IBS-D (Lotronex, Viberzi, Xifaxan) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
08-01-2024	08-01-2024

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Lotronex® (alosetron) Tablet*	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 • not responded adequately to conventional therapy. Severe IBS includes diarrhea and 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	*generic available	5
Viberzi® (eluxadoline) Tablet	Treatment of irritable bowel syndrome with diarrhea in adults		1
Xifaxan® (rifaximin) Tablet	Treatment of travelers' diarrhea (TD) caused by noninvasive strains of Escherichia coli in adult and pediatric patients 12 years of age and older Reduction in risk of overt hepatic encephalopathy (HE) recurrence in adults Treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults Limitations of Use: TD - Do not use in patients with diarrhea complicated by fever or blood in the stool or diarrhea due to pathogens other than Escherichia coli		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Guidelines

Irritable Bowel Syndrome (IBS) is defined as recurrent abdominal pain, on average, at least 1 day/week in the past 3 months, associated with two or more of the following:(3,4,6)

- Related to defecation
- Associated with a change in stool frequency
- Associated with a change in stool form (appearance)

These criteria should be fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis.(7) IBS is subtyped according to predominant bowel habit as IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed type (IBS-M), and unclassified (IBS-U).(3)

The American College of Gastroenterology (ACG) and the American Gastroenterological Association lists the following in the management of IBS-D:(4,8)

Intervention	ACG Recommendation and Strength of Evidence	AGA Recommendation and Strength of Evidence
Probiotics	Conditional, very low	NA
rifaximin (Xifaxan)	Strong, moderate	Conditional, moderate
eluxadoline (Viberzi)	Conditional, moderate	Conditional, moderate
alosetron (Lotronex)	Conditional, low	Conditional, moderate
Tricyclic Antidepressants (TCAs)	Strong, Moderate	Conditional, low
Bile acid sequestrants	Conditional, very low	NA
antispasmodics	Conditional, low	Conditional, low
loperamide	NA	Conditional, very low
Selective Serotonin Reuptake Inhibitors (SSRIs)	NA	Conditional, low

Updated ACG guidelines published in 2021, include a strong recommendation for the use of TCAs in the management of IBS-D. Although the 2021 guidelines do not address loperamide use, they do briefly discuss that loperamide is not recommended as first-line therapy for treating IBS-D symptoms because it may improve diarrhea but not improve global IBS symptoms. A recent AGA guideline on probiotics highlighted the evidence gaps in the use of probiotics in patients with IBS and concluded that future, larger, and high-quality studies are needed. In addition, studies evaluating the synergistic effects of combined treatment in IBS, which is often used in patients with moderate to severe symptoms in clinical practice, and better comparative effectiveness studies in IBS are needed. (4,8)

Safety

Alosetron was reintroduced under a risk evaluation and mitigation strategy (REMS) in June 2002, limiting use to women experiencing chronic (greater than 6 months), severe IBS-D symptoms who previously lacked response to traditional therapies. The term "traditional therapies" (or conventional therapies) has not been further defined, and multiple agents have been US FDA-approved for IBS-D in the years since the REMS protocol was established.(4)

Alosetron also carries the following black box warnings:(5)

- 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

	• Alosetron is indicated only for women with severe diarrhea predominant irritable bowel syndrome (IBS) who have not responded adequately to conventional therapy • Discontinue alosetron immediately in patients who develop constipation or symptoms of ischemic colitis. Do not resume alosetron in patients who develop ischemic colitis Alosetron carries the following contraindications:(5) • Do not initiate in patients with constipation • 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 • Concomitant use of fluvoxamine Eluxadoline carries the following contraindications:(1) • Patients without a gallbladder • Known or suspected biliary duct obstruction, or sphincter of Oddi disease or dysfunction • Alcoholism, alcohol abuse, alcohol addiction, or drink more than 3 alcoholic beverages/day • History of pancreatitis; structural diseases of the pancreas, including known or suspected pancreatic duct obstruction • Patients with a known hypersensitivity reaction to eluxadoline • Severe hepatic impairment (Child-Pugh Class C) • History of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction Rifaximin carries the following contraindications:(2) • History of hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components of rifaximin

REFERENCES

Number	Reference
1	Viberzi prescribing information. Allergan USA, Inc. June 2020.
2	Xifaxan prescribing information. Salix Pharmaceuticals, Inc. October 2023.
3	Longstreth GF, Thompson WG, Chey WD et al. Functional bowel disorders. Gastroenterology. 2006; 130:1480–91.
4	Lacy, Brian E, Pimentel, March, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. The American Journal of Gastroenterology. 2021. 116: 17-44. Available at: https://journals.lww.com/ajg/Fulltext/2021/01000/ACG_Clinical _Guideline_Management_of_Irritable.11.aspx.
5	Lotronex prescribing information. Sebela Pharmaceuticals, Inc. April 2019.
6	Reference no longer used.
7	Mearin F, Lacy BE, Chang L, et al. Bowel disorders. Gastroenterology. 2016 Feb.
8	Lembo A, Sultan S, Chang L, Heidelbaugh JJ, Smalley W, Verne GN. AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea. Gastroenterology. 2022;163(1):137-151. doi:https://doi.org/10.1053/j.gastro.2022.04.017.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	alosetron hcl tab	0.5 MG ; 1 MG	Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	Alosetron HCl Tab 0.5 MG (Base Equiv)	0.5 MG	60	Tablets	30	DAYS			
	Alosetron HCl Tab 1 MG (Base Equiv)	1 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	alosetron hcl tab	0.5 MG ; 1 MG	Medicaid
Lotronex	alosetron hcl tab	0.5 MG ; 1 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	Alosetron HCl Tab 0.5 MG (Base Equiv)	0.5 MG	Medicaid
	Alosetron HCl Tab 1 MG (Base Equiv)	1 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Alosetron	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. ALL of the following: 1. The patient has a diagnosis of irritable bowel syndrome with severe diarrhea (IBS-D) **AND** 2. The patient has an onset of IBS-D symptoms starting at least 6 months prior **AND** 3. The patient exhibits at least ONE of the following: A. Frequent and severe abdominal pain/discomfort **OR** B. Frequent bowel urgency or fecal incontinence **OR** C. Disability or restriction of daily activities due to IBS **AND** 4. The patient will NOT be using the requested agent in combination with another agent from this program for IBS-D **AND** 5. ONE of the following: A. The patient's sex is female **OR**

Module	Clinical Criteria for Approval
	B. The requested agent is medically appropriate for the patient's sex **AND** 6. The patient has had anatomic or biochemical abnormalities of the gastrointestinal tract excluded **AND** 7. ONE of the following: A. The patient's medication history includes conventional therapy AND ONE of the following: 1. The patient has had an inadequate response to at least one conventional therapy **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over conventional therapy **OR** B. The patient has an intolerance or hypersensitivity to conventional therapy **OR** C. The patient has an FDA labeled contraindication to ALL conventional therapy **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL conventional therapy cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** B. The patient has another FDA labeled indication for the requested agent **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 3 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will NOT be using the requested agent in combination with another agent from this program for a diagnosis of IBS-D **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months

Module	Clinical Criteria for Approval
	NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months