17.2 Medication Guide

MEDICATION GUIDE
LOTRONEX (LOW-trah-nex) Tablets
(alosetron hydrochloride)

Before using LOTRONEX for the first time, you should:

- Understand that LOTRONEX has serious risks for some people.
- Read and follow the directions in this Medication Guide.
- Sign a Patient-Physician Agreement with your doctor.

Read this Medication Guide carefully before you sign the Patient-Physician Agreement. You must sign the Patient-Physician Agreement before you start LOTRONEX. Read the Medication Guide you get with each refill for LOTRONEX. There may be new information. This Medication Guide does not take the place of talking with your doctor.

1. <u>What is the most important information I should know about LOTRONEX?</u>

A. LOTRONEX is a medicine only for some women with severe chronic irritable bowel syndrome (IBS) whose:

- main problem is diarrhea and
- IBS symptoms have not been helped enough by other treatments.

B. Some patients have developed serious bowel side effects while taking LOTRONEX. Serious bowel (intestine) side effects can happen suddenly, including the following.

1. **Serious complications of constipation:** About 1 out of every 1,000 women who take LOTRONEX may get serious complications of constipation. These complications **may lead to a hospital stay and, in rare cases, blood transfusions, surgery, and death.** People who are older, who are weak from illness, or who take other constipating medicines may be more likely to have serious complications of constipation with LOTRONEX.
   To lower your chances of getting serious complications of constipation, do the following:
   - **If you are constipated**, do not start taking LOTRONEX.
   - **If you get constipated while taking LOTRONEX**, stop taking it right away and call your doctor.
   - **If your constipation does not get better after stopping LOTRONEX**, call your doctor again.
   - **If you stopped taking LOTRONEX, do not start taking LOTRONEX again** unless your doctor tells you to do so.
2. **Ischemic colitis (reduced blood flow to the bowel):** About 3 out of every 1,000 women who take LOTRONEX over a 6-month period may get a serious problem

where blood flow to parts of the large bowel is reduced. This is called ischemic colitis. The chance of getting ischemic colitis when you take LOTRONEX for more than 6 months is not known. **Ischemic colitis may lead to a hospital stay and, in rare cases, blood transfusions, surgery, and death**.

To lower your chances of getting serious complications of ischemic colitis, stop taking LOTRONEX and call your doctor right away if you get:

- new or worse pain in your stomach area (abdomen) or
- blood in your bowel movements.

C. Is LOTRONEX right for you?

LOTRONEX may be right for you if <u>all</u> of these things are true about you:

- Your doctor has told you that your symptoms are due to IBS.
- Your IBS bowel problem is diarrhea.
- Your IBS has lasted for 6 months or longer.
- You tried other IBS treatments and they did not give you the relief you need.
- Your IBS is severe.

You can tell if your IBS is severe if **<u>at least 1</u>** of the following is true for you:

- You have lots of painful stomach cramps or bloating.
- You often cannot control the need to have a bowel movement, or you have "accidents" where your underwear gets dirty from diarrhea or bowel movements.
- You cannot lead a normal home or work life because you need to be near a bathroom.

Enough testing has not been done to confirm LOTRONEX works in men or children under age 18.

D. There is a special prescribing program for LOTRONEX.

Only doctors who have signed up with the company that makes LOTRONEX should write prescriptions for LOTRONEX. As part of signing up, these doctors have said that they understand about IBS and the possible side effects of LOTRONEX. They have agreed to use a special sticker on **<u>written</u>** prescriptions for LOTRONEX, so the pharmacist will know that the doctors have signed up with the company. No telephone, facsimile, or computerized prescriptions are permitted with this program. Refills may be written on prescriptions.
You may be taught about LOTRONEX by your doctor or healthcare provider under a doctor's direction. Your doctor will ask you to sign a Patient-Physician Agreement after you read this Medication Guide for the first time. Signing the Agreement means that you understand the benefits and risks of LOTRONEX and that you have read and understand this Medication Guide.

