

ANDA 200652

Alosetron Tablets

Selective 5-HT₃ antagonist

Roxane Laboratories, Inc.
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Columbus, OH 43228
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS:

- To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients for whom benefits exceed the risks.
- To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide for alosetron will be dispensed with each alosetron prescription in accordance with 21 CFR 208.24. A Medication Guide will be dispensed with each 30-tablet bottle (typical dispense is 2 bottles per month). Copies of the Medication Guide will be available on the Alosetron REMS website at www.AlosetronREMS.com or via the Alosetron REMS contact center at 1-844-267-8675.

Additionally, as part of the REMS program for alosetron, a copy of the Medication Guide will be provided to certified prescribers who will provide a Medication Guide to each patient at the initiation of each new course of alosetron therapy.

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe alosetron will be specially certified.

- a. Roxane Laboratories (Roxane) will ensure that healthcare providers who prescribe alosetron are specially certified in the Alosetron REMS Program. To become certified, each prescriber of alosetron enrolls in the Alosetron REMS Program by submitting a completed Alosetron REMS Program Prescriber Enrollment Form and attesting to the following:
 - i. I request to participate in the Alosetron REMS Program and acknowledge that I have read and understand the complete Prescribing Information and other enrollment materials for the Alosetron REMS Program. I understand the risks associated with its use and will follow the requirements of the Alosetron REMS Program described below. I understand the importance of reporting all cases of ischemic colitis and serious complications of constipation to the Alosetron REMS Program at 1-844-267-8675.
 - ii. I understand that alosetron is approved only for women with severe, diarrhea-predominant irritable bowel syndrome who have:
 - chronic irritable bowel syndrome 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 irritable bowel syndrome is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain and discomfort,
 - frequent bowel urgency or fecal incontinence
 - disability or restriction of daily activities due to irritable bowel syndrome.
- iii. I understand that if I prescribe alosetron for my patient(s), I must be able to perform the following:

- Diagnose and manage irritable bowel syndrome, ischemic colitis, constipation, and complications of constipation or refer patients to a specialist as needed.
- Ensure that all patients under my care are educated by me or a healthcare provider in my practice about the benefits and risks of the drug.

iv. I agree to:

- provide each of my patients with a copy of the Alosetron Medication Guide at initiation of alosetron treatment.
 - review the content of the Medication Guide and encourage the patient to read it and ask questions.
 - have each patient sign the Alosetron Patient Acknowledgement Form. The original signed form must be placed in the patient's medical record, and a copy given to the patient.
 - inform my patients about the Alosetron Patient Follow-Up Survey, encourage them to participate and provide them with an Alosetron Patient Follow-Up Survey Pre-Enrollment Form.
 - affix Alosetron REMS Program stickers to written prescriptions for alosetron (i.e., the original and all subsequent prescriptions). Alosetron REMS stickers will be provided as part of the Alosetron REMS Program. Refills are permitted to be written on prescriptions.
 - ensure that all prescriptions for alosetron are written and not transmitted by telephone, facsimile, or computer.
- b. Alosetron REMS Program materials can be requested via the Alosetron REMS Program website at www.AlosetronREMS.com or by phone at 1-844-267-8675.
- c. Roxane will provide prescribers an Alosetron REMS Program Kit upon their enrollment.
- d. Roxane will maintain a database of all certified enrolled alosetron prescribers.

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

- Alosetron REMS Program Prescriber Enrollment Materials:
 - Alosetron REMS Program Enrollment Letter
 - Alosetron REMS Program Prescriber Enrollment Form
 - Alosetron REMS Program Prescriber Education Slide Deck
 - Alosetron Prescribing Information and Alosetron Medication Guide

- Alosetron REMS website for the Prescriber Section web screen shots
- Alosetron REMS Program Kit:
 - Alosetron REMS Program Kit Overview Letter
 - Alosetron REMS Program Patient Acknowledgement Form
 - Alosetron Prescribing Information and Alosetron Medication Guide
 - Alosetron REMS stickers
 - Alosetron REMS Program Patient Follow-Up Survey Pre-Enrollment Form

2. Each patient prescribed alosetron must have signed an Alosetron REMS Program Patient Acknowledgment Form for documentation of safe-use conditions. By signing the Alosetron REMS Program Patient Acknowledgment Form, the patient agrees to the following:

- a. My doctor or healthcare provider under a doctor’s direction, answered my questions about treatment with alosetron. I have read and I understand the Medication Guide for alosetron, including the section “Who should not take alosetron?” I understand that about 1 out of every 1,000 women who take alosetron may get serious complications of constipation. I understand that about 3 of every 1,000 women who take alosetron over a 6-month period may get a serious problem where blood flow to parts of the large bowel is reduced (ischemic colitis). I understand that the serious condition of ischemic colitis, and other serious complications of constipation, can happen suddenly. These serious complications may lead to a hospital stay, and in rare cases, blood transfusions, surgery, and death.
- b. I understand that certain people may be more likely to develop a serious bowel condition while taking alosetron, including people who:
 - are older,
 - have other health problems,
 - take other medicines that may cause constipation.
- c. I understand alosetron is a medicine that should only be used for some women with severe chronic irritable bowel syndrome (IBS), whose main problem is diarrhea, and whose IBS symptoms have not been helped enough by other treatments.
- d. I will follow instructions in the Alosetron Medication Guide about:
 - **telling my doctor**, before taking alosetron, about any illnesses I have, or other medicines I am taking or planning to take.
 - **taking alosetron** exactly as my doctor prescribes it.

- **stopping alosetron** and calling my doctor right away if I get constipated, if I have new or worse pain in my stomach area (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 alosetron 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 alosetron** to recheck my IBS symptoms.
 - **stopping alosetron and calling my doctor** if my IBS symptoms have not improved after 4 weeks of taking 1 mg alosetron 2 times a day.
- e. If I see other doctors about my IBS or possible side effects from alosetron, I will tell the doctor who prescribed alosetron.

The following materials are part of the Alosetron REMS Program and are appended.

- Alosetron REMS Program Patient Acknowledgement Form
- Alosetron REMS website for Patients web screen shots
- Alosetron Medication Guide

3. Pharmacists will only dispense alosetron to patients with documentation of safe-use conditions:

- a. The pharmacists will only dispense a prescription for alosetron in the presence of an Alosetron REMS sticker.¹

The Alosetron REMS sticker provides verification to the pharmacist that the prescription is written by a certified prescriber enrolled in the Alosetron REMS Program.

Pharmacists will not accept telephone, facsimile, or computerized prescriptions for alosetron. The prescription may provide refills (30-day supplies).

- b. At the time of filling the prescription, pharmacists will dispense to the patient a 30-day supply which includes a copy of the Alosetron Medication Guide.

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws.

- c. Roxane will perform educational mailings to pharmacists and retail pharmacies using an Alosetron Dear Pharmacist Letter at least 2 weeks prior to first availability of the Alosetron REMS Program and annually thereafter. The mailings will remind the pharmacists about their role within the Alosetron REMS Program.
- d. Roxane will direct pharmacists to review educational materials on the pharmacist section of the Alosetron REMS Program website. The educational materials will consist of the Alosetron REMS Program Pharmacist Education Slide Deck, discussing the benefits and risks of alosetron therapy and the pharmacist role in ensuring compliance with the REMS sticker program.

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

- Alosetron Dear Pharmacist Letter
- Alosetron REMS Program Pharmacist Education Slide Deck
- Alosetron REMS website for Pharmacists Section web screen shots

C. Implementation System

The implementation system for the Alosetron REMS Program includes the following:

1. Roxane will monitor compliance with completion of the Alosetron REMS Program Prescriber Enrollment Form and the Alosetron REMS Program Patient Acknowledgement Form to help ensure alosetron is prescribed by Alosetron REMS Program-enrolled prescribers and that patients are only treated with alosetron following documentation of safe-use conditions by conducting surveys of prescribers and patients.
2. Roxane will monitor compliance with the REMS program sticker by conducting surveys of pharmacists, prescribers, and patients to help ensure alosetron prescriptions are written by Alosetron REMS Program-enrolled prescribers and dispensed by pharmacists in accordance with the requirements of the Alosetron REMS Program.
3. Based on monitoring and evaluation of the elements to assure safe use in section, II.B., Roxane will take reasonable steps to improve the implementation of these elements, if found to be inadequate, and to address non-compliance with the requirements of the Alosetron REMS Program.

Medication Guide

Alosetron (a-LOW-zeh-tron) Hydrochloride Tablets

Before using alosetron hydrochloride tablets for the first time, you should:

- Understand that alosetron hydrochloride tablets have serious risks for some people.
- Read and follow the directions in this Medication Guide.
- Sign a Patient Acknowledgement Form.

Read this Medication Guide carefully before you sign the Patient Acknowledgement Form. You must sign the Patient Acknowledgement Form before you start alosetron hydrochloride tablets. Read the Medication Guide you get with each refill for alosetron hydrochloride tablets. There may be new information. This Medication Guide does not take the place of talking with your doctor.

1. What is the most important information I should know about alosetron hydrochloride tablets?

A. Alosetron hydrochloride tablets are 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 alosetron hydrochloride tablets. 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets.

To lower your chances of getting serious complications of constipation, do the following:

- **If you are constipated,** do not start taking alosetron hydrochloride tablets.
- **If you get constipated while taking alosetron hydrochloride tablets,** stop taking it right away and call your doctor.

- **If your constipation does not get better after stopping alosetron hydrochloride tablets**, call your doctor again.
- **If you stopped taking alosetron hydrochloride tablets, do not start taking alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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. Are alosetron hydrochloride tablets right for you?

Alosetron hydrochloride tablets may be right for you if all 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 **at least 1** 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 alosetron hydrochloride tablets works in men or children under age 18.

D. There is a special prescribing program for alosetron hydrochloride tablets.

Only doctors who have signed up with the Alosetron REMS Program should write prescriptions for alosetron hydrochloride tablets. As part of signing up, these doctors have said that they understand about IBS and the possible side effects of alosetron hydrochloride tablets. They have

agreed to use a special sticker on **written** prescriptions for alosetron hydrochloride tablets, so the pharmacist will know that the doctors have signed up with the Alosetron REMS Program. No telephone, facsimile, or computerized prescriptions are permitted with this program. Refills may be written on prescriptions.

You may be taught about alosetron hydrochloride tablets by your doctor or healthcare provider under a doctor's direction. Your doctor will ask you to sign a Patient Acknowledgement Form after you read this Medication Guide for the first time. Signing the Patient Acknowledgement Form means that you understand the benefits and risks of alosetron hydrochloride tablets and that you have read and understand this Medication Guide.

2. What are alosetron hydrochloride tablets?

Alosetron hydrochloride tablets are 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.

