

Formulary Review: RELISTOR®
Generic Name: Methylnaltrexone bromide
Manufacturer: Wyeth Pharmaceuticals
FDA Approval: April 28, 2008

Executive Summary

Introduction

RELISTOR® is the first peripherally-acting opioid antagonist approved for use in the US and is indicated for the treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient.

Pharmacology

RELISTOR® is a selective antagonist at the mu-opioid receptor. However, it does not cross the blood brain barrier, so it is able to decrease constipation resulting from opioid therapy without affecting the analgesic effects in the CNS.

Pharmacokinetics

Table 1. Pharmacokinetic profile

	0.15 mg/kg	0.30 mg/kg	0.50 mg/kg
C _{max} (ng/mL)	117	239	392
t _{max} (hr)	0.5	0.5	0.5
AUC ₂₄ (ng•hr/mL)	175	362	582

Clinical Efficacy

Prior to approval, the safety and efficacy of RELISTOR® was evaluated in two randomized, double-blind, placebo-controlled studies. In both of these studies, the median age was 68 years, patients had a life-expectancy less than six months and were receiving opioid therapy. The primary diagnosis was incurable cancer. Patients remained on their current laxative regimen throughout the studies in addition to receiving RELISTOR®. Opioid-induced constipation was defined as either less than 3 bowel movements in the preceding week or no bowel movement for greater than two days. In both studies, patients receiving RELISTOR® had a significantly higher rate of laxation within four hours of the dose.

Adverse Drug Reactions

The adverse reactions reported from the two clinical studies include abdominal pain, flatulence, nausea, dizziness, diarrhea, and hyperhidrosis. Postmarketing reports have revealed rare cases of GI perforation in patients with illnesses related to a reduction of the integrity of the wall of the GI tract.

Drug Interactions

It is a weak inhibitor of CYP2D6, but has not been found to inhibit any of the other CYP enzymes.

Dosage & Administration

RELISTOR® is for subcutaneous injection only, and should be injected in the upper arm, abdomen or thigh. The usual dosing schedule is one dose every other day, as needed, but no more frequently than one dose in a 24-hour period.

Patient weight (kg)	Dose	Injection volume
< 38	0.15 mg/kg	**
38 to <62	8 mg	0.4 mL
62 to 114	12 mg	0.6 mL
> 114	0.15 mg/kg	**

**For patients weighing less than 38 kg or greater than 114 kg:
Multiply the patient weight in kg by 0.0075 and round up the volume to the nearest 0.1 ml.
These patients should NOT receive the prefilled syringe.

Summary

RELISTOR® is the only peripherally-acting mu-opioid antagonist indicated for opioid-induced constipation in patients with advanced illness who have failed laxatives. RELISTOR is tolerated well, and usually produces a bowel movement in 30 minutes to 4 hours.

Cost

AWP: \$50 per injection; \$350 per pack of 7 prefilled syringes