Dear Pharmacist:

Important Information for Pharmacists

Prometheus would like to remind you about important aspects of LOTRONEX® and its authorized generic and the Prescribing Program for LOTRONEX™ (PPL).

LOTRONEX/alosetron hydrochloride is a selective serotonin 5-HT₃ antagonist indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic irritable bowel syndrome symptoms (generally lasting 6 months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy.

Diarrhea-predominant irritable bowel syndrome is severe if it includes diarrhea and one 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 irritable bowel syndrome.

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. Patients who develop constipation or symptoms of ischemic colitis should discontinue use of LOTRONEX/alosetron hydrochloride immediately. Patients who develop ischemic colitis should not resume LOTRONEX/alosetron hydrochloride therapy. Because of the serious gastrointestinal adverse reactions associated with LOTRONEX/alosetron hydrochloride, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable. Clinical studies have not been performed to adequately confirm the benefits of LOTRONEX/alosetron hydrochloride in men.

The Prescribing Program for LOTRONEX was implemented in order to ensure that the benefits of LOTRONEX/alosetron hydrochloride treatment outweigh the potential risks. You, the pharmacist, play an important role in the Prescribing Program for LOTRONEX. To become familiar with the Prescribing Program for LOTRONEX, please read the attached Prescribing Information and Medication Guide.

In order to comply with the Prescribing Program for LOTRONEX, pharmacists need to:
• Dispense only prescriptions that have a Prescribing Program for LOTRONEX Sticker - never fill telephone, facsimile, or computer-generated prescriptions; refills are only permitted on written prescriptions

• If a Prescribing Program for LOTRONEX sticker is not present on the prescription, call Prometheus Client Services at 1-888-423-5227 to confirm that the prescriber is enrolled in the PPL.

• Dispense a Retail Pack for LOTRONEX or its authorized generic, which in addition to the medicine contains the Medication Guide, Prescribing Information, and Patient Follow-Up Survey Pre-Enrollment Form.

We have enclosed a copy of the Medication Guide (MG), which must be provided to patients with every filled prescription. This Medication Guide contains information that can be used to facilitate discussions about the risks of therapy. The Medication Guide explains the dosing regimen for initiating therapy with LOTRONEX and its authorized generic.

Only prescribers who have enrolled in the Prescribing Program for LOTRONEX should prescribe LOTRONEX or its authorized generic. LOTRONEX/alosetron hydrochloride is indicated only for women with severe diarrhea-predominant irritable bowel syndrome who have not responded adequately to conventional therapy.

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. Patients who develop constipation or symptoms of ischemic colitis should discontinue use of LOTRONEX/alosetron hydrochloride immediately. Patients who develop ischemic colitis should not resume LOTRONEX/alosetron hydrochloride therapy.

Enclosed for your reference are the following educational materials that will provide additional details on LOTRONEX and its authorized generic and the Prescribing Program for LOTRONEX:

• The LOTRONEX and its authorized generic full Prescribing Information
• The LOTRONEX and its authorized generic Medication Guide

For more information on the Prescribing Program for LOTRONEX, including an educational slide deck (PPL Pharmacist Educational Slide Deck) designed to educate pharmacists on their role within the PPL, contact Prometheus at 1-888-423-5227 or visit us online at www.lotronexppl.com.

Sincerely,

Medical Affairs Department
Prometheus Laboratories Inc.

LOT15044 07/15