Clinical Policy: Drugs for Diarrhea

Reference Number: OR.CP.PMN.1016
Effective Date: 4.1.2025
Last Review Date: 02.25
Line of Business: Medicaid – Trillium Oregon Health Plan Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following agents are used to treat diarrhea and require prior authorization: alostron (Lotronex), eluxadoline (Viberzi).

FDA Approved Indication(s)
Alostron 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
- Not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it 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

Limitation(s) of use:

- Because of infrequent but serious gastrointestinal adverse reactions associated with Lotronex, 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 Lotronex in men.

Viberzi is indicated in adults for the treatment of irritable bowel syndrome with diarrhea (IBS-D).

Covered Alternatives:

- Current Trillium Preferred Drug List listed at:
  - https://www.trilliumohp.com/providers/pharmacy.html

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Trillium Community Health Plan that drugs for constipation are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria:

A. Irritable Bowel Syndrome with Diarrhea (must meet all)**:**

1. Diagnosis of IBS-D;
2. Prescribed agents is to be used for treatment of an FDA-approved indication;
3. Age ≥ 18 years;
4. Failure of an anti-diarrheal agent (e.g., loperamide) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. If request is for brand Lotronex, member must use generic alosetron, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed the FDA-approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the PDL, the non-formulary policy for the relevant line of business: OR.CP.PMN.1001 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy (must meet all)**:**

A. Irritable Bowel Syndrome with Diarrhea (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA-approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or

b. For drugs NOT on the PDL, the non-formulary policy for the relevant line of business: OR.CP.PMN.1001 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
IBS-D: irritable bowel syndrome with diarrhea

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
loperamide (Imodium A-D®)	Adults: 4 mg PO followed by 2 mg after each unformed stool until diarrhea is resolved; then individualize dose. Administer optimal daily dose (4-8 mg) as single or divided doses.	If no clinical improvement after treatment with 16 mg/day for at least 10 days, symptoms are unlikely to be controlled by further use.
diphenoxylate/atropine (Lomotil®)	Initially, 5 mg (2 tablets) PO QID; Discontinue after 10 days if clinical improvement is not observed	20 mg/day (of diphenoxylate)
dicyclomine (Bentyl®)	Adults: 20 mg PO QID up to 1 week, then increase to 40 mg PO QID	160 mg/day (40 mg PO QID)
hyoscyamine (Levsin®, Levbid®)	Adults: Levsin: 0.125 – 0.25 mg PO Q 4h Levbid: 0.375 – 0.75 mg PO Q 12h	1.5 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Alosetron Contraindication(s):
  - Alosetron should not be initiated 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 Contraindication(s):
  - Patients without a gallbladder
  - Known or suspected biliary duct obstruction; or sphincter of Oddi disease or dysfunction
  - Alcoholism, alcohol abuse or alcohol addiction, or in patients who drink more than 3 alcoholic beverages per day
  - A history of pancreatitis; or structural diseases of the pancreas, including known or suspected pancreatic duct obstruction
  - Known hypersensitivity reaction to Viberzi
  - Severe hepatic impairment (Child-Pugh Class C)
  - History of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction
- Boxed warning(s):
  - Alosetron: serious gastrointestinal adverse reactions (including ischemic colitis and serious complications of constipation) have resulted in hospitalization and rarely, blood transfusion, surgery, and death
  - Eluxadoline: none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Alostron (Lotronex)	IBS-D	• Starting dose is 0.5 mg PO BID • May increase dose to 1 mg BID after 4 weeks if starting dosage is well tolerated but does not adequately control IBS symptoms Discontinue Lotronex in patients who have not had adequate control of IBS symptoms after 4 weeks of treatment with 1 mg BID	2 mg/day
Eluxadoline (Viberzi)	IBS-D	100 mg PO BID or 75 mg PO BID in patients who: • Are unable to tolerate the 100 mg dose of Viberzi • Are receiving concomitant OATP1B1 inhibitors • Have mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment • Have moderate or severe renal impairment (eGFR less than 60 mL/min/1.73m^2; and in	200 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		patients with end stage renal disease (eGFR less than 15 mL/min/1.73m^2 not yet on dialysis	

VI. Product Availability

Drug	Availability
Alostron (Lotronex)	Tablets: 0.5 mg, 1 mg
Eluxadoline (Viberzi)	Tablets: 75 mg, 100 mg

VII. References

1. Drugs for Diarrhea. Proposed Oregon Health Plan Current Drug Use Criteria. Available at: https://pharmacy.oregonstate.edu/drug-policy/meetings. Accessed January 22, 2025.
2. Lotronex Prescribing Information. Roswell, GA: Sebela Pharmaceuticals Inc.; April 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021107s029lbl.pdf. Accessed July 12, 2024.
3. Viberzi Prescribing Information. Madison, NJ: Allergan; June 2020. Available at: https://www.viberzi.com/. Accessed July 12, 2024.
4. Weinberg DS, Smalley W, Heidelbaugh JJ, Shahnaz S. American Gastroenterological Association Institute guideline on the pharmacological management of irritable bowel syndrome. *Gastroenterology*. 2014; 147(5): 1146-1149. Available at: https://www.gastrojournal.org/article/S0016-5085(14)01089-0/pdf.
5. Lembo A, Sutan S, Chang L, et al. AGA clinical practice guideline on the pharmacological management of irritable bowel syndrome with diarrhea. Gastroenterology. 2022; 164: 137-151.
6. Lacy BE, Pimentel M, Brenner DM. ACG clinical guideline: Management of irritable bowel syndrome. American Journal of Gastroenterology. 2021; 116(1): 17-44.
7. Chey WD, Chey WY, Heath AT, et al. Long-term safety and efficacy of alosetron in women with severe diarrhea-predominant irritable bowel syndrome. *Am J Gastroenterol.* 2004;99(11):2195-203.
8. Chang L, Ameen VZ, Dukes GE, et al. A dose-ranging, phase II study of the efficacy and safety of alosetron in men with diarrhea-predominant IBS. *Am J Gastroentrol*. 2005;100(1):115-23.
9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.
10. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 1, 2024

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policies CP.PMN.170 Eluxadoline (Viberzi), CP.PMN.153 Alosetron	01.23.25	02.11.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
(Lotronex) and drafted FFS criteria "Drugs for Diarrhea" presented at the February 2025 P&T meeting		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.