Alosetron hydrochloride tablets does not cure IBS, and it may not help every person who takes it. For those who are helped, alosetron hydrochloride tablets 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 alosetron hydrochloride tablets, your IBS symptoms may return within 1 or 2 weeks to what they were before you started taking alosetron hydrochloride tablets.

Alosetron hydrochloride tablets are not recommended for children.

3. Who should not take alosetron hydrochloride tablets?

Alosetron hydrochloride tablets are not right for everyone. **Do not take alosetron hydrochloride tablets 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 alosetron hydrochloride tablets.**
- 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 Acknowledgement Form, or you are not willing to follow them.
- You are taking fluvoxamine (LUVOX®).

4. What should I talk about with my doctor before taking alosetron hydrochloride tablets?

Talk with your doctor:

- about the possible benefits and risks of alosetron hydrochloride tablets.
- 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 alosetron hydrochloride tablets. Other medicines may interact with how the body handles alosetron hydrochloride tablets.
- about any allergies that you have. See the end of the Medication Guide for a complete list of ingredients in alosetron hydrochloride tablets.
- if you are pregnant, planning to get pregnant, or breastfeeding.

5. How should I take alosetron hydrochloride tablets?

- Take alosetron hydrochloride tablets exactly as your doctor prescribes it. You can take alosetron hydrochloride tablets with or without food.
- Begin with 0.5 mg two times a day for 4 weeks to see how alosetron hydrochloride tablets 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 alosetron hydrochloride tablets:
 - 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 alosetron hydrochloride tablets, 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, alosetron hydrochloride tablets is not likely to help you. You should stop taking it and call your doctor.
- **If you miss a dose of alosetron hydrochloride tablets**, 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 alosetron hydrochloride tablets?”** 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 alosetron hydrochloride tablets, tell the doctor who prescribed alosetron hydrochloride tablets.

6. What are the possible side effects of alosetron hydrochloride tablets?

Constipation is the most common side effect among women with IBS who take alosetron hydrochloride tablets. **Some patients have developed serious bowel side effects while taking**

alosetron hydrochloride tablets. Read the section “**What is the most important information I should know about alosetron hydrochloride tablets?**” at the beginning of this Medication Guide for information about the serious side effects you may get with alosetron hydrochloride tablets.

This Medication Guide does not tell you about all the possible side effects of alosetron hydrochloride tablets. 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 alosetron hydrochloride tablets?

- Store alosetron hydrochloride tablets at 68°F to 77°F (20°C to 25°C). [See USP Controlled Room Temperature.]
- Protect alosetron hydrochloride tablets from light and getting wet (moisture).

Keep alosetron hydrochloride tablets and all medicines out of the reach of children.

8. General information about the safe and effective use of alosetron hydrochloride tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you have any questions or concerns about alosetron hydrochloride tablets, ask your doctor. Do not use alosetron hydrochloride tablets 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 alosetron hydrochloride tablets that was written for healthcare professionals. You can also contact the Alosetron REMS Program (toll free) at 1-844-267-8675 or at www.AlosetronREMS.com.

9. What are the ingredients of alosetron hydrochloride tablets?

Active Ingredient: alosetron hydrochloride.

Inactive Ingredients: lactose (anhydrous), magnesium stearate, microcrystalline cellulose, and pregelatinized starch.

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

Roxane Laboratories, Inc.

Columbus, Ohio 43216

MM/YYYY

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Alosetron REMS Program Enrollment Materials Letter

<Date>

<Name>

< Address>

<City, State, and Zip Code>

Re: Alosetron REMS Program Enrollment Materials

Dear <Name>:

Please find enclosed the following program enrollment materials to support your enrollment in the Alosetron REMS Program:

- Alosetron REMS Program Prescriber Enrollment Form
- Alosetron REMS Program Prescriber Education Slide Deck
- Alosetron Prescribing Information
- Alosetron Medication Guide

To complete enrollment in the Alosetron REMS Program, review the Prescriber Education Slide Deck, complete the Prescriber Enrollment Form and then fax it to the program at 1-800-535-6805. Alternatively, you may enroll by accessing the 'For Prescribers' tab on the Alosetron REMS Program website at www.AlosetronREMS.com.

If you have any questions or require additional information or further copies of any Alosetron REMS Program documents, please call the Alosetron REMS contact center at 1-844-267-8675 or visit www.AlosetronREMS.com.

Sincerely,

Alosetron REMS Program Team

Alosetron REMS Program
Prescriber Enrollment Form

The generic supplier of alosetron will ensure that healthcare providers who prescribe alosetron are specially certified in the Alosetron REMS Program. To become certified, each prescriber of alosetron enrolls in the Alosetron REMS Program by submitting a completed Alosetron REMS Program Prescriber Enrollment Form and attesting to the following:

I request to participate in the Alosetron REMS Program and acknowledge that I have read and understand the complete Prescribing Information and other enrollment materials for the Alosetron REMS Program. I understand the risks associated with its use and will follow the requirements of the Alosetron REMS Program described below. I understand the importance of reporting all cases of ischemic colitis and serious complications of constipation to the Alosetron REMS Program at 1-844-267-8675.

I understand that alosetron is approved only for women with severe, diarrhea-predominant irritable bowel syndrome who have:

- chronic irritable bowel syndrome 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 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.

I understand that if I prescribe alosetron for my patient(s), I must be able to perform the following:

- diagnose and manage irritable bowel syndrome, ischemic colitis, constipation, and complications of constipation or refer patients to a specialist as needed.

- ensure that all patients under my care are educated by me or a healthcare provider in my practice about the benefits and risks of the drug.

I agree to:

- provide each of my patients with a copy of the Alosetron Medication Guide at initiation of alosetron treatment.
- review the content of the Medication Guide and encourage the patient to read it and ask questions.
- have each patient sign the Alosetron Patient Acknowledgement Form. The original signed form must be placed in the patient’s medical record, and a copy given to the patient.
- inform my patients about the Alosetron Patient Follow-Up Survey, encourage them to participate and provide them with an Alosetron Patient Follow-Up Survey Pre-Enrollment Form.
- affix Alosetron REMS stickers to written prescriptions for alosetron (i.e., the original and all subsequent prescriptions). Alosetron REMS stickers will be provided as part of the Alosetron REMS Program. Refills are permitted to be written on prescriptions.
- ensure that all prescriptions for alosetron are written and not transmitted by telephone, facsimile, or computer.

***Indicates Required Field**

Name of Prescriber (print)*

(First)

(Last)

Signature*

Date*

NPI Number*

Office Name

Office Address*

Office City*

_____ State* _____ Zip Code* _____

Office Phone Number*

_____ Office Fax Number* _____

Email*

Confirmation Correspondence Preference (please select one): Fax Email

Upon enrollment, you will receive a program kit for alosetron with Prescribing Information, Alosetron REMS stickers, multiple copies of the Medication Guide, Patient Acknowledgment Form, Patient Follow-Up Survey Pre-Enrollment Form, and instructions for ordering additional supplies of Program materials.

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

If you have any questions regarding the Alosetron REMS Program, please call 1-844-267-8675.

To enroll, visit www.AlosetronREMS.com or complete this form in its entirety and mail or fax it to the Alosetron REMS Program to the following address:

Alosetron REMS

PO Box 29292, Phoenix, AZ 85038

Fax Number: 1-800-535-6805

THE ALOSETRON REMS PROGRAM

Prescriber Education Slide Deck

Understanding the Benefits and Risks of Alosetron

The Alosetron REMS Program - Please see
complete Prescribing Information for
Alosetron Tablets for full details.

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THE ALOSETRON REMS PROGRAM

Prescriber Education Slide Deck

Understanding the Benefits and Risks of Alosetron

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 1:

Purpose

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 1:
Purpose

Purpose of the Prescriber Educational Slide Deck for Alosetron

- By reviewing the information provided in this presentation, prescribers who prescribe alosetron hydrochloride (alosetron) will better understand the:
 - **Restricted distribution process for this product;**
 - **Risks and benefits of alosetron;**
 - **Etiology of irritable bowel syndrome;**
 - **The Alosetron REMS Program**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Purpose of the Prescriber Educational Slide Deck for Alosetron

- By reviewing the information provided in this presentation, prescribers who prescribe alosetron hydrochloride (alosetron) will better understand the:
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 - **Risks and benefits of alosetron;**
 - **Etiology of irritable bowel syndrome;**
 - **The Alosetron REMS Program**

Risk Evaluation and Mitigation Strategy (REMS)

The Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for alosetron to ensure the benefits of the drug outweigh the risk of serious gastrointestinal adverse reactions. A REMS is a strategy to address the serious risks associated with a drug. The REMS can range from periodic assessment of a product's postmarketing safety profile to strict limitations on the way a drug is prescribed, distributed, or dispensed.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Risk Evaluation and Mitigation Strategy (REMS)

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Goal of The Alosetron REMS Program and Key Elements

The Alosetron REMS Program was implemented to help reduce the risks of serious GI adverse events.

The Goals of the Alosetron REMS Program are:

•To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients in whom benefits exceed the risks.

•To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Goal of The Alosetron REMS Program and Key Elements

The Alosetron REMS Program was implemented to help reduce the risks of serious GI adverse events.

The Goals of the Alosetron REMS Program are:

- **To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients in whom benefits exceed the risks.**
- **To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.**

Goal of The Alosetron REMS Program and Key Elements (cont'd)

The Key Elements of the Alosetron REMS are:

- only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, can prescribe alosetron.
- **pharmacists may only dispense alosetron from prescriptions with a sticker and written by prescribers participating in the Alosetron REMS Program.¹**

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Goal of The Alosetron REMS Program and Key Elements (cont'd)

The Key Elements of the Alosetron REMS are:

- only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, can prescribe alosetron.
- **pharmacists may only dispense alosetron from prescriptions with a sticker and written by prescribers participating in the Alosetron REMS Program.¹**

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws.

