Clinical Policy: Methylnaltrexone Bromide (Relistor)

Reference Number: ERX.NPA.99
Effective Date: 12.01.18
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Methylnaltrexone bromide (Relistor®) is an opioid antagonist.

FDA Approved Indication(s)
Relistor tablets and injection are indicated for the treatment of opioid-induced constipation (OIC) in adult patients 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 injection is also indicated for the treatment of OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

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 Relistor is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of OIC;
2. Age ≥ 18 years;
3. For members with chronic non-cancer pain ONLY: Member has been taking opioid(s) for ≥ 4 weeks;
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. Dose does not exceed the following:
   a. Tablets: 450 mg (3 tablets) per day;
   b. Injection: FDA-approved weight-based dosing (see Section V).

Approval duration: 6 months

B. 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. Opioid-Induced Constipation (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. Member continues to receive opioid therapy;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed the following:
   a. Tablets: 450 mg (3 tablets) per day;
   b. Injection: FDA-approved weight-based dosing (see Section V).

Approval duration: 12 months

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

FDA: Food and Drug Administration
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
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	68.8 mg sennosides/day (8 tablets/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) PO 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®)	50-300 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 and at increased risk of recurrent obstruction
- Boxed warning(s): none reported

Appendix D: General Information

- Advanced illness is defined as life-ending or terminal disease. In Relistor clinical trials, opioid induced constipation was defined as less than three bowel movements in the preceding week or no bowel movement for 2 days.
- The use of Relistor beyond four months has not been studied.

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>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.

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>Refer to dosing regimen</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>
</table>

VI. Product Availability

- Tablets: 150 mg
- Injection:
  - 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

VII. References

1. Relistor Prescribing Information. Bridgewater, NJ: Salix Pharmaceuticals; April 2020. Available at: https://www.relistor.com/. Accessed July 26, 2022.
2. 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.
3. Argoff CE, Brennan MJ, Camilleri M, et al. Consensus Recommendations on Initiating Prescription Therapies for Opioid-Induced Constipation. *Pain Med*. 2015;16(12):2324-37.
4. 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.
5. Nelson AD, Camilleri M. Chronic opioid induced constipation in patients with nonmalignant pain: challenges and opportunities. *Therap Adv Gastroenterol*. 2015;8(4):206-20.
6. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. *Ther Adv Chronic Dis*. 2016;7(2):121–134.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/.
8. Camilleri M, Lembo A, Katzka DA. Opioids in Gastroenterology: Treating Adverse Effects and Creating Therapeutic Benefits. *Clin Gastroenterol Hepatol*. 2017;15(9):1338-1349.
9. 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
Policy created	07.30.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	09.10.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	06.30.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	06.24.21	11.21
4Q 2022 annual review: no significant changes; general information (appendix D) added; references reviewed and updated.	07.26.22	11.22

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.