

Clinical Policy: Methylnaltrexone Bromide (Relistor)

Reference Number: CP.CPA.274

Effective Date: 11.16.16

Last Review Date: 11.19

Line of Business: Commercial

[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 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.

It is the policy of health plans affiliated with Centene Corporation® 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 \geq 18 years;
3. 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®;
4. Dose does not exceed the following:
 - a. Tablets: 450 mg per day (3 tablets per day);
 - b. Injection: FDA-approved weight-based dosing (*see Section V*).

Approval duration: 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

II. Continued Therapy

A. Opioid Induced Constipation (must meet all):

1. Currently receiving medication via Centene benefit 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 per day (3 tablets per day);
 - b. Injection: FDA-approved weight-based dosing (*see Section V*).

Approval duration: 6 months or to member's renewal period, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

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 policies – CP.CPA.09 for commercial.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

OIC: opioid induced constipation

OTC: over the counter

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 for all relevant lines of business and may require prior authorization.

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) PO QD if necessary	40 gm per day (60 mL or 2 to 4 packets daily)
Amitiza [®] (lubiprostone)	OIC: 24 mcg PO BID	48 mcg/day
Movantik [®] (naloxegol)	25 mg PO QD	25 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
OTC Agents not covered by majority of plans		
docusate sodium (Colace [®])	50 to 300 mg/day PO 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 PO; 10 mg/day rectally
polyethylene glycol 3350 (MiraLax [®])	17 g PO QD	34 g/day
senna (Senokot [®])	1 to 2 tablets (8.6 to 17.2 mg sennosides) PO BID	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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose	
OIC in adult patients with advanced illness or pain caused by active cancer who require opioid dose escalation for palliative care	The 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	
	<u>Weight-Based Dosing of Relistor Injection</u>		
	Weight of Adult Patient		Subcutaneous Dose and Corresponding Injection Volume
	Less than 38 kg		0.15 mg/kg*
	38 kg to less than 62 kg		8 mg= 0.4 mL
	62 kg to 114 kg		12 mg=0.6 mL
More than 114 kg	0.15 mg/kg*		
*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.			
OIC in adult patients with	12 mg SC QD or 450 mg PO QD	12 mg/day SC 450 mg/day PO	

Indication	Dosing Regimen	Maximum Dose
chronic non-cancer pain		

VI. Product Availability

- 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

VII. References

1. Relistor Prescribing Information. Bridgewater, NJ: Salix Pharmaceuticals; November 2018 Available at: <https://www.relistor.com/>. Accessed August 30, 2019.
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.
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.
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.
5. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 30, 2019.
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7. Clinical Pharmacology Web site. Available at <http://clinicalpharmacology-ip.com/>. Accessed August 30, 2019.
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.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	06.13.17	11.17
4Q 2018 annual review: no significant changes; added age requirement; in continued therapy section, added requirement that member is still receiving opioid therapy per PI; references reviewed and updated.	07.27.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.30.19	11.19

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.

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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.

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