Section 2:

Indication and Usage

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 2:
Indication and Usage

Indication and Usage

Alosetron is indicated **ONLY** for women with severe diarrhea-predominant IBS who have:

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

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

9

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Indication and Usage (cont'd)

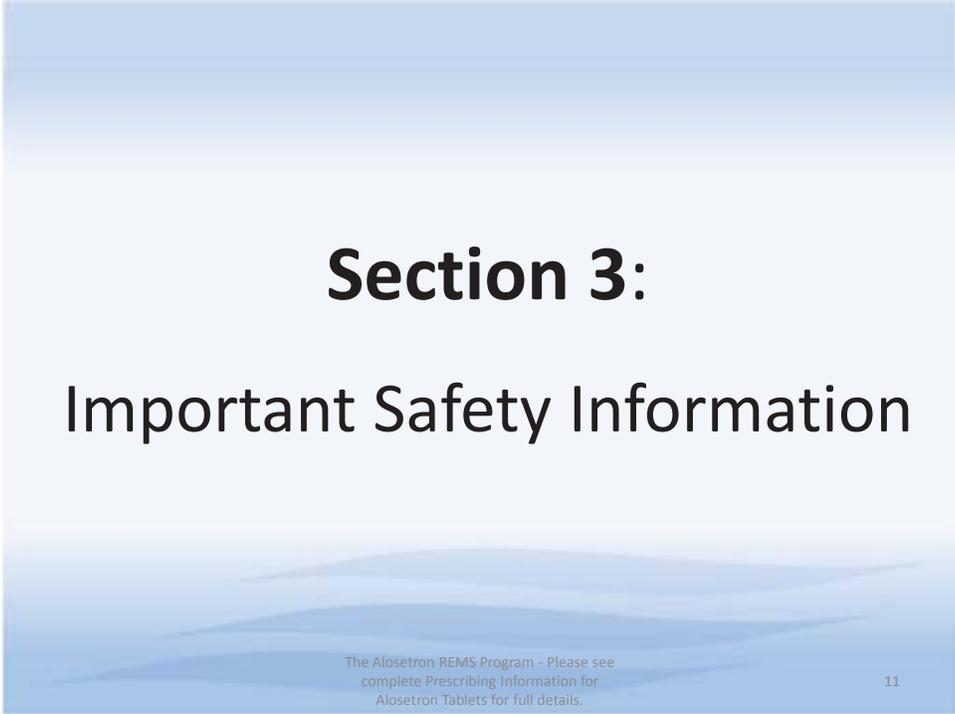
- Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:
 - **frequent and severe abdominal pain/discomfort,**
 - **frequent bowel urgency or fecal incontinence,**
 - **disability or restriction of daily activities due to IBS.**
- Because of infrequent but serious GI adverse reactions associated with alosetron, 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 alosetron in men.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Indication and Usage (cont'd)

- Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:
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- Because of infrequent but serious GI adverse reactions associated with alosetron, 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 alosetron in men.



Section 3:
Important Safety Information

Boxed Warning

WARNING: SERIOUS GASTROINTESTINAL ADVERSE REACTIONS

- Infrequent but serious gastrointestinal adverse reactions have been reported with the use of alosetron. These events, including ischemic colitis and serious complications of constipation, have resulted in hospitalization, and rarely, blood transfusion, surgery, and death.
- The Alosetron REMS Program was implemented to help reduce risks of serious gastrointestinal adverse reactions. Only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, should prescribe alosetron.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Boxed Warning

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- The Alosetron REMS Program was implemented to help reduce risks of serious gastrointestinal adverse reactions. Only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, should prescribe alosetron.

Boxed Warning (cont'd)

- Alosetron is indicated only for women with severe diarrhea-predominant IBS who have not responded adequately to conventional therapy. Before receiving the initial prescription for alosetron, the patient must read and sign the Patient Acknowledgement Form for alosetron.
- Alosetron should be discontinued immediately in patients who develop constipation or symptoms of ischemic colitis. Patients should immediately report constipation or symptoms of ischemic colitis to their prescriber. Alosetron should not be resumed in patients who develop ischemic colitis. Patients who have constipation should immediately contact their prescriber if the constipation does not resolve after alosetron is discontinued. Patients with resolved constipation should resume alosetron only on the advice of their treating prescriber.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Boxed Warning (cont'd)

- Alosetron is indicated only for women with severe diarrhea-predominant IBS who have not responded adequately to conventional therapy. Before receiving the initial prescription for alosetron, the patient must read and sign the Patient Acknowledgement Form for alosetron.
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Warnings and Precautions

Serious Complications of Constipation

- Some patients have experienced serious complications of constipation without warning. Examples include:
 - **obstruction, ileus, impaction, toxic megacolon, and secondary bowel ischemia have been reported with use of alosetron during clinical trials.**
 - **in addition, rare cases of intestinal perforation and death have been reported from postmarketing clinical practice.**
 - **in some cases, complications of constipation required intestinal surgery, including colectomy.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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 - **in some cases, complications of constipation required intestinal surgery, including colectomy.**

Warnings and Precautions (cont'd)

Serious Complications of Constipation (cont'd)

- The incidence of serious complications of constipation was ~0.1%, or 1 per 1,000 patients, in women receiving either alosetron or placebo.
- Patients who are elderly, debilitated, or taking additional medications that decrease GI motility may be at greater risk for complications of constipation.
- Alosetron should be discontinued immediately in patients who develop constipation.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

Serious Complications of Constipation (cont'd)

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- Alosetron should be discontinued immediately in patients who develop constipation.

Warnings and Precautions (cont'd)

Ischemic Colitis

- Some patients have experienced symptoms of ischemic colitis without warning.
- Ischemic colitis has been reported in patients receiving alosetron in clinical trials as well as during marketed use of the drug.
- In IBS clinical trials:
 - **cumulative incidence of ischemic colitis in women receiving alosetron was:**
0.2%, or 2 per 1,000 patients (95% CI 1 to 3), over 3 months
0.3%, or 3 per 1,000 patients (95% CI 1 to 4), over 6 months
 - **patient experience in controlled clinical trials is insufficient to estimate the incidence of ischemic colitis in patients taking alosetron for longer than 6 months**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

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 - **patient experience in controlled clinical trials is insufficient to estimate the incidence of ischemic colitis in patients taking alosetron for longer than 6 months**

Warnings and Precautions (cont'd)

Ischemic Colitis (cont'd)

- Alosetron should be discontinued immediately in patients with signs of ischemic colitis, e.g., rectal bleeding, bloody diarrhea, or new or worsening abdominal pain.
- Because ischemic colitis can be life threatening, patients with signs or symptoms of ischemic colitis should be evaluated promptly and have appropriate diagnostic testing performed.
- Treatment with alosetron should not be resumed in patients who develop ischemic colitis.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

Ischemic Colitis (cont'd)

- Alosetron should be discontinued immediately in patients with signs of ischemic colitis, e.g., rectal bleeding, bloody diarrhea, or new or worsening abdominal pain.
- Because ischemic colitis can be life threatening, patients with signs or symptoms of ischemic colitis should be evaluated promptly and have appropriate diagnostic testing performed.
- Treatment with alosetron should not be resumed in patients who develop ischemic colitis.

Contraindications

- Alosetron should not be initiated in patients with constipation.
- Alosetron is contraindicated in patients with a 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.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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 - **Crohn's disease or ulcerative colitis;**
 - **diverticulitis;**
 - **severe hepatic impairment.**

Contraindications (cont'd)

- Alosetron should not be used by patients who are unable to understand or comply with the Patient Acknowledgement Form.
- Concomitant administration of alosetron with fluvoxamine is contraindicated.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Contraindications (cont'd)

- Alosetron should not be used by patients who are unable to understand or comply with the Patient Acknowledgement Form.
- Concomitant administration of alosetron with fluvoxamine is contraindicated.

Drug Interactions

In vivo data suggest that alosetron is primarily metabolized by cytochrome P450 (CYP) 1A2, with minor contributions from CYP3A4 and CYP2C9. Therefore, inducers or inhibitors of these enzymes may change the clearance of alosetron.

- Concomitant administration of alosetron and fluvoxamine is contraindicated.
- Concomitant administration of alosetron and moderate CYP1A2 inhibitors, including quinolone antibiotics and cimetidine, has not been evaluated, but should be avoided unless clinically necessary because of similar potential drug interactions.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Drug Interactions (cont'd)

- Caution should be used when alosetron and ketoconazole are administered concomitantly.
- Coadministration of alosetron and strong CYP3A4 inhibitors, such as clarithromycin, telithromycin, protease inhibitors, voriconazole, and itraconazole has not been evaluated but should be undertaken with caution because of similar potential drug interactions.
- The effect of induction or inhibition of other pathways on exposure to alosetron and its metabolites is not known.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Drug Interactions (cont'd)

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- The effect of induction or inhibition of other pathways on exposure to alosetron and its metabolites is not known.

Use in Specific populations

- Pregnancy Category B.
- It is not known whether alosetron is excreted in human milk; caution should be exercised when alosetron is administered to a nursing woman.
- Safety and effectiveness in pediatric patients have not been established.
- Postmarketing experience suggests that elderly patients may be at greater risk for complications of constipation; therefore, appropriate caution and follow-up should be exercised if alosetron is prescribed for these patients.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Use in Specific populations (cont'd)

- Increased exposure to alosetron and/or its metabolites is likely to occur in patients with hepatic impairment. Alosetron should not be used in patients with severe hepatic impairment and should be used with caution in patients with mild or moderate hepatic impairment.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Use in Specific populations (cont'd)

- Increased exposure to alosetron and/or its metabolites is likely to occur in patients with hepatic impairment. Alosetron should not be used in patients with severe hepatic impairment and should be used with caution in patients with mild or moderate hepatic impairment.

Adverse Reactions Reported in ≥ 1% of IBS Patients^a

Gastrointestinal Adverse Reactions	Alosetron 1 mg BID (n=8,328 ^b)	Placebo (n=2,363)
Constipation ^c	29%	6%
Abdominal discomfort and pain	7%	4%
Nausea	6%	5%
GI discomfort and pain	5%	3%
Abdominal distention	2%	1%
Regurgitation and reflux	2%	2%
Hemorrhoids	2%	1%

^a Reported in ≥1% of alosetron patients and occurring more frequently on alosetron 1 mg twice-a-day than on placebo.
^b Data reported from 22 repeat-dose studies in patients with IBS treated for 8 to 24 weeks.
^c $P < 0.0001$ vs placebo.

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Adverse Reactions

Constipation is a frequent and dose-related side effect of treatment with alosetron.

- In clinical studies constipation was reported in ~29% of patients with IBS treated with alosetron 1 mg twice daily (n=9,316).
 - **The effect was statistically significant compared with placebo ($P<0.0001$);**
 - **11% of patients treated with alosetron 1 mg twice daily withdrew from the studies due to constipation.**
- Although the number of IBS patients treated with alosetron 0.5 mg twice daily is relatively small (n=243), 11% of patients reported constipation and 4% of patients withdrew from clinical studies due to constipation.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Overdosage

- No specific antidote available for overdose of alosetron.
- Patients should be managed with appropriate supportive therapy.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 4:
How to Prescribe and Dispense
Alosetron Tablets

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 4:
How to Prescribe and Dispense Alosetron Tablets

Dosage and Administration

For safety reasons, only prescribers who enroll in the Alosetron REMS Program can prescribe alosetron.

