Clinical Policy: Gastrointestinal Agents

Reference Number: IL.ERX.NPA.122
Effective Date: 06.01.21
Last Review Date: 08.21
Line of Business: Illinois Medicaid

Revision Log

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

Description
The following gastrointestinal agents are used to treat either constipation or diarrhea of different etiologies.

**The following criteria apply to Illinois Medicaid.*

FDA Approved Indication(s)
- Linaclotide (Linzess®), lubiprostone (Amitiza®), and plecanatide (Trulance®) are indicated for:
  - Chronic idiopathic constipation (CIC) in adults
  - Irritable bowel syndrome with constipation (IBS-C) in adults
    - Amitiza only indicated for women ≥18 years of age
- Prucaloprode (Motegrity™) is indicated for:
  - CIC in adults
- Tegaserod (Zelnorm®) is indicated for:
  - IBS-C in women (≤ 65 years of age)
- Amitiza, naloxegol (Movantik®), methylnaltrexone bromide (Relistor®), and naldemedine (Symproic®) are indicated for:
  - 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
- Relistor is also indicated for:
  - Treatment of OIC in adults with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care
- Eluxadoline (Viberzi®) and alosetron (Lotronex®) are indicated for:
  - Irritable bowel syndrome with diarrhea (IBS-D) in adults
    - Lotronex only indicated for women with severe IBS-D who have chronic IBS symptoms (generally lasting 6 months or longer), had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and have not responded adequately to conventional therapy

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that the requested agent 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. Request is for Amitiza, Linzess, Motegrity, or Trulance;
4. Failure of one of each of the following categories, unless clinically significant adverse effects are experienced or all are contraindicated (a-e);

a. An increase of dietary fiber with lifestyle modifications;
b. Stool softening agent (e.g., docusate);
c. Saline laxative (e.g., magnesium citrate, milk of magnesia);
d. Stimulant laxative (e.g., bisacodyl, senna);
e. Osmotic laxative (e.g., polyethylene glycol (MiraLax®));

5. Dose does not exceed the FDA approved maximum (see section V).

Approval duration: 3 months

B. Opioid-Induced Constipation (must meet all)**:**

1. Diagnosis of OIC;
2. Age ≥ 18 years;
3. Request is for Amitiza, Movantik, Relistor, or Symproic;
4. For OIC with chronic non-cancer pain: Member has been taking opioid(s) for ≥ 4 weeks due to chronic pain not caused by active cancer;
5. For OIC secondary to treatment of an advanced illness (e.g., incurable cancer, end-stage COPD, heart failure, Alzheimer's disease with dementia, HIV/AIDS): All of the following are met (a, b, and c):
   a. Member has a life expectancy ≤ 6 months;
   b. Member is receiving palliative care;
   c. Member is receiving opioid therapy;
6. Failure of one of each of the following categories, unless clinically significant adverse effects are experienced or all are contraindicated (a-e);
   a. An increase of dietary fiber with lifestyle modifications;
   b. Stool softening agent (e.g., docusate);
   c. Saline laxative (e.g., magnesium citrate, milk of magnesia);
   d. Stimulant laxative (e.g., bisacodyl, senna);
   e. Osmotic laxative (e.g., polyethylene glycol (MiraLax));
7. Dose does not exceed the FDA approved maximum (see section V).

Approval duration: 3 months

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

1. Diagnosis of IBS-C;
2. Member meets one of the following (a, b, or c):
   a. For Amitiza: both of the following (i and ii):
      i. Member is a female;
      ii. Age ≥ 18 years;
   b. For Zelnorm: all of the following (i, ii, and iii):
      i. Member is a female;
      ii. Age ≤ 65 years;
      iii. Member does not have any of the following contraindications: a history of myocardial infarction, stroke, transient ischemic attack, or angina;
   c. For Linzess and Trulance: Age ≥ 18 years;
3. Documentation of recurrent abdominal pain or discomfort ≥ 1 day a week in the last 3 months with ≥ 2 of the following: improvement with defecation, onset associated with change in frequency of stool, and/or onset associated with change in form (appearance) of stool;
4. Failure of one of each of the following categories, unless clinically significant adverse effects are experienced or all are contraindicated (a-e);
   a. An increase of dietary fiber with lifestyle modifications;
   b. Stool softening agent (e.g., docusate);
   c. Saline laxative (e.g., magnesium citrate, milk of magnesia);
   d. Stimulant laxative (e.g., bisacodyl, senna);
   e. Osmotic laxative (e.g., polyethylene glycol (MiraLax));
5. Dose does not exceed the FDA approved maximum (see section V).

Approval duration: 3 months

D. Irritable Bowel Syndrome with Diarrhea (must meet all)**:**
1. Diagnosis of IBS-D;
2. Age ≥ 18 years;
3. One of the following (a or b):
   a. Request is Viberzi;
   b. Request is for Lotronex and member is a female;
4. Documentation of recurrent abdominal pain or discomfort ≥ 1 day a week in the last 3 months with ≥ 2 of the following: improvement with defecation, onset associated with change in frequency of stool, and/or onset associated with change in form (appearance) of stool;
5. Failure of one of each of the following categories, unless clinically significant adverse effects are experienced or all are contraindicated (a-c);
   a. An increase of dietary fiber with lifestyle modifications;
   b. Antidiarrheals and bile acid sequestrants (e.g., cholestyramine, loperamide);
   c. Tricyclic antidepressants (e.g., amitriptyline);
6. Dose does not exceed the FDA approved maximum (see section V).

