Effective Date: 03/01/2013
Last P&T Approval/Version: 04/27/2022
Next Review Due By: 04/2023
Policy Number: C5113-C

Amitiza (lubiprostone)

PRODUCTS AFFECTED

Amitiza (lubiprostone)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
irritable bowel syndrome with constipation, chronic idiopathic constipation, opioid-induced constipation

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy wasapproved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-bycase basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. OPIOID INDUCED CONSTIPATION:
   1. Documented diagnosis of opioid-induced constipation
      AND
   2. Documentation that member has chronic use of an opioid agent in the past 30 days as documented within claims history or if new to Molina a documented medical chart note of last fill date and/or prescription drug monitoring report
      AND

3. Prescriber attests that member is not currently receiving a diphenylheptane opioid (e.g., methadone)
   AND
4. The member has tried and failed (2 week trial for each agent) or is intolerant to atleast 2 of the following with or without a stool softener in the past 3 months: At least one stimulant laxative (e.g., bisacodyl); OR At least one osmotic laxative (e.g.PEG3350); OR At least one saline laxative (e.g. magnesium citrate)
   AND
5. Amitiza (lubiprostone) will not be used in combination with other functional gastro-intestinal disorder drugs [Linzess (linaclotide), Motegrity (prucalopride), Trulance (plecanatide), Movantik (naloxegol oxalate), Symproic (naldemedine tosylate), Relistor (methylnaltrexone)or Zelnorm (tegserod maleate)]
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by theprescriber within the documentation submitted for review [Contraindications to Amitiza (lubiprostone) include members with known or suspected mechanical gastrointestinal obstruction]
   AND
7. IF NON-FORMULARY/NON-PREFERRED: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried,dates of trial(s) and reason for treatment failure(s).

B. IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C)

1. Documented diagnosis of IBS-C
   AND
2. Documentation of a minimum of TWO of the following symptoms for the last 3 months: (a) Straining during at least 25% of defecations, (b) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (c) Lumpy or hard stools in at least 25% of defecations, (d) Manual maneuvers to facilitate at least 25% of defecations (e.g. digital evacuation, support of the pelvic floor) (e) Sensation of incomplete evacuation for at least 25% of defecations OR (f) Fewer than three spontaneous bowel movements per week
   AND
3. Documentation ruling out IBS-C organic disease (alarm symptoms), dys-synergic defecation, IBS-D or slow colonic transit.
   AND
4. The member has tried and failed (2 week trial for each agent) or is intolerant to at least 2 of the following with or without a stool softener in the past 3 months: At least one stimulant laxative (e.g. bisacodyl); OR At least one osmotic laxative (e.g. PEG 3350); OR At least one saline laxative (e.g. magnesium citrate)
   AND
5. Amitiza (lubiprostone) will not be used in combination with other functional gastro-intestinal disorder drugs [Linzess (linaclotide), Motegrity (prucalopride), Trulance (plecanatide), Movantik (naloxegol oxalate), Symproic (naldemedine tosylate), Relistor (methylnaltrexone) or Zelnorm (tegserod maleate)]
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Amitiza (lubiprostone) include members with known or suspected mechanical gastrointestinal obstruction]
   AND
7. IF NON-FORMULARY/NON-PREFERRED: Documentation of trial/failure of or intolerance toa majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

