the serious risks of IC and CoC associated with LOTRONEX/alosetron hydrochloride, the importance of understanding that LOTRONEX/alosetron hydrochloride should only be used in severely affected diarrhea-predominant irritable bowel syndrome patients for whom the benefits

exceed the risks, and the importance of counseling patients about the risks of IC and serious CoC, using the prescribing information and the following materials in the REMS Training Kit:

- i. REMS letter for Healthcare Providers
 - ii. LOTRONEX REMS Program Prescriber Education Slide Deck
 - iii. LOTRONEX REMS Program Safety Information Fact Sheet for Prescribers
 - iv. LOTRONEX REMS Program Patient Education Sheet
 - v. Prescriber Completion of LOTRONEX REMS Program Training Form
- b. In order to facilitate training, Sebela will:
- i. Ensure that training is provided to healthcare providers who prescribe LOTRONEX/alosetron hydrochloride by mailing or emailing the REMS Training Kit to healthcare providers who are likely to prescribe, or have prescribed LOTRONEX/alosetron hydrochloride in the 24 months preceding the REMS modification approval (01/2016). The REMS Training Kit will be distributed within 60 days after approval of the modified LOTRONEX REMS Program. Likely prescribers include, but are not limited to, general practitioners, family practitioners, internists, gastroenterologists, and nurse practitioners/physician assistants.
 - ii. Send a REMS letter for Professional Societies to the following professional societies and organizations, requesting that the letter or the content be provided to their membership within 6 and 12 months after approval of the modified LOTRONEX REMS Program.
 - American Academy of Family Physicians
 - American Academy of Nurse Practitioners
 - American Academy of Physicians Assistants
 - American College of Gastroenterology
 - American College of Physicians
 - American Gastroenterological Association
 - American Medical Association
 - iii. Ensure that prescribers can notify Sebela when they have completed training via the LOTRONEX REMS Program website or by faxing or mailing a Prescriber Completion of LOTRONEX REMS Program Training Form.
 - iv. Provide acknowledgement of completion of training electronically or by mail to prescribers upon receiving notification that training was completed.
 - v. Make REMS Training Materials available at professional society meetings and at medical educational venues where Sebela has a presence.
 - vi. Maintain a LOTRONEX REMS Program Website [www.lotronexrems.com] and call center (1-844-851-3395) to support prescribers.
 - vii. Monitor distribution and prescription data monthly. Contact all prescribers identified as not having completed training and provide training within 30 days of identification. Contact and provide training to all prescribers who do not report completion of training after the first contact up to two additional times, or until the prescriber reports completion, within 180 days of being first identified.

- viii. Maintain a validated, secure database of healthcare providers who have notified Sebela of completion of training, which will be defined as all training materials were reviewed independently by the healthcare provider.
- ix. Ensure that the REMS materials listed below are available on the LOTRONEX REMS Program Website or by calling the REMS Coordinating Center.

The following materials are part of the REMS and are appended:

REMS Training Kit

- REMS letter for Healthcare Providers
- LOTRONEX REMS Program Prescriber Education Slide Deck
- LOTRONEX REMS Program Safety Information Fact Sheet for Prescribers
- LOTRONEX REMS Program Patient Education Sheet
- Prescriber Completion of LOTRONEX REMS Program Training Form

Other appended REMS materials:

- REMS Website for Prescriber Section screenshots
- REMS Website for Patients Section screenshots
- REMS letter for Professional Societies

III. Timetable for Submission of Assessments

Sebela will submit REMS Assessments to the FDA 18 months after the date of approval of the modified REMS (01/2016) and every 12 months thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Sebela will submit each assessment so that it will be received by the FDA on or before the due date.