Policy: Drugs for Constipation

Reference Number: OR.CP.PMN.1005
Effective Date: 10.1.2021
Last Review Date: 06.25
Line of Business: Medicaid – Trillium Oregon Health Plan Revision Log

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

Description
The following agents are used to treat constipation and require prior authorization: linaclotide (Linzess), lubiprostone (Amitiza), methylnaltrexone (Relistor), naldemedine (Symproic), naloxegol (Movantik), plecanatide (Trulance), prucalopride (Motegrity), tenapanor (Ibsrela).

Covered Alternatives
- Current Trillium Preferred Drug List listed at:
  - https://www.trilliumohp.com/providers/pharmacy.html

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 Trillium Community Health Plan that drugs for constipation are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria:

A. All Indications (must meet all)**:**

1. Prescribed indication is FDA-approved (see Appendix A);
2. One of the following is met (a or b):
   a. OHP covered diagnosis that is adversely affected by constipation or secondary to constipation;
   b. Member is eligible for EPSDT review and was born in or after the year 2004;
3. Prescribed by or in consultation with one of the following (a, b, c, or d):
   a. Gastroenterologist;
   b. Dietician;
   c. Pain management specialist;
   d. Any provider type prescribing within their scope of practice if member has been approved for long-term use of opioids;
4. Failure of at least 2 recommended conventional first-line treatments including dietary modifications each used for least 4 weeks (see Appendix B);
5. If request is for prucalopride, brand Motegrity, brand Amitiza, Linzess, or Zelnorm: member has tried and failed generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for brand Motegrity, member must use generic prucalopride, unless contraindicated or clinically significant adverse effects are experienced;

7. If request is for Relistor or Symproic: member has tried and failed Movantik unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed the FDA-approved maximum recommended dose.

Approval duration: 6 months

II. Continued Therapy:

A. All Indications (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 prucalopride, brand Motegrity, brand Amitiza, Linzess, or Zelnorm: member has tried and failed generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for brand Motegrity, member must use generic prucalopride, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for Relistor or Symproic: member has tried and failed Movantik unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, new dose does not exceed the FDA-approved maximum recommended dose.

Approval duration: 6 months

III. Appendices/General Information

Appendix A. Gastrointestinal Drugs FDA-Approved for Treatment of Constipation in an Outpatient Setting

Generic (Brand Name)	Indications
Linaclotide (LINZESS)	• CIC in adults • IBS-C in adults • FC in pediatric patients aged 6 to 17 yo
Lubiprostone (AMITIZA)	• CIC in adults • IBS-C in females > 18 yo • OIC in adults: 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
Methylnaltrexone (RELISTOR)	• OIC in adults with advanced illness (injection only) • OIC in adults with chronic, non-cancer pain (tablets and injection)
Naldemedine (SYMPROIC)	• OIC in adults with chronic, non-cancer pain
Naloxegol (MOVANTIK)	• OIC in adults with chronic, non-cancer pain

Generic (Brand Name)	Indications
Plecanatide (TRULANCE)	• CIC in adults • IBS-C in adults
Prucalopride (MOTEGRITY)	• CIC in adults
Tenapanor (IBSRELA)	• IBS-C in adults
Abbreviations: CIC = chronic idiopathic constipation; FC = functional constipation; IBS-C = irritable bowel syndrome with constipation; IBS-D = irritable bowel syndrome with diarrhea; OIC = opioid-induced constipation; yo = years old	

Appendix B. Initial Management Strategies for Constipation

Strategy	Product
Dietary Modification	Increased dietary fiber (25 grams/day) and increased fluid consumption
Bulk-forming Laxatives	Psyllium (not recommended for opioid-induced constipation)
Osmotic Laxatives	Polyethylene glycol, lactulose, magnesium hydroxide, milk of magnesia
Stool Softener	Docusate
Stimulant Laxatives	Senna, bisacodyl

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Ibsrela: patients < 6 years of age due to the risk of serious dehydration; patients with known or suspected mechanical gastrointestinal obstruction
  - Linzess: patients less than 2 years of age; patients with known or suspected mechanical gastrointestinal obstruction
  - Lubiprostone: patients with known or suspected mechanical gastrointestinal obstruction
  - Movantik:
    - Patients with known or suspected gastrointestinal obstruction or at increased risk of recurrent obstruction
    - Concomitant use with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole)
    - Known serious or severe hypersensitivity reaction to Movantik or any of its excipients
  - Prucalopride: hypersensitivity to Motegrity; intestinal perforation or obstruction due to structural or functional disorder of the gut wall, obstructive ileus, severe inflammatory conditions of the intestinal tract such as Crohn's disease, ulcerative colitis, and toxic megacolon/megarectum
  - Relistor: patients with known or suspected mechanical gastrointestinal obstruction and at increased risk of recurrent obstruction
  - Symproic: patients with known or suspected gastrointestinal obstruction or at increased risk of recurrent obstruction, patients with a history of a hypersensitivity reaction to naldemedine