- Usual Dose in Adults
 - **To lower the risk of constipation, alosetron should be started at 0.5 mg twice-a-day.**
 - **Patients well controlled on 0.5 mg twice-a-day may be maintained on this regimen.**
 - **If, after 4 weeks, the 0.5 mg twice-a-day dosage is tolerated but does not adequately control IBS symptoms, increase dose to 1 mg twice-a-day, the dose used in controlled clinical trials.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Dosage and Administration (cont'd)

- Usual Dose in Adults
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 - If after 4 weeks, the 0.5 mg twice-a-day dosage is well tolerated but does not adequately control the IBS symptoms, then the dosage can be increased up to 1 mg twice-a-day.
 - **Alosetron should be discontinued in patients who have not had adequate control of IBS symptoms after 4 weeks of treatment with 1 mg twice-a-day.**
 - Alosetron should be discontinued immediately in patients who develop constipation or signs of ischemic colitis.
 - Alosetron should not be restarted in patients who develop ischemic colitis.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Dosage and Administration (cont'd)

- Usual Dose in Adults
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Dosage and Administration (cont'd)

- Clinical trial and postmarketing experience suggest that debilitated patients or patients taking additional medications that decrease GI motility may be at greater risk of serious complications of constipation.
- Therefore, appropriate caution and follow-up should be exercised if alosetron is prescribed for these patients.
- Alosetron can be taken with or without food.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Dosage and Administration (cont'd)

- Clinical trial and postmarketing experience suggest that debilitated patients or patients taking additional medications that decrease GI motility may be at greater risk of serious complications of constipation.
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Section 5: Alosetron REMS Program

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 5:
Alosetron REMS Program

Enrolling in the Alosetron REMS Program

- Prescribers must read the full PI and understand the benefits and risks of treatment with alosetron for severe diarrhea-predominant IBS.
- Prescribers then complete the Prescriber Enrollment Form at www.AlosetronREMS.com or return it by mail or by fax.
- **The form must be returned to the sponsor before a prescriber can be considered enrolled in the Alosetron REMS Program.**
- Alosetron REMS Program Kits, including Medication Guides and stickers that need to be affixed to every prescription, are provided after enrollment.

The Alosetron REMS Program - Please see
complete Prescribing Information for
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Overview of Prescriber Responsibilities

Step 1: Review and provide Medication Guide to the patient.

Step2: Have the patient complete the Patient Acknowledgment Form.
Place the original in the patient's medical record and give a copy to the patient.

Step 3: Provide patient with written prescription with affixed Alosetron REMS sticker.
Refills are permitted on written prescription.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Step 3: Provide patient with written prescription with affixed Alosetron REMS sticker.

Refills are permitted on written prescription.

Informing the Patients about the Requirements of the Alosetron REMS Program

- Once an appropriate patient has been selected for therapy, review the Medication Guide and explain the risks of alosetron therapy to the patient.
- Answer any questions the patient may have.
- Instruct the patient to complete the Patient Acknowledgement Form. Place the original signed form in the patient's medical record and give a copy to the patient.

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- Answer any questions the patient may have.
- Instruct the patient to complete the Patient Acknowledgement Form. Place the original signed form in the patient's medical record and give a copy to the patient.

The Alosetron REMS Sticker

- The Alosetron REMS sticker must be affixed to every prescription:



- Refills may be written on prescriptions.
- No telephone, facsimile, or computerized prescriptions are permitted with this program.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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The Alosetron REMS Sticker

- The Alosetron REMS sticker must be affixed to every prescription:

Alosetron Tablets

The sticker indicates that this prescription is in compliance with the

Alosetron REMS

REFILL PERMITTED

- Refills may be written on prescriptions.
- No telephone, facsimile, or computerized prescriptions are permitted with this program.

Patient Responsibilities

Patients should be instructed to:

- read the Medication Guide before starting alosetron and each time they refill their prescription.
- not take alosetron if they are constipated.
- immediately discontinue alosetron and contact their prescriber if they become constipated or have symptoms of ischemic colitis such as new or worsening abdominal pain, bloody diarrhea, or blood in the stool.
- immediately contact their prescriber again if their constipation does not resolve after discontinuation of alosetron.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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- immediately contact their prescriber again if their constipation does not resolve after discontinuation of alosetron.

Patient Responsibilities(cont'd)

Patients should be instructed to:

- resume alosetron only if their constipation has resolved and after discussion with and the agreement of their treating prescriber.
- stop taking alosetron and contact their prescriber if alosetron does not adequately control IBS symptoms after 4 weeks of taking 1 mg twice-a-day.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Patient Responsibilities(cont'd)

Patients should be instructed to:

- resume alosetron only if their constipation has resolved and after discussion with and the agreement of their treating prescriber.
- stop taking alosetron and contact their prescriber if alosetron does not adequately control IBS symptoms after 4 weeks of taking 1 mg twice-a-day.

Encourage the Patients to Enroll in the Voluntary Follow-Up Survey for Alosetron

- Sponsors offer a patient survey to monitor the process of prescribing alosetron in clinical practice.
- The survey is important for monitoring the Alosetron REMS Program.
- The Alosetron REMS Program Patient Follow-up Survey Pre-Enrollment Form will be sent to prescribers after enrollment and is available upon request.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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- You have now reached the end of this Education Slide Deck.
- If you have questions or want to enroll in the Alosetron REMS Program, please call 1-844-267-8675 or visit www.AlosetronREMS.com.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Prescriber Enrollment Kit Overview Letter

<Date>

<Name>

< Address>

<City, State, and Zip Code>

Re: Prescriber Enrollment Kit

Dear <Prescriber Name>:

To support your enrollment in the Alosetron REMS Program the following program materials are enclosed:

- Alosetron Medication Guide
- Alosetron Prescribing Information
- Alosetron Patient Acknowledgement Form
- Alosetron Patient Follow-up Survey Pre Enrollment Form
- Alosetron REMS Stickers (Qty 80 per sheet)

If you have any questions or require additional information or further copies of any Alosetron REMS Program documents, please call the Alosetron REMS contact center at 1-844-267-8675 or visit www.AlosetronREMS.com.

Sincerely,

Alosetron REMS Program Team

Alosetron REMS Program

Patient Acknowledgment Form

Alosetron 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. Alosetron has not been shown to help men with irritable bowel syndrome (IBS) or patients under age 18. My doctor, or a healthcare provider under a doctor's direction, answered my questions about treatment with alosetron. I have read and I understand the Medication Guide for alosetron including the section "Who should not take alosetron?" and,

- I understand that about 1 out of every 1,000 women who take alosetron may get serious complications of constipation. I understand that about 3 of every 1,000 women who take alosetron over a 6-month period may get a serious problem where blood flow to parts of the large bowel is reduced (ischemic colitis). I understand that the serious condition of ischemic colitis, and other serious complications of constipation, can happen suddenly. These serious complications may lead to a hospital stay, and in rare cases, blood transfusions, surgery, and death.

- I understand that certain people may be more likely to develop a serious bowel condition while taking alosetron, including people who:
 - are older,
 - have other health problems,
 - take other medicines that may cause constipation.

- I understand alosetron is a medicine that should only be used for some women with severe chronic irritable bowel syndrome (IBS), whose main problem is diarrhea, and whose IBS symptoms have not been helped enough by other treatments.

- I will follow instructions in the Alosetron Medication Guide about:
 - **telling my doctor**, before taking alosetron, about any illnesses I have, or other medicines I am taking or planning to take.
 - **taking alosetron** exactly as my doctor prescribes it.
 - **stopping alosetron** and calling my doctor right away if I get constipated, if I have new or worse pain in my stomach area (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 alosetron 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 alosetron** to recheck my IBS symptoms.
 - **stopping alosetron and calling my doctor** if my IBS symptoms have not improved after 4 weeks of taking 1 mg alosetron 2 times a day.
- If I see other doctors about my IBS or possible side effects from alosetron, I will tell the doctor who prescribed alosetron.

My signature below indicates that I have read, understood, and agree with all the statements made above, that I have asked all the questions that I have about alosetron treatment. I would like to begin treatment with alosetron.

Patient Signature _____ **Date** _____

First Name _____ **Last Name** _____

After the patient signs this Alosetron REMS Program Patient Acknowledgement Form, the patient should receive a copy and the original signed form should be kept in the patient's medical record.

For questions regarding the Alosetron REMS Program, please call 1-844-267-8675 or visit the program website at www.AlosetronREMS.com.

***Patient Follow-Up Survey for Alosetron Hydrochloride Tablets
Pre-Enrollment Form***

What is the purpose of the Survey?

The Follow-Up Survey for the Alosetron REMS Program will help the supplier of alosetron hydrochloride learn more about alosetron. Everyone who takes alosetron is invited to voluntarily sign up. If you sign up you will get questions in the mail or by email about how you are doing on alosetron. You do not have to sign up if you do not wish to, but signing up will help us learn more about alosetron. The Survey is being done by the generic supplier of alosetron hydrochloride. The Survey results will be shared with the US Food and Drug Administration (FDA) to help all patients; however, your identity and individual responses will be kept confidential.

How will the Survey work?

By sending in this Pre-Enrollment Form, you agree to participate in the Survey and be contacted by mail, email, and/or phone. Detailed information about the Survey, including the consent form and initial Survey questions, will be sent to you after you agree to sign up. You will receive a small payment for your time.

Will my information be confidential?

The information that you provide on this Pre-Enrollment Form will be kept confidential by the generic supplier of alosetron.

How do I enroll in the Follow-Up Survey for the Alosetron REMS Program?

Please complete the Pre-Enrollment Form now and mail or fax it to the Alosetron REMS Program using the information provided on the bottom of the form. **You need to send in the Pre-Enrollment Form only once.** Once received by the Alosetron REMS Program, a program contact center representative will mail or email you the program materials. The timing of this contact may not be immediate, as it is based upon our survey response requirements from the FDA. If you get more Pre-Enrollment forms from your healthcare provider and have already enrolled, please discard them.

What if I still have more questions?

If you have any questions about enrolling in the Survey, please call the Alosetron REMS Program at 1-844-267-8675.

Pre-Enrollment Contact Information

I agree to be contacted by mail, email, and/or phone about participating in the Patient Follow-Up Survey for the Alosetron REMS Program.

(Please print)

Name _____
First Middle Initial Last

E-mail _____

Address _____

City _____ State _____ Zip _____

Telephone Number (with area code) _____

Date of Birth _____ Female/Male
Month/Day/Year (Circle One)

Your Signature _____ Date _____

Are you currently under 18 years of age? Yes No
(If yes, your parent or guardian must sign this form below.)

Parent/Guardian Signature _____ Date _____

Dear Pharmacist:

Important Information for Pharmacists

The generic supplier of alosetron, Roxane Laboratories Inc., would like to inform you about important aspects of alosetron tablets and a Risk Evaluation and Mitigation Strategy (REMS) for alosetron.

