Clinical Policy: Lubiprostone (Amitiza)

Reference Number: PA.CP.PMN.142
Effective Date: 10.17.18
Last Review Date: 10.17.18

Revision Log

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 PA Health & Wellness® 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. Failure of one bulk forming laxative [e.g., psyllium (Metamucil®), methylcellulose (Citrucel®), calcium polycarbophil (FiberCon®)] unless all are contraindicated or clinically significant adverse effects are experienced;
3. Failure of one stimulant laxative (e.g., bisacodyl, senna) unless all are contraindicated or clinically significant adverse effects experienced;
4. Failure of polyethylene glycol (MiraLax®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects experienced;
5. Dose does not exceed 48 mcg per day (2 capsules per day).

Approval duration: 12 months

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

1. Diagnosis of IBS-C;
2. Failure of one bulk forming laxative [e.g., psyllium (Metamucil), methylcellulose (Citrucel), calcium polycarbophil (FiberCon)] unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 16 mcg per day (2 capsules per day).

Approval duration: 12 months

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

Approval duration: 12 months

D. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. All Indications in Section I(must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
   a. IBS-C: 16 mcg per day (2 capsules per day);
   b. CIC or OIC: 48 mcg per day (2 capsules per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIC: chronic idiopathic constipation
FDA: Food and Drug Administration
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®)	1,000 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 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)
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

1. Amitiza Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; June 2018. Available at https://www.amitiza.com/. Accessed July 20, 2018.
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4. 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.
5. 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.
6. Kumar L, Barker C, Emmanuel A. Opioid-Induced Constipation: Pathophysiology, Clinical Consequences, and Management. Gastroenterology Research and Practice. 2014;2014:141737. doi:10.1155/2014/141737.
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10. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy Created	10/18	

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.