

Methylnaltrexone for Refractory Opioid-Induced Constipation

Staff information sheet

**Medical staff - please remember to complete an audit sheet
and place it in the audit folder in the doctors office**

How does methylnaltrexone work?

Methylnaltrexone blocks the action of opioids on the gastrointestinal tract (a 'mu opioid receptor antagonist'). However, it doesn't penetrate the blood brain barrier, so shouldn't interfere with their analgesic effect.

When should it be used?

It is licensed for opioid-induced constipation that hasn't responded to usual measures (laxatives) in palliative care patients. It costs ~£20 per ampoule.

Consider it in patients provided:

- They are not known to be allergic to methylnaltrexone *and*
- They do not have mechanical gastrointestinal obstruction *and*
- Titration and switching of laxatives and rectal measures is ineffective or inappropriate *and*
- Opioids are thought to be a significant cause of their constipation *and*
- They are inpatients. This is not a requirement of the license, but is a precaution in case colic needs urgent treatment. This will be reviewed in the light of the audit.

If in doubt, discuss with a consultant or other experienced colleague.

What to include when seeking informed consent

Information should always be tailored to individual patient's wishes and circumstances. Verbal consent should be documented including what was discussed. This may include:

- **This is a new treatment.** We have little experience of its use, but a large research study found it to be safe and effective, and it has been scrutinised and approved by the UK regulatory authorities
- **The main alternative option** would be to continue to use enemas and/or larger doses of oral laxatives. These are established treatments, though some people find enemas uncomfortable
- **The commonest adverse effects** ('side effects') are diarrhoea, nausea, griping/colic, stinging at the injection site, and dizziness. With the exception of the last two, these are similar to the adverse effects seen with enemas/laxatives.

How to prescribe methylnaltrexone

Regular laxatives are continued alongside methylnaltrexone

Prescribe a one off SCut dose on day 1. Dose is according to weight (if in doubt, use lower dose):

- >60Kg Methylnaltrexone 12mg
- <60Kg Methylnaltrexone 8mg

Consider a lower dose with renal or hepatic impairment

Consider a lower test dose with colostomy, diverticulosis, or faecal impaction

In everyone: prescribe hyoscine butylbromide 20mg SCut p.r.n. in case of colicky pain

Thereafter:

- *If no response*, repeat dose on day 2
- *If partial response*, consider repeat dose on day 3
- Further doses can be given alternate days until laxatives have been titrated to an effective dose
- If an effective dose is difficult to achieve consider switching laxatives or a laxative-sparing opioid (e.g. transdermal fentanyl)

What to look out for in patients receiving methylnaltrexone

Preparation: Similar to enemas. Bowel action can occur quickly (average is 30-60mins after the dose is given) and can be diarrhoea, so consider inco sheets, commode at bedside if appropriate.

Flush: If giving via a SCut line, flush with sodium chloride 0.9%. Rotate site if reaction occurs.

Adverse effects to look for:

- Injection site reaction – if bothersome, give analgesia (consider topical hydrocortisone 0.5% cream b.d.-q.d.s. if marked)
- Colicky pain – give hyoscine butylbromide 20mg SCut p.r.n.
- Diarrhoea – if marked and needs treatment, give hyoscine butylbromide 20mg SCut p.r.n.
- Dizziness – lie patient down, reassure, encourage to drink plenty, and check observations. If in doubt, discuss with medical team
- Nausea – treat with a centrally acting antiemetic such as cyclizine 50mg SCut/PO p.r.n. t.d.s or haloperidol 0.5-1.5mg SCut/PO p.r.n. b.d.-q.d.s.

Pharmacological details for prescribers

For more information, see the summary of product characteristics at <http://emc.medicines.org.uk/>

- Absorption: Peak plasma concentration 30mins after SCut injection
- Distribution: Blood brain barrier penetration is minimal
- Metabolism and elimination: Around 1/3 is metabolised to either inactive or partially active compounds. These, plus the un-metabolised parent drug, are predominantly renally excreted. Half-life is ~8 hours.
- Therefore dose reduction is advised in renal impairment, and caution is advised with severe renal and severe hepatic impairment. Discuss use in such patients with a consultant.

References

- Summary of product characteristics (see <http://emc.medicines.org.uk/>)
- Thomas et al (2008) *Methylnaltrexone for opioid-induced constipation in advanced illness*. The New England Medical Journal 358: 2332-43

Audit: Methylnaltrexone for refractory opioid-induced constipation

Completed by medical team

Name (or sticker): DoB:	Diagnosis:
	If cancer , is there known intra-abdominal/pelvic disease? <div><input type="checkbox"/> Yes <input type="checkbox"/> No</div>
What's already been tried? Laxatives tried and titrated: Rectal measures tried:	
Methylnaltrexone used Was a lower initial test dose tried? Y / N Dose used (record highest dose, if lower test dose used): Total number of doses given and how often:	
Has the patient expressed a view or preference about the treatment? (e.g. how did the patient feel about the treatment? Did they express a preference about future treatment?)	
What is the MDTs opinion about the treatment? Effective? (e.g. Did it work? How quickly? Did it affect length of stay?) Any problems? (e.g. Was the bowel movement comfortable? Site reactions? Other problems?)	

Thank you for helping with this audit. Please return form to audit folder in doctor's office