Alosetron 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 alosetron. 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 alosetron immediately. Patients who develop ischemic colitis should not resume alosetron therapy. Because of the serious gastrointestinal adverse reactions associated with alosetron, 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 alosetron in men.

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

In order to comply with the Alosetron REMS Program, pharmacists need to:

- **Dispense only prescriptions that have an Alosetron REMS sticker² - never fill telephone, facsimile, or computer-generated prescriptions; refills are only permitted on written prescriptions (Figure 1)**
- **If an Alosetron REMS sticker is not present on the prescription, call the Alosetron REMS Program contact center at 1-844-267-8675 to confirm that the prescriber is enrolled in the Alosetron REMS Program.**



Figure 1. The Alosetron REMS sticker ensures appropriate prescribing and dispensing of alosetron

We have enclosed a copy of the Alosetron 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 alosetron.

Only prescribers who have enrolled in the Alosetron REMS Program should prescribe alosetron. Alosetron 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 alosetron. 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 alosetron immediately. Patients who develop ischemic colitis should not resume alosetron therapy.

Enclosed for your reference are the following educational materials that will provide additional details on alosetron and the Alosetron REMS Program:

- The Alosetron full Prescribing Information

² In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws.

- The Alosetron Medication Guide

For more information on the Alosetron REMS Program, including an educational slide deck (Alosetron REMS Program Pharmacist Education Slide Deck) designed to educate pharmacists on their role within the program, please call 1-844-267-8675 or visit the program website at www.AlosetronREMS.com.

Sincerely,

Roxane Laboratories Inc., The Generic Supplier of alosetron

THE ALOSETRON REMS PROGRAM

Pharmacist Education Slide Deck

Understanding the Benefits and Risks of Alosetron

The Alosetron REMS Program - Please see
complete Prescribing Information for
Alosetron Tablets for full details.

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THE ALOSETRON REMS PROGRAM

Pharmacist Education Slide Deck

Understanding the Benefits and Risks of Alosetron

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details

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The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 1:

Purpose

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 1: Purpose

Purpose of the Pharmacist Educational Slide Deck for Alosetron

- By reviewing the information provided in this presentation, pharmacists who dispense alosetron hydrochloride (alosetron) will better understand the:
 - **Restricted distribution process for this product;**
 - **Risks and benefits of alosetron;**
 - **Etiology of irritable bowel syndrome;**
 - **The Alosetron REMS Program**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Purpose of the Pharmacist Educational Slide Deck for Alosetron

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 - **Restricted distribution process for this product;**
 - **Risks and benefits of alosetron;**
 - **Etiology of irritable bowel syndrome;**
 - **The Alosetron REMS Program**

Risk Evaluation and Mitigation Strategy (REMS)

The Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for alosetron to ensure the benefits of the drug outweigh the risk of serious gastrointestinal adverse reactions. A REMS is a strategy to address the serious risks associated with a drug. The REMS can range from periodic assessment of a product's postmarketing safety profile to strict limitations on the way a drug is prescribed, distributed, or dispensed.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Risk Evaluation and Mitigation Strategy (REMS)

The Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for alosetron to ensure the benefits of the drug outweigh the risk of serious gastrointestinal adverse reactions. A REMS is a strategy to address the serious risks associated with a drug. The REMS can range from periodic assessment of a product's postmarketing safety profile to strict limitations on the way a drug is prescribed, distributed, or dispensed.

Goal of The Alosetron REMS Program and Key Elements

The Alosetron REMS Program was implemented to help reduce the risks of serious GI adverse events.

The Goals of the Alosetron REMS Program are:

•To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients in whom benefits exceed the risks.

•To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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- **To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.**

Goal of The Alosetron REMS Program and Key Elements (cont'd)

The Key Elements of the Alosetron REMS are:

- only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, can prescribe alosetron.
- **pharmacists may only dispense alosetron from prescriptions with an Alosetron REMS sticker and written by prescribers participating in the Alosetron REMS Program.** ¹

¹. In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

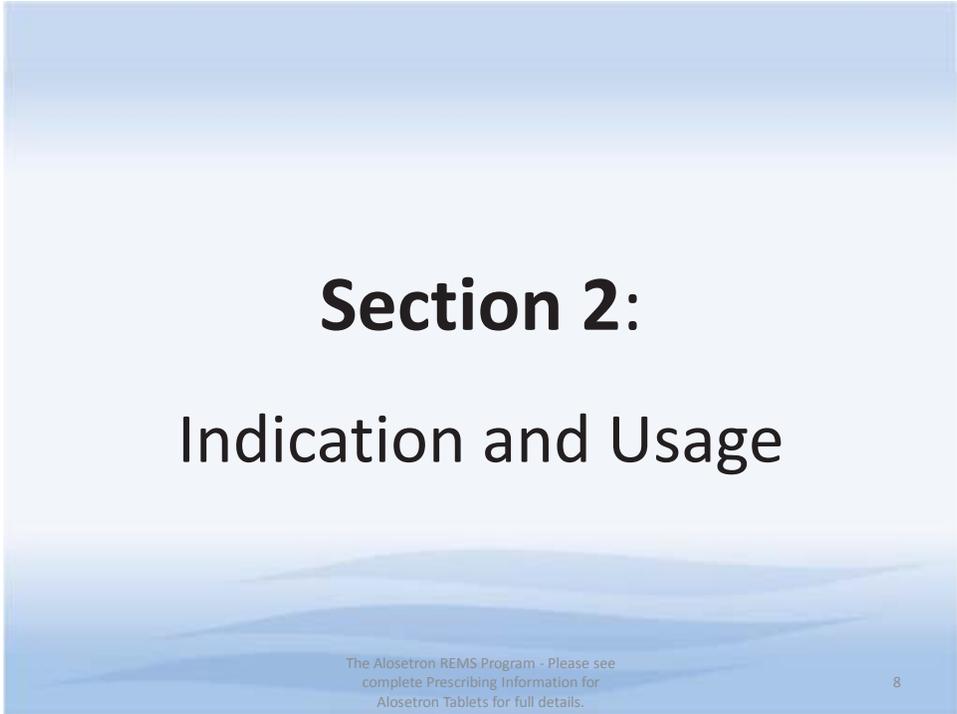
7

Goal of The Alosetron REMS Program and Key Elements (cont'd)

The Key Elements of the Alosetron REMS are:

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Section 2:
Indication and Usage

Indication and Usage

Alosetron is indicated **ONLY** for women with severe diarrhea-predominant IBS who have:

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

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Indication and Usage (cont'd)

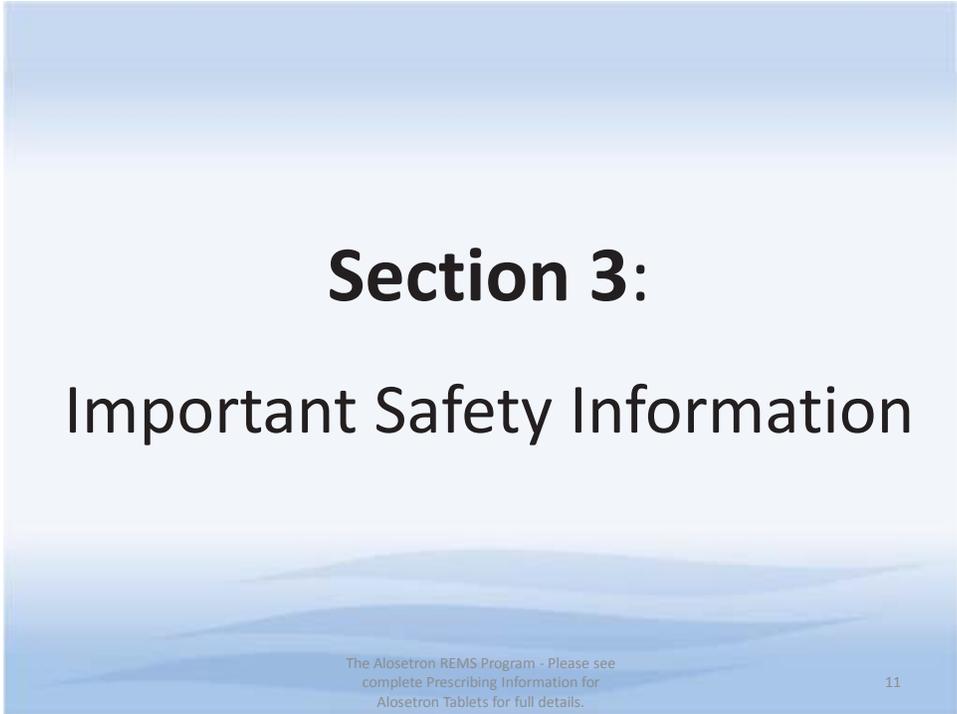
- Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:
 - **frequent and severe abdominal pain/discomfort,**
 - **frequent bowel urgency or fecal incontinence,**
 - **disability or restriction of daily activities due to IBS.**
- Because of infrequent but serious GI adverse reactions associated with alosetron, 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 alosetron in men.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Indication and Usage (cont'd)

- Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:
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Section 3:
Important Safety Information

Boxed Warning

WARNING: SERIOUS GASTROINTESTINAL ADVERSE REACTIONS

- Infrequent but serious gastrointestinal adverse reactions have been reported with the use of alosetron. These events, including ischemic colitis and serious complications of constipation, have resulted in hospitalization, and rarely, blood transfusion, surgery, and death.
- The Alosetron REMS Program was implemented to help reduce risks of serious gastrointestinal adverse reactions. Only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, should prescribe alosetron.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Boxed Warning (cont'd)

- Alosetron is indicated only for women with severe diarrhea-predominant IBS who have not responded adequately to conventional therapy. Before receiving the initial prescription for alosetron, the patient must read and sign the Patient Acknowledgement Form for alosetron.
- Alosetron should be discontinued immediately in patients who develop constipation or symptoms of ischemic colitis. Patients should immediately report constipation or symptoms of ischemic colitis to their prescriber. Alosetron should not be resumed in patients who develop ischemic colitis. Patients who have constipation should immediately contact their prescriber if the constipation does not resolve after alosetron is discontinued. Patients with resolved constipation should resume alosetron only on the advice of their treating prescriber.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Boxed Warning (cont'd)

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Warnings and Precautions

Serious Complications of Constipation

- Some patients have experienced serious complications of constipation without warning. Examples include:
 - **obstruction, ileus, impaction, toxic megacolon, and secondary bowel ischemia have been reported with use of alosetron during clinical trials.**
 - **in addition, rare cases of intestinal perforation and death have been reported from postmarketing clinical practice.**
 - **in some cases, complications of constipation required intestinal surgery, including colectomy.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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 - **in some cases, complications of constipation required intestinal surgery, including colectomy.**

Warnings and Precautions (cont'd)

Serious Complications of Constipation (cont'd)

- The incidence of serious complications of constipation was ~0.1%, or 1 per 1,000 patients, in women receiving either alosetron or placebo.
- Patients who are elderly, debilitated, or taking additional medications that decrease GI motility may be at greater risk for complications of constipation.
- Alosetron should be discontinued immediately in patients who develop constipation.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

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- Alosetron should be discontinued immediately in patients who develop constipation.

