

FDA Required REMS Safety Information

LOTRONEX[®] and its authorized generic alosetron hydrochloride tablets: Modified REMS

- **RISK OF SERIOUS GASTROINTESTINAL ADVERSE REACTIONS**
 - Infrequent but serious gastrointestinal adverse reactions have been reported with the use of LOTRONEX/alosetron hydrochloride. These events, including ischemic colitis and serious complications of constipation, have resulted in hospitalization and, rarely, blood transfusion, surgery, and death.
- **INDICATED ONLY** for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have not responded adequately to conventional therapy
- **DISCONTINUE** immediately in patients who develop constipation or symptoms of ischemic colitis. Do not resume LOTRONEX/alosetron hydrochloride in patients who develop ischemic colitis.
- **Contraindicated in patients with:**
 - Constipation
 - History of chronic or severe constipation or sequelae from constipation; intestinal obstruction, stricture, toxic megacolon, gastrointestinal perforation, and/or adhesions; ischemic colitis; impaired intestinal circulation, thrombophlebitis, or hypercoagulable state; Crohn's disease or ulcerative colitis; diverticulitis; severe hepatic impairment
 - Concomitant use of fluvoxamine (LUVOX[®])

Important Safety Notice

The FDA has required Sebela Pharmaceuticals Inc. to distribute this safety notice to your organization as part of the LOTRONEX REMS (Risk Evaluation and Mitigation Strategy) Program. We request that you inform your members about the following serious risks associated with Lotronex/alosetron hydrochloride and of changes to the LOTRONEX REMS Program:

Risk of Serious Gastrointestinal Adverse Reactions

- **Counsel** patients to discontinue LOTRONEX/alosetron hydrochloride immediately and contact their prescriber right away if they develop constipation or symptoms of ischemic colitis
- **Evaluate** patients with signs of ischemic colitis (e.g., rectal bleeding, bloody diarrhea, new or worsening abdominal pain)
- **Discontinue** LOTRONEX/alosetron hydrochloride immediately if signs of ischemic colitis occur, such as rectal bleeding, bloody diarrhea, or new or worsening abdominal pain.

Changes to the REMS Program

- ❶ Prescribers are **no** longer required to affix prescribing program stickers to written prescriptions for LOTRONEX/alosetron hydrochloride
- ❷ Pharmacies are **no** longer required to only dispense LOTRONEX/alosetron hydrochloride for a paper prescription with an affixed prescribing program sticker. **Electronic prescriptions are now allowed**
- ❸ Patients are no longer required to complete and submit a Patient Acknowledgment Form. Instead, a Patient Education Sheet is available for the prescriber to discuss with the patient.

Healthcare providers who prescribe LOTRONEX/alosetron hydrochloride will be provided training to ensure the benefits of LOTRONEX/alosetron hydrochloride continue to outweigh the risks of ischemic colitis and serious complications of constipation. Training materials can be found at www.lotronexREMS.com or by calling 1-844-851-3395. By completing the LOTRONEX REMS Program Training Form a healthcare professional will be entered into a database for trained prescribers.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information on these risks, and a link to the Prescribing Information including the BOXED WARNING are available at www.lotronexREMS.com.

Indication:

LOTROXEX/alosetron hydrochloride is a selective serotonin 5-HT₃ antagonist indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have chronic IBS symptoms (generally lasting 6 months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and not responded adequately to conventional therapy.

Severe IBS includes diarrhea and 1 or more of the following:

- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

This letter does not contain the complete safety profile for LOTRONEX/alosetron hydrochloride. Please visit www.lotronexREMS.com for more information.

Reporting Adverse Events:

You are encouraged to report all suspected adverse events associated with LOTRONEX/alosetron hydrochloride to the FDA at www.fda.gov/medwatch, or 1-800-FDA-1088 or Sebelo Pharmaceuticals Inc. at 1-844-732-3521.

Sincerely,

Sebelo Pharmaceuticals, Inc.

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