NHS
Pan Mersey
Area Prescribing Committee

Prescribing Support Information

METHADONE TABLETS IN PAIN MANAGEMENT

AMBER patient retained by specialist

Your patient has been identified as being suitable to receive methadone tablets in accordance with the indication detailed below. They have been commenced on treatment either in clinic or during an inpatient admission at a tertiary centre and have been stabilised on a suitable dose by the specialist pain team. Once stabilised, your patient will be reviewed annually in the pain clinic.

When prescribing methadone, prescribers should consider NICE NG193 (07 April 2021): Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. Chronic primary pain is pain with no clear underlying cause, or pain (or its impact) that is out of proportion to any observable injury or disease and NICE recommends that opioids are not initiated in this type of pain.
For other chronic pain conditions, prescribers should continue to follow the appropriate NICE guidelines, including those on headaches, low back pain and sciatica, rheumatoid arthritis, osteoarthritis, spondyloarthritis, endometriosis, neuropathic pain and irritable bowel syndrome, some of which include opioids as an option.

This medicine has been considered as appropriate for prescribing in primary care and the information contained in this document has been provided to support you to prescribe methadone for your patient in the community. A full, individualised plan has been agreed with the patient and this must be communicated with the GP before prescribing is transferred to primary care.

Your patient will remain under the care of the specialist team whilst receiving this medicine.

Indication

Pan Mersey Area Prescribing Committee has RAG rated methadone as Amber Patient Retained, which means that it is suitable for prescribing in primary care following initiation by a consultant in pain medicine in a tertiary centre for the treatment of:

1. Refractory neuropathic pain, unresponsive to any other opioid (e.g. central post stroke pain, spinal cord injury pain, painful diabetic neuropathy etc.)
2. Severe, iatrogenic opioid dependency patients with positive response to oral ketamine treatment, who require a stabilisation phase prior to rotation to a different opioid or cessation of all opioid therapy.
3. Patients with chronic pain responsive to doses of strong opioids (<100mg Morphine Equivalent and 50% pain reduction) that require regular rotations between opioids and achieve good pain relief on low dose methadone.

Name of Drug, Form and Dose

Methadone 5mg tablet

Methadone is approximately 2-4 times more potent than oral morphine, mainly due to the NMDA antagonising effect[1]. The patient will have their dose of methadone titrated up and stabilised at the tertiary centre. The normal dosage range for patients prescribed methadone from the pain clinic is 15-45mg per day.

Due to the increased risk of accumulation, the use of methadone is cautioned in patients with renal or hepatic disease. However, as methadone has no active metabolites and as it is eliminated via both the faeces and urine, it is relatively safe in patients with renal impairment. Patients will have baseline U&Es and LFTs checked prior to commencing methadone.

Monitoring recommendations

No additional monitoring is required for patients established on methadone by the pain clinic. As methadone can lead to QTc interval prolongation, it is contra-indicated in patient with QT prolongation including congenital QT prolongation. Prior to the initiation of methadone, patients will have had a baseline ECG and the results of this will be communicated in correspondence from the specialist.
A list of drugs that prolong QT interval can be found at www.crediblemeds.org following free registration.

How long the medicine should be prescribed for

Patients with refractory neuropathic pain and opioid responsive chronic pain who required regular opioid rotation may remain on methadone indefinitely. The specialist should ensure that the wishes of the patient are considered at all times. Patients should be supported with dose reduction wherever possible.

Patients with iatrogenic opioid dependency may remain on methadone for several months to allow the opioid receptors to recover. They will then be switched/rotated to alternative opioids if opioid responsive, under the care of the pain specialist, or weaned off opioids altogether.