Approval duration: 6 months

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. For OIC: Member continues to receive opioid therapy;
3. For Zelnorm, member does not have any of the following contraindications: a history of myocardial infarction, stroke, transient ischemic attack, or angina;
4. Member is responding positively to therapy;
5. If request is for a dose increase, new dose does not exceed the FDA approved maximum (see section V).

Approval duration: 3 months (for OIC); 12 months (for all other indications)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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
IBS-D: irritable bowel syndrome with diarrhea
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
docusate sodium (Colace®)	50-300 mg/day PO given in single or divided doses	360 mg/day
magnesium citrate	195 to 300 mL PO given in single or divided doses	300 mL/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	4 tablets (34.4 mg sennosides) PO twice daily
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) PO QD if necessary	60 mL or 2 to 4 packets daily
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
loperamide (Imodium A-D®)	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.
amitriptyline (Elavil®)	10 to 25 mg QHS	150 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
See respective Prescribing Information for listed contraindications and boxed warnings

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
alosetron (Lotronex®)	IBS-D	Starting dose is 0.5 mg PO BID May increase dose to 1 mg BID after 4 weeks if starting dosage is well tolerated but does not adequately control IBS symptoms	2 mg/day
eluxadoline(Viberzi®)	IBS-D	100 mg PO BID	200 mg/day
linaclotide (Linzess®)	CIC, IBS-C	CIC: 72 mcg or 145 mcg PO QD IBS-C: 290 mcg PO QD	CIC: 145 mcg/day IBS-C: 290 mcg/day
lubiprostone (Amitiza®)	CIC, OIC, IBS-C	CIC and OIC: 24 mcg PO BID IBS-C: 8 mcg PO BID	CIC and OIC: 48 mcg/day IBS-C: 16 mcg/day
methylnaltrexone bromide (Relistor®)	OIC in adult patients with chronic non-cancer pain	12 mg SC QD or 450 mg PO QD	12 mg/day SC 450 mg/day PO
	OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dose	Recommended dosage regimen is one dose administered SC QOD, as needed. Do not administer more frequently than one dose per 24-hour period.	Refer to dosing regimen

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td></td><td>escalation for palliative care</td><td>Weight-Based Dosing of Relistor Injection
<table>
<tr><th>Weight of Adult Patient</th><th>Subcutaneous Dose</th></tr>
<tr><td>Less than 38 kg</td><td>0.15 mg/kg*</td></tr>
<tr><td>38 kg to less than 62 kg</td><td>8 mg = 0.4 mL</td></tr>
<tr><td>62 kg to 114 kg</td><td>12 mg = 0.6 mL</td></tr>
<tr><td>More than 114 kg</td><td>0.15 mg/kg*</td></tr>
</table>
*Calculate the injection volume for these patients by multiplying the patient weight in kilograms by 0.0075 and then rounding up the volume to the nearest 0.1 mL.</td><td></td></tr>
<tr><td>naldemedine (Symproic®)</td><td>OIC</td><td>0.2 mg PO QD with or without food</td><td>0.2 mg/day</td></tr>
<tr><td>naloxegol (Movantik®)</td><td>OIC</td><td>25 mg PO QD; if not tolerated, reduce to 12.5 mg PO QD</td><td>25 mg/day</td></tr>
<tr><td>plecanatide (Trulance®)</td><td>CIC, IBS-C</td><td>3 mg PO QD</td><td>3 mg/day</td></tr>
<tr><td>prucaloprode (Motegrity™)</td><td>CIC</td><td>Adults: 2 mg PO once daily</td><td>2 mg/day</td></tr>
<tr><td>tegaserod (Zelnorm®)</td><td>IBS-C</td><td>6 mg PO BID at least 30 minutes before meals</td><td>12 mg/day</td></tr>
</table>

VI. Product Availability

Drug Name	Availability
alosetron (Lotronex®)	tablets: 0.5 mg, 1 mg
eluxadoline(Viberzi®)	tablets: 75 mg, 100 mg
linaclotide (Linzess®)	capsules: 72 mcg, 145 mcg, 290 mcg
lubiprostone (Amitiza®)	capsules: 8 mcg, 24 mcg
methylnaltrexone bromide (Relistor®)	tablet: 150 mg injections: 8 mg/0.4 mL single-dose pre-filled syringe, 12 mg/0.6 mL single-dose pre-filled syringe and vial
naldemedine (Symproic®)	tablet: 0.2 mg
naloxegol (Movantik®)	tablets: 12.5 mg, 25 mg
plecanatide (Trulance®)	tablet: 3 mg
prucaloprode (Motegrity™)	tablets: 1 mg, 2 mg
tegaserod (Zelnorm®)	tablet: 6 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created (MRX P.229)	04.22.21	05.21
3Q 2021 annual review: no significant changes; references reviewed and updated.	07.16.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.