# Clinical Policy: Linaclotide (Linzess)

Reference Number: CP.PMN.71
Effective Date: 11.01.15
Last Review Date: 11.24
Line of Business: Medicaid

Revision Log

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

## Description

Linaclotide (Linzess®) is a guanylate cyclase-C agonist.

## FDA Approved Indication(s)

Linzess is indicated for the treatment of:

- Irritable bowel syndrome with constipation (IBS-C) in adults
- Chronic idiopathic constipation (CIC) in adults
- Functional constipation (FC) in pediatric patients 6 to 17 years of age

## Policy/Criteria

*Provider must submit documentation (including 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® that Linzess is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

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

1. Diagnosis of IBS-C;
2. Age ≥ 18 years;
3. Failure of one bulk forming laxative (e.g., psyllium (Metamucil®), methylcellulose (Citrucel®), calcium polycarbophil (FiberCon®)), unless clinically significant adverse effects are experienced or all are contraindicated;
4. Failure of generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed both of the following (a and b):
   a. 290 mcg per day;
   b. 1 capsule per day.

**Approval duration: 12 months**

**B. Chronic Idiopathic Constipation** (must meet all)**:**

1. Diagnosis of CIC;
2. Age ≥ 18 years;
3. Failure of one bulk forming laxative (e.g., psyllium [Metamucil], methylcellulose [Citrucel], calcium polycarbophil [FiberCon]), unless clinically significant adverse effects are experienced or all are contraindicated;

4. Failure of one stimulant laxative (e.g., bisacodyl, senna), unless clinically significant adverse effects are experienced or all are contraindicated;
5. Failure of polyethylene glycol (MiraLax®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed both of the following (a and b):
   a. 145 mcg per day;
   b. 1 capsule per day.

**Approval duration: 12 months**

**C. Functional Constipation** (must meet all)**:**

1. Diagnosis of FC;
2. Age ≥ 6 to ≤ 17 years;
3. Failure of one bulk forming laxative (e.g., psyllium [Metamucil], methylcellulose [Citrucel], calcium polycarbophil [FiberCon]), unless clinically significant adverse effects are experienced or all are contraindicated;
4. Failure of polyethylene glycol (MiraLax®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of at least ONE of the following (a, b, or c), unless clinically significant adverse effects are experienced or all are contraindicated:
   a. Stimulant laxative (e.g., bisacodyl, senna);
   b. Osmotic laxative (e.g., lactulose, magnesium hydroxide);
   c. Lubricant laxative (e.g., mineral oil);
6. Dose does not exceed 72 mcg (1 capsule) per day.

**Approval duration: 12 months**

**D. 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.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.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.PMN.53 for Medicaid.

## II. Continued Therapy

**A. All Indications in Section I** (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 any of the following (a, b, or c):
   a. IBS-C (i and ii):
      i. 290 mcg per day;
      ii. 1 capsule per day;
   b. CIC (i and ii):
      i. 145 mcg per day;
      ii. 1 capsule per day;
   c. FC: 72 mcg (1 capsule) per day.

**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 formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: 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.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.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*

CIC: chronic idiopathic constipation
FC: functional constipation
FDA: Food and Drug Administration
IBS-C: irritable bowel syndrome with constipation