C. CHRONIC IDIOPATHIC CONSTIPATION:
1. Documented diagnosis of chronic idiopathic constipation
   AND
2. Documentation of a minimum of TWO of the following symptoms for the last 3 months: (a) Straining during at least 25% of defecations, (b) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (c) Lumpy or hard stools in at least 25% of defecations, (d) Manual maneuvers to facilitate at least 25% of defecations (e.g. digital evacuation, support of the pelvic floor) (e) Sensation of incomplete evacuation for at least 25% of defecations OR (f) Fewer than three spontaneous bowel movements per week
   AND
3. Prescriber attests to ruling out secondary causes of chronic constipation (drug-induced, IBS-C, Inflammatory bowel disease, colorectal cancer, hypothyroidism, electrolyte imbalances)
   AND
4. The member has trial and failure (2 week trial of each agent) or is intolerant to at least 2 of the following with or without a stool softener in the past 3 months: At least one stimulant laxative (e.g. bisacodyl); OR At least one osmotic laxative (e.g.PEG3350); OR At least one saline laxative (e.g. magnesium citrate) OR bulk- forming laxative (e.g. psyllium or methylcellulose)
   AND
5. Amitiza (lubiprostone) will not be used in combination with other functional gastro-intestinal disorder drugs [Linzess(linaclotide), Motegrity (prucalopride), Trulance (plecanatide), Movantik (naloxegol oxalate), Symproic (naldemedine tosylate), Relistor (methylnaltrexone) or Zelnorm (tegserod maleate)]
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Amitiza (lubiprostone) include: Patients with known or suspected mechanical gastrointestinal obstruction]
   AND
7. IF NON-FORMULARY/NON-PREFERRED: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary alternatives for the given diagnosis. Submit documentation including medication(s) tried,dates of trial(s) and reason for treatment failure(s).

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:
1. Documentation that the member has demonstrated a beneficial response to Amitiza, per the prescribing physician (e.g., increased number of bowel movements from baseline)
   AND
2. Documentation of no intolerable adverse effectsor drug toxicity
   AND
3. FOR OIC: Documentation member is still on opioid therapy

DURATION OF APPROVAL:

Initial authorization:12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

None

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
CIC and OIC: 24mcg twice daily
IBS-C: 8mcg twice daily
Max of #60 capsules per 30 days

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Gastrointestinal Chloride Channel Activators

FDA-APPROVED USES:
Treatment of irritable bowel syndrome with constipation (IBS-C) in women ≥ 18 years old, treatment of chronic idiopathic constipation (CIC) in adults, treatment of opioid-induced constipation (OIC) in adults with chronic, non-cancer pain, including chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation

Limitation of Use: Effectiveness of Amitiza in the treatment of OIC in patients taking diphenylheptane opioids (e.g., methadone) has not been established

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Rome IV Diagnostic Criteria for Constipation

Must include two or more of the following criteria for diagnosis:
*Criteria should be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

- Straining during at least 25% of defecations
- Sensation of anorectal obstruction/blockage for at least 25% of defecations
- Lumpy or hard stools in at least 25% of defecations
- Manual maneuvers to facilitate at least 25% of defecations (e.g. digital evacuation, support of the pelvicfloor)
- Sensation of incomplete evacuation for at least 25% of defecations
- Fewer than three spontaneous bowel movements per week.

Rome IV Diagnostic Criteria for IBS-C

Must include two or more of the following criteria for diagnosis:
*Criteria should be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

- Recurrent abdominal pain on average at least 1 day/week in the last 3 months-

Related to defecation

- Associated with a change in the frequency of stool
- Associated with a change in the form (appearance) of stool

American Gastroenterological Association Institute Guideline on the Medical Management of Opioid-Induced Constipation- Gastroenterology 2019;156:218–226

Intestinal Secretagogues

Intestinal chloride ion secretagogues act through the guanylate cyclase C receptor with associated secretion of water into the intestinal lumen. Chloride ions secreted from enterocytes or colonocytes enter the cell through the basolateral Na-K-Cl co-transporter. Lubiprostone is a bicyclic fatty acid derived from prostaglandin E1 that activates apical membrane chloride channels to stimulate intestinal and colonic secretion of chloride-rich fluidinto the intestinal lumen. It has been shown to accelerate intestinal and colonic transport without significantly impacting colonic motility or sensation.