- Trulance: patients less than 6 years of age due to the risk of serious dehydration, patients with known or suspected mechanical gastrointestinal obstruction

- Boxed warning(s):
  - Ibsrela: contraindicated in patients < 6 years of age; avoid use of Ibsrela in patients 6 years to < 12 years of age; the safety and effectiveness of Ibsrela have not been established in patients < 18 years of age
  - Linzess: risk of serious dehydration in pediatric patients less than 2 years of age
  - Trulance: risk of serious dehydration in pediatric patients
  - None reported for lubiprostone, Movantik, prucalopride, Relistor or Symproic.

IV. Dosage and Administration

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td rowspan="3">Linaclotide (Linzess)</td><td>IBS-C</td><td>290 mcg PO QD</td><td>290 mcg/day</td></tr>
<tr><td>CIC</td><td>72 mcg or 145 mcg PO QD</td><td>145 mcg/day</td></tr>
<tr><td>FC</td><td>72 mcg PO QD</td><td>72 mcg/day</td></tr>
<tr><td rowspan="2">Lubiprostone (Amitiza)</td><td>CIC and OIC</td><td>24 mcg PO BID</td><td>48 mcg/day</td></tr>
<tr><td>IBS-C</td><td>8 mcg PO BID</td><td>16 mcg/day</td></tr>
<tr><td rowspan="2">Methylnaltrexone bromide (Relistor)</td><td rowspan="1">OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dose escalation for palliative care</td><td>The recommended dosage regimen is one dose administered SC QOD, as needed. Do not administer more frequently than one dose per 24-hour period.</td><td>Refer to dosing regimen</td></tr>
<tr><td colspan="2">Weight-Based Dosing of Relistor Injection
<table>
<tr><th>Weight of Adult Patient</th><th>Subcutaneous Dose and Corresponding Injection Volume</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></tr>
<tr><td>OIC in adult patients with chronic non-cancer pain</td><td>12 mg SC QD or 450 mg PO QD</td><td>12 mg/day SC
450 mg/day PO</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>Prucalopride (Motegrity)</td><td>CIC</td><td>Adults: 2 mg PO once daily</td><td>2 mg/day</td></tr>
</table>

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tenapanor (Ibsrela)	IBS-C	50 mg PO BID	100 mg/day

V. Product Availability

Drug Name	Availability
Linaclotide (Linzess)	Capsules: 72 mcg, 145 mcg, and 290 mcg
Lubiprostone (Amitiza)	Capsules: 8 mcg and 24 mcg
Methylnaltrexone bromide (Relistor)	Tablet: 150 mg Injections: • 8 mg/0.4 mL methylnaltrexone bromide in a single-dose pre-filled syringe • 12 mg/0.6 mL methylnaltrexone bromide in a single-dose pre-filled syringe, or single-dose vial
Naldemedine (Symproic)	Tablet: 0.2 mg
Naloxegol (Movantik)	Tablets: 12.5 mg and 25 mg
Plecanatide (Trulance)	Tablet: 3 mg
Prucalopride (Motegrity)	Tablets: 1 mg, 2 mg
Tenapanor (Ibsrela)	Tablet: 50 mg Tablets: 10 mg, 20 mg, 30 mg

VI. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy TCHP.PHAR.185 Drugs for Constipation. Added requirement to try and fail the authorized generic Amitiza prior to initial approval of brand Amitiza, Linzess, Motegrity, Trulance, Zelnorm per SDC recommendation.	06.30.21	07.15.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	03.17.22	04.07.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Per February SDC and prior clinical guidance, added redirection to Movantik for initial Relistor and Symproic requests; template changes applied to continued therapy section; references reviewed and updated	03.13.23	04.06.23
Per December SDC, added redirection to generic lubiprostone and Linzess for Trulance requests	01.09.24	02.20.24
1Q 2025 annual review: updated to reflect changes in FFS criteria "Drugs for Constipation" presented at the February 2025 P&T meeting; removed Zelnorm from criteria as product has been removed from the market; removed alvimopan from criteria as drug is not used in outpatient settings; updated appendixes and tables; references reviewed and updated.	01.24.25	02.11.25
Per March SDC, added redirection to generic prucalopride for initial approval criteria and continued therapy, removed step through Linzess for Trulance.	05.13.25	06.10.25

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.