2. <u>What is LOTRONEX?</u>

LOTRONEX is a medicine only for some women with severe chronic IBS whose:

- main problem is diarrhea and
- IBS symptoms have not been helped enough by other treatments.

LOTRONEX does not cure IBS, and it may not help every person who takes it. For those who are helped, LOTRONEX reduces lower stomach area (abdominal) pain and discomfort, the sudden need to have a bowel movement (bowel urgency), and diarrhea from IBS. If you stop taking LOTRONEX, your IBS symptoms may return within 1 or 2 weeks to what they were before you started taking Lotronex.

LOTRONEX is not recommended for children.

3. Who should not take LOTRONEX?

LOTRONEX is not right for everyone. **Do not take LOTRONEX if any of the following apply to you:**

- Your main IBS problem is constipation or you are constipated most of the time.
- You have had a serious problem from constipation. **If you are constipated now, do not start taking LOTRONEX.**
- You have had serious bowel blockages.
- You have had blood flow problems to your bowels, such as ischemic colitis.
- You have had blood clots.
- You have had Crohn's disease, ulcerative colitis, diverticulitis, or severe liver disease.
- You do not understand this Medication Guide or the Patient-Physician Agreement, or you are not willing to follow them.
- You are taking fluvoxamine (LUVOX®).

4. What should I talk about with my doctor before taking LOTRONEX?

Talk with your doctor:

- about the possible benefits and risks of LOTRONEX.
- about how much of a problem IBS is in your life and what treatments you have tried.
- about any other illnesses you have and medicines you take or plan to take. These include prescription and non-prescription medicines, supplements, and herbal remedies. Certain illnesses and medicines can increase your chance of getting serious side effects while taking LOTRONEX. Other medicines may interact with how the body handles LOTRONEX.
- about any allergies that you have. See the end of the Medication Guide for a complete list of ingredients in LOTRONEX.
- if you are pregnant, planning to get pregnant, or breastfeeding.

5. How should I take LOTRONEX?

- Take LOTRONEX exactly as your doctor prescribes it. You can take LOTRONEX with or without food.
- Begin with 0.5 mg two times a day for 4 weeks to see how LOTRONEX affects you. You and your doctor may decide that you should keep taking this dose if you are doing well.
- Check with your doctor 4 weeks after starting LOTRONEX:
  - If you try 0.5 mg two times a day for 4 weeks, it may not control your symptoms. If you do not get constipation or other side effects from LOTRONEX, your doctor may

increase your dose up to 1 mg two times a day.
    - If 1 mg two times a day does not work after 4 weeks, LOTRONEX is not likely to help you. You should stop taking it and call your doctor.
- **If you miss a dose of LOTRONEX**, just skip that dose. Do **not** take 2 doses the next time. Wait until the next time you are supposed to take it and then take your normal dose.
- **Follow the important instructions in the section "What is the most important information I should know about LOTRONEX?"** about when you must stop taking the medicine and when you should call your doctor.
- **If you see other doctors** about your IBS or side effects from LOTRONEX, let the doctor who prescribed LOTRONEX know.

6. What are the possible side effects of LOTRONEX?

Constipation is the most common side effect among women with IBS who take LOTRONEX. **Some patients have developed serious bowel side effects while taking LOTRONEX.** Read the section **"What is the most important information I should know about LOTRONEX?"** at the beginning of this Medication Guide for information about the serious side effects you may get with LOTRONEX.

This Medication Guide does not tell you about all the possible side effects of LOTRONEX. Your doctor or pharmacist can give you a more complete list.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

7. How should I store LOTRONEX?

- Store LOTRONEX between 59ºF to 86ºF (15ºC to 30ºC).
- Protect LOTRONEX from light and getting wet (moisture).

Keep Lotronex and all medicines out of the reach of children.

8. General information about the safe and effective use of LOTRONEX

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you have any questions or concerns about LOTRONEX, ask your doctor. Do not use LOTRONEX for a condition for which it was not prescribed. Do not share your medicine with other people. It may harm them.