*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.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| psyllium (Metamucil®) | 1 rounded teaspoonful, tablespoonful, or premeasured packet in 240 mL of fluid PO, 1 to 3 times per day (2.4 g of soluble dietary fiber per dose) | 7.2 g (as soluble dietary fiber)/day |
| calcium polycarbophil (FiberCon®) | 1,000 mg 1 to 4 times per day or as needed | 6,000 mg/day |
| methylcellulose (Citrucel®) | Caplet: 2 caplets (total 1 g methylcellulose) PO with at least 240 ml (8 oz) of liquid, up to 6 times per day as needed<br><br>Powder: 1 heaping tablespoonful (2 g methylcellulose per 19 g powder) in at least 240 ml (8 oz) of water PO, given 1 to 3 times per day as needed | Caplet: 12 caplets/day<br>Powder: 6 grams/day |
| sennosides (Senokot®) | 1 to 2 tablets (8.6 to 17.2 mg sennosides) PO BID | 68.8 mg sennosides/day |
| bisacodyl (Dulcolax®) | 5 to 15 mg/day (1 to 3 tablets) PO given as a single dose, or 1 suppository or retention enema (10 mg) PR QD<br><br>Either a suppository or oral tablet(s) may be used up to 3 times per week | 15 mg/day PO or 10 mg/day PR |
| polyethylene glycol 3350 (MiraLax®) | 17 g (approximately 1 heaping tablespoon) of powder in 120 to 240 mL of fluid PO QD | 34 grams/day |
| magnesium hydroxide (milk of magnesia) | Varies | Varies |
| mineral oil | 10 mL to 90 mL per day PO as needed to relieve constipation<br><br>60 mg mL or 120 mL rectally as a single dose | 90 mL/day PO or 120 mL/day PR |
| lubiprostone (Amitiza®) | CIC: 24 mcg PO BID<br>IBS-C: 8 mcg PO BID | CIC: 48 mcg/day<br>IBS-C: 16 mcg/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*

- Contraindication(s): patients less than 2 years of age; patients with known or suspected mechanical gastrointestinal obstruction
- Boxed warning(s): risk of serious dehydration in pediatric patients less than 2 years of age

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| IBS-C | 290 mcg PO QD | 290 mcg/day |
| CIC | 72 mcg or 145 mcg PO QD | 145 mcg/day |
| FC | 72 mcg PO QD | 72 mcg/day |

## VI. Product Availability

Capsules: 72 mcg, 145 mcg, and 290 mcg

## VII. References

1. Linzess Prescribing Information. Irvine, CA: Allergan; June 2023. Available at: https://www.linzess.com/. Accessed July 12, 2024.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed August 1, 2024.

*Irritable Bowel Syndrome*

3. 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.
4. Lacy BE, Pimentel M, Brenner DM. ACG clinical guideline: Management of irritable bowel syndrome. American Journal of Gastroenterology. 2021; 116(1): 17-44.
5. Chang L, Sultan S, Lembo A, et al. AGA clinical practice guideline on the pharmacological management of irritable bowel syndrome with constipation. Gastroenterology. 2022;163:118-136.
6. Ford AC, Moayyedi P, Lacy BE, et al. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. *Am J Gastroenterol*. 2014;109:S2-S26.
7. Paquette IM, Varma M, Ternent C, et al. The American Society of Colon and Rectal Surgeons' Clinical Practice Guideline for the Evaluation and Management of Constipation. *Dis Colon Rectum.* 2016;59:479-492.

*Chronic Idiopathic Constipation*

8. American Gastroenterological Association, Bharucha AE, Dorn SD et al. American Gastroenterological Association medical position statement on constipation. *Gastroenterol*. 2013 Jan;144(1):211-7. doi: 10.1053/j.gastro.2012.10.029.
9. Lin C, Chey WD, Imdad A, et al. American Gastroenterological Assocation-American College of Gastroenterology clinical practice guideline: Pharmacological management of chronic idiopathic constipation. Gastroenterology 2023;164:1086-1106.

*Functional Constipation*
10. de Geus A, Koppen IJN, Flint RB, Benninga MA, and Tabbers MM. An update of pharmacological management in children and functional constipation. Pediatric Drugs 2023;25:343-358.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 4Q 2020 annual review: no significant changes; references reviewed and updated. | 06.29.20 | 11.20 |
| Removed HIM line of business per March SDC. | 03.26.21 | 05.21 |
| Per June SDC and prior clinical guidance, added requirement for use of generic lubiprostone; HIM line of business added to policy (retire HIM.PA.157). | 06.02.21 | 08.21 |
| 4Q 2021 annual review: no significant changes; legacy WCG Medicaid to apply (WCG.CP.PMN.71 to be retired); references reviewed and updated. | 08.11.21 | 11.21 |
| 4Q 2022 annual review: no significant changes; contraindications and boxed warnings updated per PI; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. | 07.26.22 | 11.22 |
| 4Q 2023 annual review: references reviewed and updated.<br>RT4: new indication functional pediatric constipation added; contraindications updated per PI. | 07.05.23 | 11.23 |
| Per August SDC, removed HIM line of business. | 08.22.23 | 12.23 |
| 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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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.