Clinical Policy: Lubiprostone (Amitiza)

Reference Number: CP.PMN.142
Effective Date: 12.01.14
Last Review Date: 11.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Lubiprostone (Amitiza®) is a chloride channel activator.

FDA Approved Indication(s)

Amitiza is indicated for the treatment of:

- Chronic idiopathic constipation (CIC) in adults
- Irritable bowel syndrome with constipation (IBS-C) in women ≥ 18 years old
- Opioid-induced constipation (OIC) in adults with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.
  - Limitation(s) of use: Effectiveness of Amitiza in the treatment of OIC in patients taking diphenylheptane opioids (e.g., methadone) has not been established.

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® that Amitiza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. 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 experienced;
6. Member must use generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed both of the following (a and b):
   a. 48 mcg per day;
   b. 2 capsules per day.

Approval duration: 12 months

B. 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. Member must use generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed both of the following (a and b):
   a. 16 mcg per day;
   b. 2 capsules per day.

Approval duration: 12 months

C. Opioid-Induced Constipation (must meet all)**:**
1. Diagnosis of OIC;
2. Age ≥ 18 years;
3. Member has been taking opioid(s) for ≥ 4 weeks due to chronic pain, not caused by active cancer;
4. Failure of one agent from each of the following classes while on opioid therapy, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):
   a. Stimulant laxative (e.g., bisacodyl, senna);
   b. Osmotic laxative (e.g., lactulose, polyethylene glycol);
   c. Stool softener (e.g., docusate);
5. Member has used one of the aforementioned agents in the past 30 days, unless contraindicated;
6. Member must use generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed both of the following (a and b):
   a. 48 mcg per day;
   b. 2 capsules per day.

Approval duration: 6 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.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and 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;
2. 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);*
3. Member is responding positively to therapy;
4. Member must use generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. IBS-C (i and ii):
      i. 16 mcg per day;
      ii. 2 capsules per day;
   b. CIC or OIC (i and ii):
      i. 48 mcg per day;
      ii. 2 capsules 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.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIC: chronic idiopathic constipation
FDA: Food and Drug Administration
PAMORA: peripherally acting mu-opioid receptor antagonist
IBS-C: irritable bowel syndrome with constipation
OIC: opioid-induced 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®)	1,250 mg calcium polycarbophil 1 to 4 times PO per day or as needed	5,000 mg/day calcium polycarbophil
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 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 Powder: 6 g/day
bisacodyl (Dulcolax®)	Oral: 5 to 15 mg QD Rectal: Enema, suppository: 10 mg (1 enema or suppository) QD	15 mg/day PO; 10 mg/day rectally
senna (Senokot®)	1 to 2 tablets (8.6 to 17.2 mg sennosides) PO BID	8 tablets/day (68.8 mg sennosides/day)
lactulose	10 to 20 g (15 to 30 mL or 1 to 2 packets) PO QD; may increase to 40 g (60 mL or 2 to 4 packets) QD if necessary	40 g/day (60 mL or 2 to 4 packets/day)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
polyethylene glycol 3350 (MiraLax®)	17 g (approximately 1 heaping tablespoon) of powder in 120 to 240 mL of fluid given PO QD	34 g/day
docusate sodium (Colace®)	50 to 300 mg/day PO given in single or divided doses	360 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

- Contraindication(s): patients with known or suspected mechanical gastrointestinal obstruction
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CIC and OIC	24 mcg PO BID	48 mcg/day
IBS-C	8 mcg PO BID	16 mcg/day

VI. Product Availability

Capsules: 8 mcg and 24 mcg

VII. References

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2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed July 11, 2023.
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Chronic Idiopathic Constipation

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Irritable Bowel Syndrome
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Opioid-Induced Constipation
10. Argoff CE, Brennan MJ, Camilleri M, et al. Consensus Recommendations on Initiating Prescription Therapies for Opioid-Induced Constipation. *Pain Med*. 2015 Dec;16(12):2324-37.
11. Pergolizzi JV, Raffa RB, Pappagallo M, et al. Peripherally acting μ-opioid receptor antagonists as treatment options for constipation in noncancer pain patients on chronic opioid therapy. *Patient preference and adherence*. 2017;11:107-119. doi:10.2147/PPA.S78042.
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14. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. *Ther Adv Chronic Dis.* 2016 Mar; 7(2): 121–134.
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16. Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guidelines on the Medical Management of Opioid-Induced Constipation. *Gastroenterol*. 2019;156:218-226.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.30.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	06.29.20	11.20
Added requirement for use of generic lubiprostone per March SDC and prior clinical guidance.	03.26.21	05.21
Per SDC and prior clinical guidance, added Commercial line of business; revised reference from HIM.PHAR.21 to HIM.PA.154.	06.02.21	08.21
4Q 2021 annual review: no significant changes; modified reference from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.11.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; 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

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.