Your doctor or pharmacist can give you more information about LOTRONEX that was written for healthcare professionals. You can also contact the company that makes LOTRONEX (toll free) at 1-888-423-5227 or at www.lotronex.com.

9. What are the ingredients of LOTRONEX?

Active Ingredient: alosetron hydrochloride.

Inactive Ingredients: lactose (anhydrous), magnesium stearate, microcrystalline cellulose, and pregelatinized starch. The white film-coat for the 0.5 mg tablet contains hypromellose, titanium dioxide, and triacetin. The blue film-coat for the 1 mg tablet contains hypromellose, titanium dioxide, triacetin, and indigo carmine.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised April 2008 LX002A08

17.3 FDA-Approved Patient-Physician Agreement

PATIENT-PHYSICIAN AGREEMENT FOR LOTRONEX

SECTION FOR THE PATIENT

LOTRONEX (alosetron hydrochloride) is only for women with severe irritable bowel syndrome (IBS) whose main problem is diarrhea and who did not get the relief needed from other treatments. LOTRONEX has not been shown to help men with IBS or patients under age 18.

My doctor, or a healthcare provider under a doctor's direction, answered my questions about treatment with LOTRONEX. I have read and I understand the Medication Guide for LOTRONEX, and

- I understand that some patients using LOTRONEX have had serious bowel conditions (ischemic colitis and complications of constipation). I understand that these serious conditions can happen suddenly, and that they may lead to a hospital stay, and in rare cases, blood transfusions, surgery, and death. I also understand that certain patients may be more likely to develop a serious bowel condition while taking LOTRONEX. These include older patients, those who have other health problems and those who take other medicines that may cause constipation.
- My doctor and I agree that my IBS is severe and that other treatments have not given me the relief that I need. I also agree that I meet all of the requirements described in the section of the Medication Guide "What is the most important information I should know about LOTRONEX?" I understand that these requirements help to make sure that LOTRONEX is used only by patients who are likely to have more benefit from treatment than risk.
- I don't have any problems listed in the section of the Medication Guide "Who should not take LOTRONEX?" that prevents me from taking LOTRONEX.
- I will follow instructions in the Medication Guide about:
  - **telling my doctor**, before taking LOTRONEX, about any illnesses I have, or other medicines I am taking or planning to take.
  - **taking LOTRONEX** exactly as my doctor prescribes it.
  - **stopping LOTRONEX** and calling my doctor right away if I get constipated, if I have new or worse pain in my abdomen, or if I see blood in my bowel movements.
  - **calling my doctor** again if the constipation I called about before has not gotten better.
  - **not starting LOTRONEX again** unless my doctor tells me to do so, if I stopped taking it because I got constipated.
  - **talking with my doctor 4 weeks after starting LOTRONEX** to recheck my IBS symptoms.

- **stopping LOTRONEX and calling my doctor** if my IBS symptoms have not improved after 4 weeks of taking 1 mg 2 times a day.

I understand that LOTRONEX should be prescribed only by doctors who have signed up with the company that makes the drug. Doctors in the program must:

- fully discuss the drug's benefits and risks with each patient.
- sign this agreement with each patient before giving the initial prescription. It is not necessary to sign an agreement more than once.
- use a special sticker on written LOTRONEX prescriptions so that pharmacists know the doctor has signed up. No telephone, facsimile, or computerized prescriptions are permitted with this program. Refills may be written on prescriptions.

If I see other doctors about my IBS or possible side effects from LOTRONEX, I will let the doctor who prescribed LOTRONEX know.

My signature below indicates I have read, understood, and agree with all the statements made above. I would like to begin treatment with LOTRONEX.

_____

Name of Patient (print)

_____ _____

Signature Date

SECTION FOR THE PHYSICIAN

I am enrolled in the Prescribing Program for LOTRONEX, and I will continue to follow the requirements of the Program.