In patients with OIC, the AGA makes no recommendation for the use of lubiprostone. No recommendation, evidence gap. Limited consistent evidence exists to support a recommendation for the use of lubiprostone for the treatment of OIC. Three large phase 3 RCTs55–57 compared the use of lubiprostone to placebo for the treatment of OIC in adult patients with non-cancer pain on stable opiate doses for at least 30 days before enrollment. Lubiprostone 24 mg twice daily with meals and 8 ounces of fluid was administered for 12 weeks in each study. The pooled SBM response rate was RR of 1.15 (95% CI, 0.97–1.37) with38% of patients in the lubiprostone arm achieving SBM response compared with 32.7% of patients in the placebo arm. Compared with placebo, there was some improvement in SBM frequency with an increase of 0.6 to 0.8 more SBMs. In the Spierings et al study, however, no improvement in SBM frequency was reported, but there was a small reduction in straining and an improvement in stool consistency, however, it was unclear whether these small reductions correlated with clinically meaningful improvements. No meaningful changes in quality of life were noted. Overall, 6.4% of patients who received lubiprostone had adverse effects that led totreatment discontinuation compared to 3.0% in the placebo arm. The majority of side effects were diarrhea, nausea, abdominal pain, headache, and vomiting. The quality of the evidence for lubiprostone was low. Overall, there was concern about selective reporting bias across the studies and imprecision. Also, it was unclear if the differences reported were clinically meaningful improvements. **Based on the low quality of evidence and the limitations of theevidence, the AGA made no recommendation for lubiprostone and identified this area asan evidence gap.**

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Amitiza is a type-2 chloride channel activator that stimulates chloride secretion in the GI tract. Through this action, Amitiza enhances GI fluid secretion and transit time which alleviates constipation. Amitiza is minimally absorbed and has low systemic bioavailability after oral administration. Amitiza is indicated for the treatment of 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; chronic idiopathic constipation (CIC) in adults; and irritable bowel syndrome with constipation (IBS-C) in women ≥ 18years of age. A limitation of use for Amitiza in OIC is that its efficacy has not been established in patients taking diphenylheptane opioids (e.g., methadone).

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Amitiza (lubiprostone) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Amitiza is contraindicated with known or suspected bowl obstruction.

OTHER SPECIAL CONSIDERATIONS:

Precaution for patients with a history of hypotension and/or will concomitantly be using antihypertensive drugs since may increase risk of hypotension and syncope

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Amitiza CAPS 24MCG
Amitiza CAPS 8MCG

REFERENCES

1. Amitiza (lubiprostone) [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America; November 2020.
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3. Pare P, Bridges R, Champion MC, et al. Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. Can J Gastroenterol. 2007 Apr;21 Suppl B:3B-22B
4. Bove A, Bellini M, Battaglia E, et al. Consensus statement AIGO/SICCR diagnosis and treatment of chronic constipation and obstructed defecation (part II: treatment). World J Gastroenterol. 2012 Sep 28;18(36):4994-5013
5. Bharucha A, Dorn S, Lembo A. 'American Gastroenterological Association medical position statement on constipation. Gastroenterology. 2013 Jan;144(1):211-7
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7. Tarumi Y, Wilson MP, Szafran O, Spooner GR. Randomized, double-blind, placebo- controlled trial of oral docusate in the management of constipation in hospice patients. J PainSymptom Manage 2013;45:2-13.
8. Weitzel KW, Goode JR. Constipation. In Krinsky DL, Ferreri SP, Hemstreet B, et al, Eds. Handbook of Nonprescription Drugs. 18th ed. Washington, DC: American Pharmaceutical Association, 2015.
9. American Gastroenterological Association Institute Guideline on the Medical Management of Opioid-Induced Constipation.Crockett SD, Greer KB, Heidelbaugh JJ, Falck-Ytter Y, Hanson BJ, Sultan S, American Gastroenterological Association Institute Clinical Guidelines Committee. Gastroenterology. 2019;156(1):218. Epub 2018 Oct 16.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Other Special Consideration	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file