

# RGH Pharmacy E-Bulletin

Volume 35 (5): August 24, 2009

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH

© Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia 5041

## Methylnaltrexone

Methylnaltrexone is a peripherally acting mu ( $\mu$ ) opioid-receptor antagonist, predominantly active in the gastrointestinal tract, marketed in Australia as Relistor®. It does not cross the blood-brain barrier, or interact significantly with the delta or kappa opioid receptors. Methylnaltrexone is indicated for use in opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. It is available only as a subcutaneous injection to be given when the patient has not experienced a bowel motion for at least 3 days.

Patient weight	Dose	Injection volume
<38kg	0.15mg/kg	Patient weight x 0.0075, rounded to nearest 0.1mL
38-61kg	8mg	0.4mL
62-114kg	12mg	0.6mL
>114kg	0.15mg/kg	Patient weight x 0.0075, rounded to nearest 0.1mL

The usual dosing interval is alternate days, although the interval can be longer. If there has been no bowel motion within 24 hours of the last dose, another dose can be given. Methylnaltrexone is contraindicated in known or suspected bowel obstruction. A 50% dose reduction is recommended in patients with an estimated GFR of less than 30mL/minute.

In clinical trials, methylnaltrexone 0.15mg/kg or placebo was given to patients who had received opioids for two or more weeks and who had received stable doses of opioids and laxatives for three or more days without relief of opioid-induced constipation. Opioid-induced constipation was defined as either fewer than three laxations during the preceding week and no clinically meaningful laxation within 24 hours before the first study dose. Patients could continue their baseline laxative regimen throughout the study and take rescue laxatives as needed, though not within 4 hours of a dose of study drug. 71 patients received placebo and 63 were given methylnaltrexone. 48% of patients in the methylnaltrexone group had laxation within 4 hours compared to 15% in the placebo group.

There is no doubt that methylnaltrexone is effective at reversing opioid-induced constipation. Rapid onset of a bowel movement may occur within 30 minutes of a dose, therefore patients should remain close to toileting facilities.

It is not reported how long patients had been on their baseline laxative regimen before entry into the study although they were reported as taking between 1 - 5 drug classes of laxatives (median 2 classes). It is worth noting that for any patient in whom opioids are started with the intention of regular use, regular laxatives should be started simultaneously, and stimulant laxatives should be started early.

Methylnaltrexone does not appear to block the analgesic effect of opioids. Pain assessment scores and withdrawal scores did not differ between the active and placebo groups. Adverse effects reported with greater frequency in the methylnaltrexone group than in the placebo group are: abdominal pain, flatulence, nausea, dizziness, and diarrhoea.

Methylnaltrexone is not PBS listed, and syringes of 12mg/0.6 ml cost approximately \$A50 each. There is no clear maximum duration of use; the open-label extension of clinical trials lasted up to three months.

Given the cost of methylnaltrexone, it could be reserved for use in palliative care patients receiving chronic opioids who have constipation-related discomfort and reduced frequency of bowel motions, despite maximal use of regular laxatives.

Acknowledgment – This E-Bulletin is based on work by Jenny Casanova, Senior Clinical Pharmacist, RGH.

**FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: [chris.alderman@rgh.sa.gov.au](mailto:chris.alderman@rgh.sa.gov.au)**  
Information in this E-Bulletin is derived from critical analysis of available evidence – individual clinical circumstances should be considered when making treatment decisions. You are welcome to forward this E-bulletin by email to others you might feel would be interested, or to print the E-Bulletin for wider distribution. Reproduction of this material is permissible for purposes of individual study or research.