I, or a healthcare provider under a physician's direction, have given the patient named above:

- a copy of the Medication Guide for LOTRONEX, and instructed the patient to read it carefully before signing this Agreement, and to take it home.
- counseling about the benefits and risks of LOTRONEX.
- appropriate instructions for taking LOTRONEX.
- answers to all of the patient's questions about treatment with LOTRONEX.
- a prescription for LOTRONEX that has the program sticker affixed on it to alert pharmacists I am enrolled in the Prescribing Program for LOTRONEX.

The patient signed the Patient-Physician Agreement in my presence after I counseled the patient, asked if the patient had any questions about treatment with LOTRONEX, and answered all questions to the best of my ability.

_____

Name of Physician (print)

_____ _____

Signature Date

After the patient and the physician sign this Patient-Physician Agreement, give a copy to the patient and put the original signed form in the patient's medical record.

17.4 FDA-Approved Physician Enrollment Form

PRESCRIBING PROGRAM FOR LOTRONEX:
PHYSICIAN ENROLLMENT FORM

The Prescribing Program for LOTRONEX was implemented to help reduce risks of serious gastrointestinal adverse reactions, some fatal, associated with this medicine. The program is intended to help physicians and their patients understand the benefits and risks of treatment with LOTRONEX in order to make fully informed decisions.

I wish to participate in the Prescribing Program for LOTRONEX (PPL) and acknowledge that I have read the complete Prescribing Information for LOTRONEX and understand and will follow the requirements of the PPL described below.

- For safety reasons, LOTRONEX is approved only for women with severe, diarrhea-predominant irritable bowel syndrome (D-IBS) who have:
  - chronic IBS symptoms (generally lasting for 6 months or longer),
  - had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
  - not responded adequately to conventional therapy.

  Diarrhea-predominant IBS 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 IBS.
- Physicians who enroll in the PPL should be able to diagnose and manage IBS, ischemic colitis, constipation, and complications of constipation, or refer patients to a specialist as needed.
- Patients considering treatment with LOTRONEX must be educated on the benefits and risks of the drug, given a copy of the Medication Guide, instructed to read it, and encouraged to ask questions. The patient may be educated by the enrolled physician or a healthcare provider under a physician's direction.
- After reviewing the Medication Guide prior to the initial prescription, the physician and the patient must both sign the Patient-Physician Agreement form. The original signed form must be placed in the patient's medical record, and a copy given to the patient.
- Program stickers must be affixed to <u>written</u> prescriptions for LOTRONEX (i.e., the original and all subsequent prescriptions). Stickers will be provided as part of the Prometheus Prescribing Program for LOTRONEX. Refills are permitted to be written on prescriptions.
- All prescriptions for LOTRONEX must be written and not transmitted by telephone,

facsimile, or computer.

- Prescribers must report all serious adverse reactions with LOTRONEX to Prometheus at 1-888-423-5227 or to the Food and Drug Administration at 1-800-FDA-1088.

_____

Name of Physician (print)

_____ _____

Signature Date

DEA Number _____

Office Address: _____

_____

_____

Office Phone Number: _____

Office Fax Number: _____

Upon enrollment, you will receive a prescribing kit for LOTRONEX with the complete Prescribing Information, Prescribing Program for LOTRONEX stickers, multiple copies of the Medication Guide and Patient-Physician Agreement for LOTRONEX, and instructions for ordering additional supplies of Program materials.

You only need to enroll once, and you are under no obligation to prescribe LOTRONEX.

If you have any questions, please call the Prescribing Program for LOTRONEX at 1-888-423-5227 or visit www.lotronex.com.

TO ENROLL, VISIT WWW.LOTRONEX.COM OR PHONE 1-888-423-5227 OR COMPLETE THIS FORM IN ITS ENTIRETY AND MAIL OR FAX TO THE FOLLOWING ADDRESS:

Prescribing Program for Lotronex
Prometheus Client Services
9410 Carroll Park Drive
San Diego, CA 92121
1-888-423-5227
Fax Number: 1-888-824-0896

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