

Methylnaltrexone (Relistor) for Opioid-Induced Constipation

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STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

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Methylnaltrexone (Relistor) is labeled for the treatment of opioid-induced constipation in patients with advanced illness who have not responded to laxative therapies.¹ As a selective antagonist of peripheral mu-opioid

receptors, methylnaltrexone inhibits opioid-induced gastrointestinal (GI) hypomotility without central nervous system effects such as sedation or change in mental status.²

Drug	Starting dosage	Dose form	Approximate cost*
Methylnaltrexone (Relistor)	0.15 mg per kg subcutaneously every other day as needed	Single-use vials with 12 mg per 0.6 mL or 8 mg per 0.4 mL, or as a seven-dose kit	\$48 per single-dose vial or \$336 for a seven-dose kit

*—Average wholesale cost, based on Red Book. Montvale, N.J.: Medical Economics Data; 2010.

SAFETY

Methylnaltrexone is safe and unlikely to cause adverse effects. Less than 1 percent of patients have severe diarrhea requiring discontinuation of treatment. Methylnaltrexone does not reverse analgesia from opioids or cause opiate withdrawal symptoms.²⁻⁴ The use of methylnaltrexone has not been studied beyond four months' duration in adults, and it has not been evaluated in children. It is contraindicated in patients with GI obstruction. Methylnaltrexone is U.S. Food and Drug Administration pregnancy category B and its excretion in breast milk has not been determined.¹

TOLERABILITY

The most common adverse effects of methylnaltrexone are abdominal pain (17 to 30 percent versus 10 to 13 percent with placebo), flatulence (8 to 13 percent versus 6 to 7 percent), and nausea (11 to 21 percent versus 5 to 7 percent).^{1,3,4} In clinical trials, discontinuation rates because of adverse events have been low: 6 percent of patients taking methylnaltrexone compared with 7 percent of those taking placebo.²

EFFECTIVENESS

One study involved older patients (median age: 72 years) with advanced illness who received a median of 150 mg oral morphine equivalents per day (mean dosage: 417 mg per day) and had fewer than three stools per week. Patients had been on opioids for at least two weeks before the methylnaltrexone intervention, and laxative therapy had failed. The median number of laxative drug classes used was two, with contact laxatives/stimulants (81 percent), stool softeners (41 percent), and osmotic agents (30 percent) used most often.⁴

About 60 percent of patients taking methylnaltrexone had a bowel movement within four hours, usually within 30 minutes of the first dose, compared with about 14 percent of those on placebo (number needed to treat = 2.2). Thirty-five percent responded after the second dose of methylnaltrexone 24 hours later, and 26 percent after the third dose. About 74 percent of patients rated themselves as "slightly to much better" with treatment, compared with 35 percent taking placebo.¹

On average, methylnaltrexone reduces GI transit time by 52 minutes versus placebo.⁵ ▶

PRICE

The average wholesale price of methylnaltrexone is \$48 per single-use vial or \$336 for a seven-dose kit. A generic form is not available.

SIMPLICITY

Methylnaltrexone is typically given every other day as a subcutaneous injection in the upper arm, abdomen, or thigh as needed to induce a bowel movement. It should not be used more than once every 24 hours. The dose is 8 mg for patients weighing 84 to less than 136 lb (38 to less than 62 kg) and 12 mg for patients weighing 136 to 251 lb (62 to 114 kg). Patients above or below these weight ranges receive 0.15 mg per kg. The dose is decreased by 50 percent in patients with creatinine clearance less than 30 mL per minute per 1.73 m² (0.50 mL per second per 1.73 m²). No dose adjustment is necessary for patients with mild to moderate hepatic dysfunction.¹

Methylnaltrexone should be stored at room temperature away from light, and should be injected within 24 hours after being drawn into a syringe. Patients should discard the syringe if the medication is discolored or if particles are visible.

Bottom Line

Methylnaltrexone can temporarily relieve opioid-induced constipation in patients with advanced illness who have not responded to laxative treatment. However, it must be given by injection, is expensive, and has been studied only for short-term use.

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Author disclosure: Nothing to disclose.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Air Force, the U.S. Department of Defense, or the U.S. Government.

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