Warnings and Precautions (cont'd)

Ischemic Colitis

- Some patients have experienced symptoms of ischemic colitis without warning.
- Ischemic colitis has been reported in patients receiving alosetron in clinical trials as well as during marketed use of the drug.
- In IBS clinical trials:
 - **cumulative incidence of ischemic colitis in women receiving alosetron was:**
0.2%, or 2 per 1,000 patients (95% CI 1 to 3), over 3 months
0.3%, or 3 per 1,000 patients (95% CI 1 to 4), over 6 months
 - **patient experience in controlled clinical trials is insufficient to estimate the incidence of ischemic colitis in patients taking alosetron for longer than 6 months**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

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 - **patient experience in controlled clinical trials is insufficient to estimate the incidence of ischemic colitis in patients taking alosetron for longer than 6 months**

Warnings and Precautions (cont'd)

Ischemic Colitis (cont'd)

- Alosetron should be discontinued immediately in patients with signs of ischemic colitis, e.g., rectal bleeding, bloody diarrhea, or new or worsening abdominal pain.
- Because ischemic colitis can be life threatening, patients with signs or symptoms of ischemic colitis should be evaluated promptly and have appropriate diagnostic testing performed.
- Treatment with alosetron should not be resumed in patients who develop ischemic colitis.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Warnings and Precautions (cont'd)

Ischemic Colitis (cont'd)

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- Because ischemic colitis can be life threatening, patients with signs or symptoms of ischemic colitis should be evaluated promptly and have appropriate diagnostic testing performed.
- Treatment with alosetron should not be resumed in patients who develop ischemic colitis

Contraindications

- Alosetron should not be initiated in patients with constipation.
- Alosetron is contraindicated in patients with a 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.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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 - **ischemic colitis, impaired intestinal circulation, thrombophlebitis, or hypercoagulable state;**
 - **Crohn’s disease or ulcerative colitis;**
 - **diverticulitis;**
 - **severe hepatic impairment.**

Contraindications (cont'd)

- Alosetron should not be used by patients who are unable to understand or comply with the Patient Acknowledgement Form.
- Concomitant administration of alosetron with fluvoxamine is contraindicated.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Contraindications (cont'd)

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Drug Interactions

In vivo data suggest that alosetron is primarily metabolized by cytochrome P450 (CYP) 1A2, with minor contributions from CYP3A4 and CYP2C9. Therefore, inducers or inhibitors of these enzymes may change the clearance of alosetron.

- Concomitant administration of alosetron and fluvoxamine is contraindicated.
- Concomitant administration of alosetron and moderate CYP1A2 inhibitors, including quinolone antibiotics and cimetidine, has not been evaluated, but should be avoided unless clinically necessary because of similar potential drug interactions.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Drug Interactions (cont'd)

- Caution should be used when alosetron and ketoconazole are administered concomitantly.
- Coadministration of alosetron and strong CYP3A4 inhibitors, such as clarithromycin, telithromycin, protease inhibitors, voriconazole, and itraconazole has not been evaluated but should be undertaken with caution because of similar potential drug interactions.
- The effect of induction or inhibition of other pathways on exposure to alosetron and its metabolites is not known.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Drug Interactions (cont'd)

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- The effect of induction or inhibition of other pathways on exposure to alosetron and its metabolites is not known.

Use in Specific populations

- Pregnancy Category B.
- It is not known whether alosetron is excreted in human milk; caution should be exercised when alosetron is administered to a nursing woman.
- Safety and effectiveness in pediatric patients have not been established.
- Postmarketing experience suggests that elderly patients may be at greater risk for complications of constipation; therefore, appropriate caution and follow-up should be exercised if alosetron is prescribed for these patients.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Use in Specific populations

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- It is not known whether alosetron is excreted in human milk; caution should be exercised when alosetron is administered to a nursing woman.
- Safety and effectiveness in pediatric patients have not been established.
- Postmarketing experience suggests that elderly patients may be at greater risk for complications of constipation; therefore, appropriate caution and follow-up should be exercised if alosetron is prescribed for these patients.

Use in Specific populations (cont'd)

- Increased exposure to alosetron and/or its metabolites is likely to occur in patients with hepatic impairment. Alosetron should not be used in patients with severe hepatic impairment and should be used with caution in patients with mild or moderate hepatic impairment.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Use in Specific populations (cont'd)

- Increased exposure to alosetron and/or its metabolites is likely to occur in patients with hepatic impairment. Alosetron should not be used in patients with severe hepatic impairment and should be used with caution in patients with mild or moderate hepatic impairment.

Adverse Reactions Reported in ≥ 1% of IBS Patients^a

Gastrointestinal Adverse Reactions	Alosetron 1 mg BID (n=8,328 ^b)	Placebo (n=2,363)
Constipation ^c	29%	6%
Abdominal discomfort and pain	7%	4%
Nausea	6%	5%
GI discomfort and pain	5%	3%
Abdominal distention	2%	1%
Regurgitation and reflux	2%	2%
Hemorrhoids	2%	1%

^a Reported in ≥1% of alosetron patients and occurring more frequently on alosetron 1 mg twice-a-day than on placebo.

^b Data reported from 22 repeat-dose studies in patients with IBS treated for 8 to 24 weeks.

^c $P < 0.0001$ vs placebo.

The Alosetron REMS Program - Please see
complete Prescribing Information for
Alosetron Tablets for full details.

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Adverse Reactions Reported in ≥ 1% of IBS Patients^a

Gastrointestinal Adverse Reactions	Alosetron 1 mg BID (n=8,328 ^b)	Placebo (n=2,363)
Constipation^c	29%	6%
Abdominal discomfort and pain	7%	4%
Nausea	6%	5%
GI discomfort and pain	5%	3%
Abdominal distention	2%	1%
Regurgitation and reflux	2%	2%
Hemorrhoids	2%	1%

^a Reported in ≥1% of alosetron patients and occurring more frequently on alosetron 1 mg twice-a-day than on placebo.

^b Data reported from 22 repeat-dose studies in patients with IBS treated for 8 to 24 weeks.

^c $P < 0.0001$ vs placebo.

Adverse Reactions

Constipation is a frequent and dose-related side effect of treatment with alosetron.

- In clinical studies constipation was reported in ~29% of patients with IBS treated with alosetron 1 mg twice daily (n=9,316).
 - **The effect was statistically significant compared with placebo ($P<0.0001$);**
 - **11% of patients treated with alosetron 1 mg twice daily withdrew from the studies due to constipation.**
- Although the number of IBS patients treated with alosetron 0.5 mg twice daily is relatively small (n=243), 11% of patients reported constipation and 4% of patients withdrew from clinical studies due to constipation.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Adverse Reactions

Constipation is a frequent and dose-related side effect of treatment with alosetron.

- In clinical studies constipation was reported in ~29% of patients with IBS treated with alosetron 1 mg twice daily (n=9,316).
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- Although the number of IBS patients treated with alosetron 0.5 mg twice daily is relatively small (n=243), 11% of patients reported constipation and 4% of patients withdrew from clinical studies due to constipation.

Overdosage

- No specific antidote available for overdose of alosetron.
- Patients should be managed with appropriate supportive therapy.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Overdosage

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- Patients should be managed with appropriate supportive therapy.

Section 4:

Alosetron

REMS Program

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Section 4:
Alosetron REMS Program

Prescriber Enrollment in the Alosetron REMS Program

- Prescribers must read the full PI and understand the benefits and risks of treatment with alosetron for severe diarrhea-predominant IBS.
- Prescribers then complete the Prescriber Enrollment Form at www.AlosetronREMS.com or return it by mail or by fax.
- **The form must be returned to the sponsor before a prescriber can be considered enrolled in the Alosetron REMS Program.**
- Alosetron REMS Program Kits, including Medication Guides and stickers that need to be affixed to every prescription, are provided after enrollment.

The Alosetron REMS Program - Please see
complete Prescribing Information for
Alosetron Tablets for full details.

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Prescriber Enrollment in the Alosetron REMS Program

- Prescribers must read the full PI and understand the benefits and risks of treatment with alosetron for severe diarrhea-predominant IBS.
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- **The form must be returned to the sponsor before a prescriber can be considered enrolled in the Alosetron REMS Program.**
- Alosetron REMS Program Kits, including Medication Guides and stickers that need to be affixed to every prescription, are provided after enrollment.

Prescriber Requirements in the Alosetron REMS Program

- Once an appropriate patient has been selected for therapy, the Medication Guide and risks of alosetron therapy must be discussed with the patient.
- Any questions from the patient should be initially addressed by the prescriber or a healthcare provider under the prescriber's direction.
- Instruct the patient to complete the Patient Acknowledgement Form. The original signed form should be placed in the patient's medical record and another copy should be given to the patient.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Prescriber Requirements in the Alosetron REMS Program

- Once an appropriate patient has been selected for therapy, the Medication Guide and risks of alosetron therapy must be discussed with the patient.
- Any questions from the patient should be initially addressed by the prescriber or a healthcare provider under the prescriber's direction.
- Instruct the patient to complete the Patient Acknowledgement Form. The original signed form should be placed in the patient's medical record and another copy should be given to the patient.

Overview of Prescriber Responsibilities

Step 1: Review and provide Medication Guide to the patient.

Step 2: Have the patient complete the Patient Acknowledgment Form.
Place the original in the patient's medical record and give a copy to the patient.

Step 3: Provide patient with written prescription with affixed Alosetron REMS sticker.
Refills are permitted on written prescription.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Overview of Prescriber Responsibilities

Step 1: Review and provide Medication Guide to the patient.

Step 2: Have the patient complete the Patient Acknowledgment Form.

Place the original in the patient's medical record and give a copy to the patient.

Step 3: Provide patient with written prescription with affixed Alosetron REMS sticker.

Refills are permitted on written prescription.

Section 5:

Role of the Pharmacist in the Alosetron REMS Program

The Alosetron REMS Program - Please see
complete Prescribing Information for
Alosetron Tablets for full details.

