

## **Clinical Policy: Alosetron (Lotronex)**

Reference Number: CP.PMN.153

Effective Date: 11.16.16

Last Review Date: 11.24

Line of Business: Commercial, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Alosetron (Lotronex<sup>®</sup>) is a selective serotonin 5-HT<sub>3</sub> antagonist.

### **FDA Approved Indication(s)**

Lotronex 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.

### **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 health plans affiliated with Centene Corporation<sup>®</sup> that Lotronex is **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

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

1. Diagnosis of diarrhea-predominant IBS;
2. Age  $\geq$  18 years;
3. 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;

4. Failure of an antispasmodic agent (e.g., dicyclomine) 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 both of the following (a and b):
  - a. 2 mg per day;
  - b. 2 tablets per day.

**Approval duration:**

**Medicaid** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**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 formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 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.CPA.09 for commercial and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**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 brand Lotronex, member must use generic alosetron, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
  - a. 2 mg per day;
  - b. 2 tablets per day.

**Approval duration:**

**Medicaid** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**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 formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 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.CPA.09 for commercial and 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.CPA.09 for commercial and 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: irritable bowel syndrome

*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 for all relevant lines of business and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
loperamide (Imodium A-D <sup>®</sup> )	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 <sup>®</sup> )	Initially, 5 mg (2 tablets) PO QID; Discontinue after 10 days if clinical improvement is not observed	20 mg/day (of diphenoxylate)
dicyclomine (Bentyl <sup>®</sup> )	Adults: 20 mg PO QID up to 1 week, then increase to 40 mg PO QID	160 mg/day (40 mg PO QID)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hyoscyamine (Levsin <sup>®</sup> , Levbid <sup>®</sup> )	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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Lotronex 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
- Boxed warning(s): serious gastrointestinal adverse reactions (including ischemic colitis and serious complications of constipation) have resulted in hospitalization and rarely, blood transfusion, surgery, and death

*Appendix D: General Information*

- Commercially available Lotronex is prescribed and distributed under a restricted distribution program, which is intended to control its access and to educate program participants (clinicians, pharmacists, patients) about the risks and benefits of the drug. The Lotronex REMS program was implemented to help reduce the risks of a serious gastrointestinal (GI) adverse event and to ensure the benefits of the drug outweigh the risk.
- One study of 662 men with diarrhea-predominant IBS showed Lotronex 1 mg twice daily provided a significantly higher average rate of adequate relief of IBS pain and discomfort during weeks 5-12 of the treatment phase (primary endpoint) compared to placebo.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
IBS-D	<ul style="list-style-type: none"> <li>• Starting dose is 0.5 mg PO BID</li> <li>• May increase dose to 1 mg BID after 4 weeks if starting dosage is well tolerated but does not adequately control IBS symptoms</li> <li>• Discontinue Lotronex in patients who have not had adequate control of IBS symptoms after 4 weeks of treatment with 1 mg BID</li> </ul>	2 mg/day

**VI. Product Availability**

Tablets: 0.5 mg, 1 mg

**VII. References**

1. Lotronex Prescribing Information. Roswell, GA: Sebelo Pharmaceuticals Inc.; April 2019. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/021107s029lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021107s029lbl.pdf). Accessed July 12, 2024.
2. Micromedex<sup>®</sup> Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 1, 2024
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: <http://www.clinicalpharmacology-ip.com/>.
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](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 Gastroenterol*. 2005;100(1):115-23.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q2020 annual review: no significant changes; references reviewed and updated.	06.26.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.06.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	10.18.21	02.22
4Q 2022 annual review: added generic redirection; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.26.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.05.23	11.23
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.12.24	11.24

**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.

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**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.

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