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BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Alosetron (Lotronex) is back: Should I use it to treat my patients with irritable bowel syndrome?

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Use of alosetron is limited because of its adverse effects

A: You should give alosetron (Lotronex) only if:

- The patient is a woman
- She has severe diarrhea-predominant irritable bowel syndrome (IBS), with continuous symptoms lasting more than 6 months
- You have tried other treatments and these have failed
- She has no contraindications to the drug, particularly certain structural diseases of the gut
- You register with the manufacturer to give the drug
- You educate the patient about the drug and she signs a patient-physician agreement.

WHAT IS ALOSETRON?

Alosetron, introduced in February 2000, is a 5-hydrotryptamine antagonist. It has been shown to improve abdominal pain, stool consistency, frequency, and urgency in women with diarrhea-predominant IBS, although symptoms rapidly return after it is stopped.[1–3]

And it has side effects, notably severe ischemic colitis (leading to death in some cases) and constipation. As of March 8, 2002, the US Food and Drug Administration (FDA) received reports of 84 cases of ischemic colitis and 113 cases of serious complications of constipation. The cumulative incidence of ischemic colitis in women receiving alosetron was 0.3% over 6 months.

GlaxoSmithKline, the manufacturer, withdrew alosetron from the market in November 2000. The FDA recently approved the remarketing of alosetron, but with strict restrictions.

Do not confuse alosetron with tegaserod (Zelnorm), which also became available recently. Tegaserod is indicated in women with *constipation*-predominant IBS, whereas alosetron is indicated for women with severe *diarrhea*-predominant IBS. There are no overlapping indications between the two medications.

WHAT IS 'SEVERE DIARRHEA-PREDOMINANT IBS'?

Irritable bowel syndrome is defined under the recently modified Rome II criteria as abdominal discomfort or pain lasting at least 12 weeks (not necessarily consecutive) in the preceding 12 months that cannot be explained by a structural or biochemical abnormality and that has at least two of the following three features:

- It is relieved with defecation
- Its onset is associated with diarrhea or constipation
- Its onset is associated with a change in the form of the stool.

Severe diarrhea-predominant IBS is defined as diarrhea and one or more of the following symptoms:

- Frequent and severe abdominal pain or discomfort
- Frequent fecal urgency or incontinence
- Disability or restriction of daily activities due to IBS.

Fewer than 5% of cases of IBS are considered severe, and only a fraction of severe cases are diarrhea-predominant IBS.

If a patient has severe diarrhea-predomi-

nant IBS, structural diseases must be excluded via laboratory, imaging, endoscopic, and histologic evaluation. Once these are excluded, the patient should be reassured and an alliance between the patient and physician should be established.

ALOSETRON IS NOT A FIRST-LINE TREATMENT

Dietary and lifestyle modifications are commonly recommended for patients with IBS.[4] Agents that have a safer side-effect profile, such as antidiarrheals, antispasmodics, and antidepressants, are usually next in line.

Alosetron is indicated only in women with severe, diarrhea-predominant IBS who have chronic symptoms (continuous symptoms lasting more than 6 months) that fail to respond to conventional therapy. Geriatric patients may be at a greater risk for complications, such as constipation. Therefore, we do not recommend using alosetron in male, pediatric, or geriatric patients.

THE PRESCRIBING PROGRAM

To prescribe alosetron, physicians must first enroll in GlaxoSmithKline's prescribing program (1-888-825-5249 or www.lotronex.com).

The FDA requires physicians who prescribe alosetron to educate their patients about the risks and benefits of the drug and to give them a copy of the FDA-approved medication guide. Patients must read and sign a patient-physician agreement before receiving their initial prescription. The forms can be found at www.fda.gov/cder/drug/infopage/lotronex/lotronex.htm.

Pharmacists are asked to fill only prescriptions that display a prescribing program sticker affixed by an enrolled physician, and to give patients a copy of the FDA-approved medication guide every time they dispense the drug.

In addition, enrolled physicians must agree to report serious adverse events to GlaxoSmithKline at 1-888-825-5249 or to the FDA at 1-800-FDA-1088.

CONTRAINDICATIONS

Alosetron should not been used in patients with:

- Chronic or severe constipation
- A history of intestinal obstruction, stricture, toxic megacolon, gastrointestinal perforation, adhesions, ischemic colitis, impaired intestinal circulation, thrombophlebitis, or a hypercoagulable state
- Current or past inflammatory bowel disease or diverticulitis.

DOSAGE

Alosetron should be started at a dosage of 1 mg daily by mouth for 4 weeks. If, after 4 weeks, the 1-mg daily dosage is well tolerated but does not adequately control IBS symptoms, it can be increased to 1 mg twice a day, the dosage used in controlled clinical trials.

Alosetron should be stopped if it does not adequately control IBS symptoms after 4 weeks of treatment with 1 mg twice a day.

To register, call 888-825-5249 or go to www.lotronex.com

REFERENCES

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3. **Camilleri M, Northcutt AR, Kong S, Dukes G, McSorley D, Mangel AW.** Efficacy and safety of alosetron in women with irritable bowel syndrome: a randomized, placebo-controlled trial. Lancet 2000; 355:1035–1040.
4. **Shen B, Soffer EE.** The challenge of irritable bowel syndrome: creating an alliance between patient and physician. Cleve Clin J Med 2001; 68:224–234.

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