PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

RELISTOR
(methylnaltrexone bromide)

Status: CVS Caremark Criteria ***REG***
Type: Initial Prior Authorization ***Ref # 505-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Relistor tablets and Relistor 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 opioid-induced constipation (OIC) in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for opioid-induced constipation in an adult patient 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

OR

- The requested drug is being prescribed for opioid-induced constipation in an adult patient with advanced illness or pain caused by active cancer who requires opioid dosage escalation for palliative care
  AND
- The request is for Relistor injection

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Relistor tablet and Relistor 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 opioid-induced constipation in adult patients with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.[1-3] Use of Relistor beyond 4 months has not been studied in the advanced illness population.[3]

Constipation is by far the most common and debilitating gastrointestinal effect of opioids, and some degree of constipation is near universal in patients taking opioid medications. Lifestyle modifications are an appropriate first step for all those with constipation, and include increasing one's fluid intake, regular moderate exercise as tolerated, and toileting as soon as possible in response to the urge to defecate. The American Gastroenterological Association (AGA) presents a strong recommendation that laxatives be used as first-line agents in this disorder. If an adequate trial of laxatives results in incomplete relief of OIC symptoms, other agents might be needed.[9] If the nonspecific regimens do not provide satisfactory relief from the gastrointestinal manifestations of opioid-induced constipation, as evidenced by a bowel function index (BFI) score of more than 30 points, then specific treatment options with peripherally restricted opioid receptor antagonists such as methylnaltrexone bromide may be more efficacious for treatment of opioid-induced constipation and may thereby improve bowel function.[5,6] The AGA suggests methylnaltrexone over no treatment in patients with laxative refractory OIC.[9]

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The National Comprehensive Cancer Network (NCCN) Adult Cancer Pain guidelines recommend a prophylactic bowel regimen with a stimulant laxative with or without a stool softener or polyethylene glycol (PEG) and to increase the dose of the laxative when increasing the dose of opioids. When response to laxative therapy has not been sufficient for opioid induced constipation in patients with advanced illness, methylnaltrexone can be used.[4]

Most studies regarding the safety and efficacy of Relistor have not exceeded 4 months in duration.[5-7] The use of methylnaltrexone beyond 4 months has not been studied in the advanced illness population.[3] The long-term effects of methylnaltrexone (i.e., > 12 weeks) have not been often evaluated.[8] One phase 3, open-label trial studied the effects of injectable methylnaltrexone for 48 weeks in patients 18 years of age or older with opioid-induced constipation (OIC) with chronic non-cancer pain. The study excluded patients with a history of chronic constipation prior to opioid treatment, patients with significant gastrointestinal (GI) disorder, patients with cardiovascular conditions, and patients with unstable hepatic, renal, pulmonary, psychiatric, or other medical conditions. The study showed overall safety and efficacy with chronic use of injectable methylnaltrexone but had several limitations and suggested further research was needed. Additional studies are needed to assess the effects of methylnaltrexone on diverse patient populations.[8] Due to the lack of information regarding extended use, Relistor will be approved for 4 months if conditions are met.

REFERENCES

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4. Swarm R, Youngwerth J, Anghelescu D, et al. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Adult Cancer Pain version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed August 17, 2021.
5. Clemens KE and Klaschik E. Managing opioid-induced constipation in advanced illness: focus on methylnaltrexone bromide. *Therapeutics and Clinical Risk Management* 2010;6:77–82.
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8. Webster LR, Michna E, Khan A, et al. Long-term safety and efficacy of subcutaneous methylnaltrexone in patients with opioid-induced constipation and chronic noncancer pain: a phase 3, open-label trial. *Pain Medicine* 2017;18:1496-1504.
9. Crockett S, Greer K, Heidelbaugh J, Falck-Ytter Y, et al. American gastroenterological association institute guideline on the medical management of opioid-induced constipation. Gastroenterology. January 2019; 156 (1):218-226.

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CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for opioid-induced constipation in an adult patient with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation?	Yes	No

	[If yes, then no further questions.]		
2	Is the requested drug being prescribed for opioid-induced constipation in an adult patient with advanced illness or pain caused by active cancer who requires opioid dosage escalation for palliative care? [If no, then no further questions.]	Yes	No
3	Is this a request for Relistor injection?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 4 months	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have one of these conditions: - You are an adult with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation and you are requesting Relistor to treat opioid-induced constipation - You are an adult with advanced illness or pain caused by active cancer who requires increases in opioid dosage for palliative care and you are requesting Relistor injection to treat opioid-induced constipation Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Approve, 4 Months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have the following condition: - You are an adult with chronic non-cancer pain, including chronic pain related to prior cancer or its treatment who does not require frequent (e.g., weekly) opioid dosage escalation and you are requesting Relistor tablets to treat opioid-induced constipation Your request has been denied based on the information we have. [Short Description: No approvable diagnosis for Relistor tablets]