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Section 5:
Role of the Pharmacist in the Alosetron REMS Program

Pharmacist Responsibilities

- Learn about the Alosetron REMS Program.
- Understand the benefits and risks of treatment with alosetron **for severe diarrhea-predominant IBS, which are described in the Prescribing Information, the Medication Guide, and the Patient Follow-Up Survey Pre-Enrollment Form.**
- To ensure documentation of safe-use conditions, pharmacists must confirm the validity of every prescription of alosetron by ensuring that the Alosetron REMS sticker is present on the prescription prior to dispensing alosetron to a patient.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Pharmacist Responsibilities

- Learn about the Alosetron REMS Program.
- Understand the benefits and risks of treatment with alosetron **for severe diarrhea-predominant IBS, which are described in the Prescribing Information, the Medication Guide, and the Patient Follow-Up Survey Pre-Enrollment Form.**
- To ensure documentation of safe-use conditions, pharmacists must confirm the validity of every prescription of alosetron by ensuring that the Alosetron REMS sticker is present on the prescription prior to dispensing alosetron to a patient.

Pharmacist Responsibilities (cont'd)

- If an Alosetron REMS sticker is not present on the prescription, call 1-844-267-8675 to confirm that the prescriber is enrolled in the Alosetron REMS.¹
- Provide each patient with their prescribed treatment of alosetron **and a copy of the alosetron Medication Guide.**

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Pharmacist Responsibilities (cont'd)

- If an Alosetron REMS sticker is not present on the prescription, call 1-844-267-8675 to confirm that the prescriber is enrolled in the Alosetron REMS.¹
- Provide each patient with their prescribed treatment of alosetron **and a copy of the alosetron Medication Guide.**

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to State substitution laws

The Alosetron REMS Program

- To prescribe alosetron, prescribers must be enrolled in the Alosetron REMS Program
- To enroll, prescribers must understand the benefits and risks of treatment with alosetron for women with severe diarrhea-predominant IBS, including the information in the Prescribing Information, Medication Guide, and Patient Acknowledgement Form.
- Pharmacists should also learn about and understand the benefits and risks associated with alosetron treatment.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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The Alosetron REMS Program

- To prescribe alosetron, prescribers must be enrolled in the Alosetron REMS Program
- To enroll, prescribers must understand the benefits and risks of treatment with alosetron for women with severe diarrhea-predominant IBS, including the information in the Prescribing Information, Medication Guide, and Patient Acknowledgement Form.
- Pharmacists should also learn about and understand the benefits and risks associated with alosetron treatment.

The Alosetron REMS Sticker

- Upon enrollment in the Alosetron REMS Program, stickers for prescriptions are provided to prescribers.



The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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The Alosetron REMS Sticker

- Upon enrollment in the Alosetron REMS Program, stickers for prescriptions are provided to prescribers.

Alosetron Tablets

The sticker indicates that this prescription is in compliance with the

Alosetron REMS

REFILL PERMITTED

The Alosetron REMS Sticker (cont'd)

- Stickers affixed to a prescription of alosetron **indicate the following:**
 - **Certifies participation of a prescriber in the Alosetron REMS;**
 - **Alosetron prescription is valid and may be filled by a pharmacist;**
 - **Prescription may include refills;**
 - **Telephone, faxed, or computerized prescriptions are NOT valid under the program.**

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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The Alosetron REMS Sticker (cont'd)

- Stickers affixed to a prescription of alosetron **indicate the following:**
 - **Certifies participation of a prescriber in the Alosetron REMS;**
 - **Alosetron prescription is valid and may be filled by a pharmacist;**
 - **Prescription may include refills;**
 - **Telephone, faxed, or computerized prescriptions are NOT valid under the program.**

Overview of Pharmacist Responsibilities

Step 1: Verify the validity of Alosetron prescription by checking for the Alosetron REMS sticker (refills are permitted on written prescriptions)

Step 2: Dispense Alosetron to the patient, including the Alosetron Medication Guide

Note to Pharmacist:

If an Alosetron REMS sticker is not present on the prescription, call 1-844-267-8675 to confirm that the prescriber is enrolled in the Alosetron REMS Program. In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitute of alosetron is permitted pursuant to State substitution laws.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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Overview of Pharmacist Responsibilities

Step 1: Verify the validity of Alosetron prescription by checking for the Alosetron REMS sticker (refills are permitted on written prescriptions)

Step 2: Dispense Alosetron to the patient, including the Alosetron Medication Guide

Note to Pharmacist:

If an Alosetron REMS sticker is not present on the prescription, call 1-844-267-8675 to confirm that the prescriber is enrolled in the Alosetron REMS Program. In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitute of alosetron is permitted pursuant to State substitution laws.

- You have now reached the end of this Education Slide Deck.
- If you have questions regarding the Alosetron REMS Program, please call 1-844-267-8675 or visit www.AlosetronREMS.com.

The Alosetron REMS Program - Please see complete Prescribing Information for Alosetron Tablets for full details.

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- You have now reached the end of this Education Slide Deck.
- If you have questions regarding the Alosetron REMS Program, please call 1-844-267-8675 or visit www.AlosetronREMS.com.

Alosetron REMS Program

Risk Evaluation and Mitigation Strategy

**Web Mockups
V10**

Footer is included on every web page. To reduce the length of the document, the screenshot is included once.

Please consult the [Prescribing Information](#) and [Important Safety Information](#).

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HOME PAGE



	For Patients	For Prescribers	For Pharmacists	Important Safety Information
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Alosetron REMS (Risk Evaluation and Mitigation Strategy)

What is the Alosetron REMS Program?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary for alosetron to ensure the benefits of the drug outweigh the risk of serious gastrointestinal (GI) adverse reactions.

The Alosetron REMS Program was implemented to help reduce the risks of a serious GI adverse event.

The goals of the Alosetron REMS Program are:

- To mitigate the risk of ischemic colitis (IC) and serious complications of constipation (CoC) associated with alosetron hydrochloride (hereinafter, referred to as alosetron) by ensuring that alosetron is used in only severely affected patients in whom the benefits exceed the risks.
- To ensure that the risk of IC and serious CoC with the use of alosetron are communicated to patients, pharmacists, and prescribers.

The key elements of the Alosetron REMS Program are:

- Only prescribers who have enrolled in the Alosetron REMS Program, based on their understanding of the benefits and risks, can prescribe alosetron.
- Pharmacists may only dispense alosetron from prescriptions with a sticker¹ and written by prescribers participating in the Alosetron REMS Program.

Alosetron is indicated **ONLY** for women with severe diarrhea-predominant IBS who have:

- Chronic irritable bowel syndrome 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.

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to state substitution laws.

PATIENT



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Patient Role in the Alosetron REMS Program

The Alosetron Medication Guide is provided to enhance patient awareness and understanding of the potential serious risks associated with the use of alosetron. The Alosetron Medication Guide includes critical information that every patient and caregiver should know about alosetron. Please use the links below to review the Medication Guide and Important Safety Information for alosetron.



[Medication Guide](#)



[Important Safety Information](#)

The Patient Follow-Up Survey for the Alosetron REMS Program will help the supplier of alosetron hydrochloride learn more about alosetron. Everyone who takes alosetron is invited to voluntarily sign up. If you sign up you will get questions in the mail or by email about how you are doing on alosetron. You do not have to sign up if you do not wish to, but signing up will help us learn more about alosetron. The Survey is being done by the generic supplier of alosetron hydrochloride. The Survey results will be shared with the U.S. Food and Drug Administration (FDA) to help all patients; however, your identity and individual responses will be kept confidential. If you are taking alosetron and want to participate, please use the link below to download, print and complete the Patient Follow-up Survey Pre-Enrollment Form and return it to the program by fax or mail as indicated on the form.



[Patient Follow-up Survey Pre-Enrollment Form](#)



PRESCRIBERS



Prescriber Role in the Alosetron REMS Program

Only prescribers who enroll in the Alosetron REMS Program, based on their understanding of the benefits and risks, can prescribe alosetron. The Alosetron REMS Program facilitates patients safety. The program requires patients, prescribers and pharmacists to understand the appropriate use of alosetron and its potential risks, as well as potential adverse events and how to handle them.

Prescribers need to comply with the following requirements of the Alosetron REMS Program:

- Complete enrollment in the Alosetron REMS Program.
- Review and provide Medication Guide to the patient.
- Have the patient complete the Patient Acknowledgment Form. Place the original in the patient's medical record and give a copy to the patient.
- Provide patient with a written prescription with affixed Alosetron REMS sticker.

Prescriber Enrollment

Prescribers must enroll in the Alosetron REMS Program prior to prescribing alosetron.

To enroll in the Alosetron REMS Program via web:

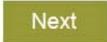
1. Review the Prescriber Education Slide Deck located in the Resources section below.
2. Press **Next** to begin the enrollment process.

To enroll in the Alosetron REMS Program via fax:

1. Review the Prescriber Education Slide Deck located in the Resources section below.
2. Complete the Prescriber Enrollment Form located in the Resources section below.
3. Fax the completed Prescriber Enrollment Form to the Alosetron REMS Program at 1-800-535-6805.

Resources

-  [Prescriber Enrollment Form](#)
-  [Medication Guide](#)
-  [Patient Acknowledgement Form](#)
-  [Important Safety Information](#)
-  [Prescribing Information](#)
-  [Prescriber Education Slide Deck](#)



PRESCRIBER AGREEMENT



For Patients

For Prescribers

For Pharmacists

Important Safety Information

The Alosetron REMS Program - Prescriber Enrollment

To begin the enrollment process, please read the attestation statements below.

I understand and agree to the following:

- I have read and understand the complete Prescribing Information and other enrollment materials for the Alosetron REMS Program. I understand the risks associated with its use and will follow the requirements of the Alosetron REMS Program described below. I understand the importance of reporting all cases of ischemic colitis and serious complications of constipation to the Alosetron REMS Program at 1-844-267-8675.
- I understand that alosetron is approved only for women with severe, diarrhea-predominant irritable bowel syndrome who have:
 - chronic irritable bowel syndrome 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 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
- I understand that if I prescribe alosetron for my patient(s), I must be able to perform the following:
 - diagnose and manage irritable bowel syndrome, ischemic colitis, constipation, and complications of constipation or refer patients to a specialist as needed
 - ensure that all patients under my care are educated by me or a healthcare provider in my practice about the benefits and risks of the drug
- I agree to provide each of my patients with a copy of the Alosetron Medication Guide at initiation of alosetron treatment.
- I agree to review the content of the Medication Guide and encourage the patient to read it and ask questions.
- I agree to have each patient sign the Alosetron Patient Acknowledgement Form. The original signed form must be placed in the patient's medical record, and a copy given to the patient.
- I agree to inform my patients about the Alosetron Patient Follow-Up Survey, encourage them to participate and provide them with an Alosetron Patient Follow-Up Survey Pre-Enrollment Form.
- I agree to affix Alosetron REMS stickers to written prescriptions for alosetron (i.e., the original and all subsequent prescriptions). Alosetron REMS stickers will be provided as part of the Alosetron REMS Program. Refills are permitted to be written on prescriptions.
- I agree to ensure that all prescriptions for alosetron are written and not transmitted by telephone, facsimile, or computer.