NB: Opioid cross-titration is RED in Pan Mersey.
Where a patient is undergoing transition from one strong opioid to another under supervision of a pain clinic specialist using “cross-titration” (gradual reduction of dose of the opioid being stopped with simultaneous gradual increase in dose of the new opioid), prescribing of both opioids should be undertaken by the specialist until the first opioid has been stopped

Contra-indications

- Hypersensitivity to the active substance or to any of the excipients
- Respiratory depression, obstructive airways disease.
- Acute alcoholism,
- Head injury or raised intracranial pressure.
- It is not recommended during an asthma attack or where there is a risk of paralytic ileus.
- Concurrent administration with monoamine oxidase inhibitors (including moclobemide), or within 2 weeks of discontinuation of treatment with them.
- Concurrent use of other central nervous system depressants (see other information)
- Methadone is not suitable for children. Babies born to mothers receiving methadone may suffer withdrawal symptoms.
- Individuals with QT prolongation, including congenital long QT syndrome (see monitoring requirements)
- As with all opioid analgesics, this product should not be administered to patients with severe hepatic impairment as it may precipitate Porto- systemic Encephalopathy in patients with severe liver damage.
- As with other opioid drugs, methadone may cause constipation which is particularly dangerous in patients with severe hepatic impairment and measures to avoid constipation should be initiated early.

Adverse effects
Very common (≥ 1/10): Nausea, vomiting

Common (≥ 1/100 to < 1/10): Fluid retention, euphoria, hallucinations, sedation, blurred vision, miosis, vertigo, constipation, transient rash, sweating, fatigue

Please note that this list is not exhaustive – please refer to summary of product characteristics (SPC) for complete list

Seek advice from the initiating specialist if there are concerns about potential adverse effects

Special warnings/cautions
Methadone should be given with caution to patients with asthma, convulsive disorders, depressed respiratory reserve, hypotension, hypothyroidism or prostatic hypertrophy.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. Any required dose adjustments will be completed by the initiating specialist.

Methadone should be administered with caution to patients at risk for the development of prolonged QT interval. Patients will undergo baseline ECG assessment (see monitoring)

See summary of product characteristics (SPC) for full list of warnings and cautions.

Interaction with other medicines
There is considerable potential for interaction with CYP 3A4 inducers and inhibitors. Inducers, such as carbamazepine, phenytoin, rifampicin, and St John's Wort have the potential to lower plasma concentrations of methadone. Inhibitors, such as clarithromycin, fluoxetine, antifungals, and HIV-1 protease inhibitors may increase plasma concentrations. It should be noted that many methadone-related deaths recorded in the literature are due to drug interactions rather than methadone alone. In addition, some antipsychotics may precipitate methadone withdrawal symptoms via an unknown mechanism.

There is an increased risk of respiratory depression if methadone is combined benodiazpines[3], if co-prescription is considered necessary, utilise the lowest effective dose for the shortest period of time – seek advice from initiating specialist.

Please refer to the British national formulary (BNF) or summary of product characteristics (SPC) for a complete list of interactions.

Other information
Best analgesic effect is usually achieved with three times a day dosing given the 6-8 hour half-life.

If the patient presents with any other pain while on methadone, manage as usual (without using other opioids), and do not adjust methadone dose. Contact the initiating specialist for advice if necessary**.**

As with other opioids, patients on methadone can develop severe constipation. In patients that are unresponsive to standard laxatives, naloxegol (12.5mg once a day to 25mg once a day) – RAG Green see Pan Mersey formulary https://www.panmerseyapc.nhs.uk/media/2236/naloxegol.pdf) may be used.

When to seek specialist advice

- If the patient suffers from a serious adverse effect
- If the patient decides to discontinue treatment for any reason (Abrupt withdrawal of methadone is very likely to trigger uncomfortable opioid abstinence symptoms (headache, myalgia, fatigue and irritability)).

Transfer of prescribing into primary care

The patient will be stabilised on a maintenance dose of methadone by the tertiary centre prior to transfer of prescribing responsibilities to primary care. Dose alteration will only be done after outpatient pain clinic review and all dose changes will be communicated to primary care in writing using the template letter. The first prescription with 1 month supply at the stabilised dose will be given by the specialist.

Contact details for advice

Please refer to the contact details included in the correspondence sent by the specialist

References

1. J Rajan, FRCA J Scott-Warren, DRCOG MRCP FRCA FFPMRCA. The Clinical Use of Methadone in Cancer and Chronic Pain Medicine. *BJA Education,* 2016; 16(3) Available from: https://academic.oup.com/bjaed/article/16/3/102/2897756
2. Summary of product characteristics. SPC
3. Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression MHRA.2021 Available from: https://www.gov.uk/drug-safety-update/benzodiazepines-and-opioids-reminder-of-risk-of-potentially-fatal-respiratory-depression
4. British National Formulary. BNF