

**Medication Policy Manual**

**Policy No:** dru161

**Topic:** Relistor<sup>®</sup>, methylnaltrexone

**Date of Origin:** September 12, 2008

**Revised/Effective Date:** September 11, 2009

**Next Review Date:** September 2010

### **IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

### **Description**

Methylnaltrexone (Relistor<sup>®</sup>) is an injectable drug used to relieve opioid-induced constipation. Because of safety concerns, it is only used in patients with advanced illness receiving palliative care.

## **Policy/Criteria**

**I.** Most contracts require prior authorization approval of methylnaltrexone prior to coverage. Methylnaltrexone may be considered medically necessary in patients with opioid-induced constipation when criteria A, B, and C below are met.

**A.** An adequate trial of a prescribed bowel regimen has been ineffective. (see Appendix A)

**AND**

**B.** The member has an advanced medical illness with a life expectancy of less than 6 months and is enrolled in a hospice program or meets hospice criteria.

**AND**

**C.** The member is receiving chronic opioid therapy.

**II.** Administration, Quantity Limitations, and Authorization Period

**A.** Regence considers methylnaltrexone to be a self-administered medication.

**B.** When prior authorization is approved, methylnaltrexone may be authorized in quantities of 14 doses per 28 days for up to 4 months.

**III.** Methylnaltrexone is considered investigational when used for all other conditions, including, but not limited to:

**A.** Use beyond four months.

**B.** Constipation not caused by opioid use.

**C.** Clinically significant acute diverticular disease.

**D.** Fecal impaction.

- E.** Surgical abdomen: Defined as a serious condition within the abdomen characterized by sudden onset, pain, tenderness, and muscular rigidity, and usually requiring emergency surgery.
- F.** Opioid-induced constipation (NOT in patients with advanced illness receiving palliative care after failing laxative therapy)

### **Position Statement**

- Standard bowel regimens are recognized as standard of care to treat opioid-induced constipation.
  - \* Standard bowel regimens are:
    - effective for most people on chronic opioid therapy and provide the best value.
    - a prescribed combination of laxatives, stool softeners, osmotic agents and/or bulk forming agents.
- When standard bowel regimens are ineffective, methylnaltrexone is an option.
- Methylnaltrexone is a selective opioid antagonist that is injected subcutaneously every other day as needed for opioid-induced constipation.
  - \* Use is limited to critically ill patients receiving palliative care.
  - \* The safety and effectiveness beyond four months has not been adequately established.
- Methylnaltrexone has been studied in critically ill patients (expected survival of less than 6 months) for whom standard laxative options have been ineffective.
- The studies of methylnaltrexone are limited to two weeks in duration. It is unknown if repeated use of methylnaltrexone will:
  - \* Continue to be effective
  - \* Affect analgesia
  - \* Cause significant adverse events

### *Clinical Efficacy*

Methylnaltrexone appears to be effective for inducing laxation in terminally ill patients, but the long term safety is unknown.

- There are two randomized, controlled studies comparing methylnaltrexone to placebo in terminally ill patients. <sup>[2,3,5]</sup> In an unpublished but reliable, blinded single-dose study, one of every two treated patients achieved laxation within four hours. The published two week trial is inconclusive because 15 to 20% of randomized patients did not complete the study.
- Neither study addresses the efficacy of methylnaltrexone with repeated use beyond two weeks.
- There is no reliable evidence for effectiveness or safety of methylnaltrexone in conditions other than opioid-induced constipation in terminally ill patients.

### *Safety*

- The prescribing information states that the use of methylnaltrexone beyond four months has not been studied.
- The safety of administration of methylnaltrexone more frequently than every other day has not been established. In clinical trials, doses were not administered more frequently than every 48 hours.
- Methylnaltrexone shares the same mechanism of action as alvimopan (Entereg<sup>®</sup>). More myocardial infarctions were reported in patients treated with alvimopan compared with placebo in a 12-month study in patients treated with opioids for chronic pain, although a causal relationship has not been established. The long-term safety of methylnaltrexone is yet to be determined.

### **References**

1. Relistor<sup>®</sup> (methylnaltrexone) prescribing information. Wyeth: Philadelphia, PA; April 2008.
2. Product Dossier: Relistor<sup>®</sup> (methylnaltrexone). Wyeth: Philadelphia, PA. May 2008.
3. FDA Center for Drug Evaluation and Treatment. Approval package for application number NDA 021964 (methylnaltrexone); Medical Review. Available at: <http://www.fda.gov/cder/foi/nda/2008/021964s000TOC.htm>. Accessed on 7/2008.

4. Thomas J, Karver S, Cooney GA, Chamberlain BH, Watt CK, Slatkin NE. Methylnaltrexone for opioid-induced constipation in advanced illness. *N Eng J Med* 2008; 358:2332-43.
5. McNicol ED, Boyce D, Schumann R, Carr DB. Mu-opioid antagonists for opioid-induced bowel dysfunction. *Cochrane Database of Systematic Reviews* 2008, Issue2. Art.No.: CD006332. DOI: 10.1002/14651858.CD006332.pub2.
6. Goodheart CR, Leavitt SB. Managing opioid-induced constipation in ambulatory-care patients. *Pain Treatment Topics*. Aug 2008.

<b>Cross References</b>
Self-Administered Injectable Medications, dru110

Codes	Number	Description
J3490		Unclassified drug

<b>Appendix A: Standard Bowel Regimens</b>
- Laxatives (examples include: bisacodyl, cascara sagrada, and senna)
- Stool softeners (examples include: docusate, lactulose, magnesium salts, polyethylene glycol, and sodium phosphate)
- Osmotic agents (examples include: milk of magnesia, magnesium citrate, and saline laxatives)
- Bulk forming agents (examples include: psyllium, calcium polycarbophil, and methylcellulose)