Pharmacy Policy Bulletin: J-0227 Lotronex (alosetron) – Commercial and Healthcare Reform	
Number: J-0227	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Drugs = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0227-011	**Original Date:** 08/07/2019
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Lotronex (alosetron)

FDA-Approved Indication(s):	• Treatment of women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:
	  ○ chronic IBS symptoms (generally lasting 6 months or longer),
	  ○ had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
	  ○ not responded adequately to conventional therapy.

Background:	• Lotronex (alosetron) is a selective serotonin 5-HT_3 antagonist. 5-HT_3 receptors are ligand-gated cation channels that are extensively distributed on enteric neurons in the human gastrointestinal tract, as well as other peripheral and central locations. Activation of these channels and the resulting neuronal depolarization affect the regulation of visceral pain, colonic transit, and gastrointestinal secretions, processes that relate to the pathophysiology of IBS.
	• Severe IBS includes diarrhea and one (1) or more of the following:
	  ○ Frequent and severe abdominal pain/discomfort
	  ○ Frequent bowel urgency or fecal incontinence
	  ○ Disability or restriction of daily activities due to IBS
	• The 2021 American College of Gastroenterology (ACG) guidelines for IBS-D emphasize a positive diagnostic strategy rather than diagnostic strategy of exclusion, as well as diagnostic testing to rule out celiac disease and irritable bowel disease (IBD). A limited trial of a low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet is recommended to improve global symptoms of IBS. Gut-directed psychotherapies to treat overall IBS symptoms as part of a comprehensive management strategy can be used in conjunction with dietary therapies and medications.
	  ○ Recommend Lotronex (alosetron) be used to relieve global IBS-D symptoms in women with severe symptoms who have failed conventional therapy (conditional recommendation, low quality of evidence)

	○ Recommend the use of rifaximin to treat global IBS-D symptoms (strong recommendation; moderate quality of evidence) ○ Recommend that tricyclic antidepressants be used to treat global symptoms of IBS. (strong recommendation; moderate quality of evidence) ○ Suggest that mixed opioid agonists/antagonists be used to treat global IBS-D symptoms (conditional recommendation, moderate quality of evidence) ○ Do not suggest the use of bile acid sequestrants to treat global IBS-D symptoms (conditional recommendation, very low quality of evidence) • The 2022 American Gastroenterological Association (AGA) guidelines for IBS-D conditionally recommend the use of Viberzi, rifaximin, Lotronex, and loperamide in patients with IBS-D. Tricyclic antidepressants, selective serotonin reuptake inhibitors and antispasmodics are conditionally recommended in patients with IBS. • Prescribing Considerations: ○ Discontinue Lotronex (alosetron) in patients who have not had adequate control of IBS symptoms after 4 weeks of treatment with 1 mg twice a day. ○ Concomitant use of fluvoxamine is contraindicated. ○ Lotronex (alosetron) is contraindicated in patients with a history of the following: ▪ 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 ○ Clinical studies have not been performed to adequately confirm the benefits of Lotronex (alosetron) in men. ○ Use of Lotronex (alosetron) is not recommended in the pediatric population, based upon the risk of serious complications of constipation and ischemic colitis in adults. ○ Lotronex (alosetron) has a black box warning for serious gastrointestinal adverse reactions, including ischemic colitis and serious complications of constipation which have resulted in hospitalization and, rarely, blood transfusion, surgery, and death.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Lotronex (alosetron) may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 18 years of age or older.

B. The member is a female.

C. The member has a diagnosis of irritable bowel syndrome with diarrhea (IBS-D) (ICD-10: K58.0), classified as severe and chronic disease.

D. The member has experienced therapeutic failure or intolerance to one (1) agent from two (2) different medication classes of the following, or all are contraindicated **(1., 2., and 3.)**:

1. anti-diarrheal (for example: loperamide)

2. anti-spasmodic (for example: dicyclomine, hyoscyamine)

3. tricyclic antidepressant (for example: amitriptyline, nortriptyline)

E. If the request is for brand Lotronex, the member has experienced therapeutic failure or intolerance to generic alosetron.

II. Reauthorization

When a benefit, reauthorization of Lotronex (alosetron) may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member's IBS-D symptoms continue to persist.
B. The member has experienced positive clinical response to therapy.
C. If the request is for brand Lotronex, the member has experienced therapeutic failure or intolerance to generic alosetron.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization:

- Commercial and HCR Plans: If approved, up to a 12 week authorization may be granted.
  - For Delaware Commercial fully-insured and ACA members, a 12 month authorization must be granted pursuant to 18 *Del. C.* §§3376(a) and 3586(a) and market conduct examination docket #5467

Reauthorization:

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Lotronex [package insert]. Roswell, Georgia: Sebela Pharmaceuticals Inc.; April 2019.
2. Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *The American Journal of Gastroenterology*. 2021 Jan; 116:17-44.
3. Lembo A, Sultan S, Chang l, et al. AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea. *Gastroenterology. 2022 July;163:137–151*