Clinical Policy Title:	methylnaltrexone bromide
Policy Number:	RxA.275
Drug(s) Applied:	Relistor®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td rowspan="2">methylnaltrexone Bromide (Relistor®)</td><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 Subcutaneous every other day, as needed. Do not administer more frequently than one dose per 24-hour period.

<u>Weight-Based Dosing of Relistor® Injection</u>
<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><td>Refer to dosing regimen</td></tr>
<tr><td>OIC in adult patients with</td><td>12 mg Subcutaneous once daily or 450 mg by mouth once daily</td><td>12 mg/day Subcutaneous</td></tr>
</table>

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
	chronic noncancer pain		450 mg/day by mouth

Dosage Forms

- Tablets: 150 mg
- Injection:
  - 8 mg/0.4 mL methylnaltrexone bromide in single-dose pre-filled syringe;
  - 12 mg/0.6 mL methylnaltrexone bromide in a single-dose pre-filled syringe, or single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of OIC;
2. Prescribed for OIC and one of the following (a or b):
   a chronic non-cancer pain;
   b In members with advanced illness or pain caused by active cancer requiring opioid dosage escalation for palliative care;
3. Age 18 years or older;
4. Failure of at least one agent from 2 different classes from the following categories below, unless contraindicated or clinically significant adverse effects are experienced:
   a. Over the counter (OTC) laxatives (e.g., docusate, bisacodyl, polyethylene glycol);
   b. Amitiza®;
   c. Movantik®;
5. If request is for chronic non-cancer pain, dose does not exceed the following:
   a. Tablets: 450 mg per day (3 tablets per day);
   b. Injection: 12 mg subcutaneously once daily.
6. If request is for members with advanced illness, dose does not exceed FDA approved weight-based dosing (See dosing information). No more than one dose in a 24-hour period.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member continues to receive opioid therapy;
3. Member is responding positively to therapy;
4. If request is for chronic non-cancer pain and is for a dose increase, new dose does not exceed the following:
   a. Tablets: 450 mg per day (3 tablets per day);
   b. Injection: 12 mg subcutaneously once daily;
5. If request is for members with advanced illness, new dose does not exceed FDA approved weight-based dosing (See dosing information). No more than one dose in a 24-hour period.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
OIC: Opioid induced constipation
OTC: Over the counter

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
lactulose	10 to 20 g (15 to 30 mL or 1 to 2 packets) daily; may increase to 40 g (60 mL or 2 to 4 packets) by mouth once daily if necessary	40 gm per day (60 mL or 2 to 4 packets daily)
Amitiza® (lubiprostone)	OIC: 24 mcg by mouth twice a day	48 mcg/day
Movantik® (naloxegol)	25 mg by mouth once daily	25 mg/day
OTC Agents not covered by majority of plans		
docusate sodium (Colace®)	50 to 300 mg/day by mouth given in single or divided doses	360 mg/day
bisacodyl (Dulcolax®)	Oral: 5 to 15 mg once daily Rectal: Enema, suppository: 10 mg (1 enema or suppository) once daily	15 mg/day by mouth; 10 mg/day rectally
polyethylene glycol 3350 (MiraLax®)	17 g by mouth once daily	34 g/day
senna (Senokot®)	1 to 2 tablets (8.6 to 17.2 mg sennosides) by mouth twice a day	8 tablets/day (68.8 mg sennosides per 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.

References

1. Relistor® Prescribing Information. Bridgewater, NJ: Salix Pharmaceuticals; April 2020. Available at: https://shared.salix.com/shared/pi/Relistor-pi.pdf?id=811664a . Accessed March 30, 2021.
2. Shaiova L, Rim F, Friedman D, et al: A review of methylnaltrexone, a peripheral opioid receptor antagonist, and its role in opioid-induced constipation. Palliat Support Care. 2007; 5(2):161-166. Accessed March 30, 2021.
3. Yuan CS, Foss JF, O'Connor M, et al: Methylnaltrexone for reversal of constipation due to chronic methadone use: a randomized controlled trial. JAMA. 2000; 283(3):367-372. Accessed March 30, 2021.
4. Yuan CS: Methylnaltrexone mechanisms of action and effects on opioid bowel dysfunction and other opioid adverse effects. Ann Pharmacother. 2007; 41(6):984-993. Accessed March 30, 2021.
5. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed March 30, 2021.
6. Relistor®. American Hospital Formulary Service Drug Information. Available at: http://www.medicinescomplete.com/mc/ahfs/current/. Accessed March 30, 2021.
7. Clinical Pharmacology Web site. Available at http://clinicalpharmacology-ip.com/ . Accessed March 30, 2021.
8. Michna E, Blonsky ER, Schulman S, et al: Subcutaneous Methylnaltrexone for Treatment of Opioid-Induced Constipation in Patients with Chronic, Nonmalignant Pain: A Randomized Controlled Study. The Journal of Pain. 2011: pp 1-9 Accessed March 30, 2021.
9. Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guidelines on the Medical Management of Opioid-Induced Constipation. Gastroenterology. 2019;156:218-226 Accessed March 30, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was revised: Currently receiving medication via RxAdvance benefit or member has previously met initial approval criteria	03/2020	
Policy was reviewed:	07/09/2020	09/14/2020

1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 2. Reference reviewed and updated.		
Policy was reviewed: 1. Approval Duration for Initial and continuation updated. 2. Abbreviated forms updated to full forms in policy. 3. Therapeutic alternative verbiage changed “Below are Suggested…” 4. Dosing criteria for initial and continued therapy creiteria was updated 5. Updated initial approval criteria to include specific use under I.A.2 6. References were updated.	03/30/2021	06/10/2021