To continue enrollment, please press the **I Agree** button.

I Agree

PRESCRIBER ONLINE ENROLLMENT FORM



- For Patients
- For Prescribers**
- For Pharmacists
- Important Safety Information

Please complete the fields below and press **Submit** to complete enrollment in the Alosetron REMS Program. All fields below are required unless otherwise indicated.

Enrolling Prescriber

First Name	<input type="text"/>
Last Name	<input type="text"/>
National Provider Identifier (NPI)	<input type="text"/>

Prescriber Office Address

Office Name	<input type="text"/>	
Address 1	<input type="text"/>	
Address 2	<input type="text"/>	(Optional)
City	<input type="text"/>	
State	<input type="text" value="-- Please select --"/>	
Zip Code	<input type="text"/>	
Phone	<input type="text"/>	
Fax	<input type="text"/>	
Email	<input type="text"/>	
Correspondence Confirmation Preference <input type="radio"/> Email <input type="radio"/> Fax		

Your signature and date are required to complete your enrollment. Please type your exact first and last name along with today's date in the spaces provided below. This will serve as your electronic signature and will certify that you have read and agreed to the terms provided for the program.

<input type="text" value="Signature (First and Last Name as typed above)"/>	<input type="text" value="Date MM/DD/YYYY"/>	<input type="button" value="Submit"/>
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PRESCRIBER ENROLLMENT CONFIRMATION



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Congratulations!

You have successfully enrolled in the Alosetron REMS Program!

Below is your Alosetron REMS Program Enrollment ID. Please note, you will receive an enrollment confirmation via your correspondence confirmation preference. Please retain this information for your records. You will also receive additional enrollment materials via postal mail in the next 7 to 10 days.

Enrollment ID: <Enrollment ID>

PHARMACISTS



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Pharmacist Role in the Alosetron REMS Program

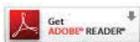
As a pharmacist you play an important role in the Alosetron REMS Program. Please read the complete Prescribing Information below, which includes the Medication Guide. To become familiar with the requirements of the program, please also review the Pharmacists Education Slide Deck below.

 [Pharmacists Education Slide Deck](#)

 [Pharmacist Letter](#)

 [Prescribing Information](#)

 [Medication Guide](#)



Pharmacists need to comply with the following requirements of the Alosetron REMS Program:

- Dispense only prescriptions that have an Alosetron REMS sticker¹.
- Never fill telephone, facsimile, or computer generated prescriptions.
- Refills are permitted on written prescriptions.
- Dispense the Medication Guide with each prescription.

¹ In the alternative, a prescription for alosetron may be dispensed in the presence of a Prescribing Program for LOTRONEX™ sticker, if generic substitution of alosetron is permitted pursuant to state substitution laws.

IMPORTANT SAFETY INFORMATION



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Important Safety Information

WARNING: SERIOUS GASTROINTESTINAL ADVERSE REACTIONS

See full prescribing information for complete boxed warning

Infrequent but serious gastrointestinal adverse reactions have been reported with the use of alosetron. These events, including ischemic colitis and serious complications of constipation, have resulted in hospitalization and, rarely, blood transfusion, surgery, and death.

- Only prescribers who have enrolled in the Alosetron REMS Program can prescribe alosetron. (5.3)
- Alosetron is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have not responded adequately to conventional therapy. (1)
- Discontinue alosetron immediately in patients who develop constipation or symptoms of ischemic colitis. Do not resume alosetron in patients who develop ischemic colitis. (2.1, 5.1, 5.2)

Alosetron is 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 who have 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.

Alosetron should not be initiated in patients with constipation. Alosetron is contraindicated in patients with a 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; inability to understand or comply with the Patient Acknowledgement Form; and concomitant use of fluvoxamine.

Please see the Full Prescribing Information for alosetron for all information including boxed warnings, and the Medication Guide for important safety information.

If you have any questions or require additional information or further copies of all the Alosetron REMS Program documents, please visit either the Alosetron REMS Program website or call the Alosetron REMS Program at 1-844-267-8675.

Promptly report suspected adverse events directly to the Alosetron REMS Program at 1-844-267-8675. You also may report adverse event information to the FDA MedWatch Reporting System by telephone at (800) FDA-1088 or by mail using Form 3500, available at www.fda.gov/medwatch.

RESOURCES



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Resources

Patient

 [Patient Follow-up Survey Pre-Enrollment Form](#)

Prescriber

 [Prescribing Information](#)

 [Medication Guide](#)

 [Prescriber Education Slide Deck](#)

 [Prescriber Enrollment Form](#)

 [Patient Acknowledgement Form](#)

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Pharmacist

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 [Medication Guide](#)

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 [Pharmacist Letter](#)



CONTACT US



For Patients

For Prescribers

For Pharmacists

Important Safety Information

Contact Us

If you have any questions or require additional information, please contact the Alosetron REMS Program utilizing the information provided below.

Phone Number

1-844-267-8675

Fax Number

1-800-535-6805

Mailing Address

Alosetron REMS Program
PO BOX 29292
PHOENIX AZ 85038-9292

MEDICATION GUIDE

ALOSETRON (a-LOW-zeh-tron) Hydrochloride Tablets

Before using alosetron hydrochloride tablets for the first time, you should:

- Understand that alosetron hydrochloride tablets have serious risks for some people.
- Read and follow the directions in this Medication Guide.
- Sign a Patient Acknowledgement Form.

Read this Medication Guide carefully before you sign the Patient Acknowledgement Form. You must sign the Patient Acknowledgement Form before you start alosetron hydrochloride tablets. Read the Medication Guide you get with each refill for alosetron hydrochloride tablets. There may be new information. This Medication Guide does not take the place of talking with your doctor.

1. What is the most important information I should know about alosetron hydrochloride tablets?

A. Alosetron hydrochloride tablets are 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 alosetron hydrochloride tablets. 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets.

To lower your chances of getting serious complications of constipation, do the following:

- **If you are constipated**, do not start taking alosetron hydrochloride tablets.
- **If you get constipated while taking alosetron hydrochloride tablets**, stop taking it right away and call your doctor.
- **If your constipation does not get better after stopping alosetron hydrochloride tablets**, call your doctor again.
- **If you stopped taking alosetron hydrochloride tablets, do not start taking alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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 alosetron hydrochloride tablets 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. Are alosetron hydrochloride tablets right for you?

Alosetron hydrochloride tablets may be right for you if all 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 **at least 1** 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 alosetron hydrochloride tablets works in men or children under age 18.

D. There is a special prescribing program for alosetron hydrochloride tablets.

Only doctors who have signed up with the Alosetron REMS Program should write prescriptions for alosetron hydrochloride tablets. As part of signing up, these doctors have said that they understand about IBS and the possible side effects of alosetron hydrochloride tablets. They have agreed to use a special sticker on **written** prescriptions for alosetron hydrochloride tablets, so the pharmacist will know that the doctors have signed up with the Alosetron REMS Program. No telephone, facsimile, or computerized prescriptions are permitted with this program. Refills may be written on prescriptions.

You may be taught about alosetron hydrochloride tablets by your doctor or healthcare provider under a doctor's direction. Your doctor will ask you to sign a Patient Acknowledgement Form after you read this Medication Guide for the first time. Signing the Patient Acknowledgement Form means that you understand the benefits and risks of alosetron hydrochloride tablets and that you have read and understand this Medication Guide.

2. What are alosetron hydrochloride tablets?

Alosetron hydrochloride tablets are 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.

Alosetron hydrochloride tablets does not cure IBS, and it may not help every person who takes it. For those who are helped, alosetron hydrochloride tablets 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 alosetron hydrochloride tablets, your IBS symptoms may return within 1 or 2 weeks to what they were before you started taking alosetron hydrochloride tablets. Alosetron hydrochloride tablets are not recommended

for children.

3. Who should not take alosetron hydrochloride tablets?

Alosetron hydrochloride tablets are not right for everyone. **Do not take alosetron hydrochloride tablets 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 alosetron hydrochloride tablets.**
- 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 Acknowledgement Form, or you are not willing to follow them.
- You are taking fluvoxamine (LUVOX®).

4. What should I talk about with my doctor before taking alosetron hydrochloride tablets?

Talk with your doctor:

- about the possible benefits and risks of alosetron hydrochloride tablets.
- 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 nonprescription medicines, supplements, and herbal remedies. Certain illnesses and medicines can increase your chance of getting serious side effects while taking alosetron hydrochloride tablets. Other medicines may interact with how the body handles alosetron hydrochloride tablets.
- about any allergies that you have. See the end of the Medication Guide for a complete list of ingredients in alosetron hydrochloride tablets.
- if you are pregnant, planning to get pregnant, or breastfeeding.

5. How should I take alosetron hydrochloride tablets?

- Take alosetron hydrochloride tablets exactly as your doctor prescribes it. You can take alosetron hydrochloride tablets with or without food.
- Begin with 0.5 mg two times a day for 4 weeks to see how alosetron hydrochloride tablets 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 alosetron hydrochloride tablets:
 - 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 alosetron hydrochloride tablets, 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, alosetron hydrochloride tablets is not likely to help you. You should stop taking it and call your doctor.
- **If you miss a dose of alosetron hydrochloride tablets, 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 alosetron hydrochloride tablets?" 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 alosetron hydrochloride tablets, tell the doctor who prescribed alosetron hydrochloride tablets.

6. What are the possible side effects of alosetron hydrochloride tablets?

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

This Medication Guide does not tell you about all the possible side effects of alosetron hydrochloride tablets. 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 alosetron hydrochloride tablets?

- Store alosetron hydrochloride tablets at 68°F to 77°F (20°C to 25°C). [See USP Controlled Room Temperature.]
- Protect alosetron hydrochloride tablets from light and getting wet (moisture).

Keep alosetron hydrochloride tablets and all medicines out of the reach of children.

8. General information about the safe and effective use of alosetron hydrochloride tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you have any questions or concerns about alosetron hydrochloride tablets, ask your doctor. Do not use alosetron hydrochloride tablets 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 alosetron hydrochloride tablets that was written for healthcare professionals. You can also contact the Alosetron REMS Program (toll free) at 1-844-267-8675 or at www.AlosetronREMS.com.

9. What are the ingredients of alosetron hydrochloride tablets?

Active Ingredient: alosetron hydrochloride.

Inactive Ingredients: lactose (anhydrous), magnesium stearate, microcrystalline cellulose, and pregelatinized starch.

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

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