



## Prescribing Support Information

### **Methadone tablets in pain management**

This medicine has been categorised as Amber Patient Retained by the Pan-Mersey Area Prescribing Committee

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 reviewed by the specialist pain team. Once stabilised your patient will be reviewed yearly in the pain clinic.

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.

Pan Mersey Area Prescribing Committee has RAG rated methadone as Amber 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.

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

### **Methadone**

Methadone is a strong opioid acting as an agonist at Mu receptors and as an antagonist at N-methyl-D-aspartate (NMDA) receptors. NMDA receptor activity is thought to provide an explanation of the efficacy of methadone in neuropathic pain. It has a less sedating effect than morphine.

### **Licensed Indication**

Methadone tablets are licensed for the management of moderate to severe pain.

## **Drug/Form/Dose**

Methadone 5mg tablet

Methadone is approximately 2-4 times more potent than oral morphine, mainly due to the NMDA antagonising effect. 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.

## **Monitoring**

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](http://www.crediblemeds.org) following free registration.

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.

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/1478/naloxegol\\_201801\\_ps144\\_v0200.pdf?U\\_NLID=988456462201811516285](https://www.panmerseyapc.nhs.uk/media/1478/naloxegol_201801_ps144_v0200.pdf?U_NLID=988456462201811516285)) may be used.

## **How long will your patient be prescribed methadone?**

Patients with refractory neuropathic pain and opioid responsive chronic pain who required regular opioid rotation may remain on methadone indefinitely.

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.

## Contra-indications

- Hypersensitivity to the active substance or to any of the excipients
- Respiratory depression, obstructive airways disease
- In cases of 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
- Obstetric use is not recommended, because in labour the prolonged duration of action increases the risk of neonatal respiratory depression
- Methadone is not suitable for children and babies born to mothers receiving methadone may suffer withdrawal symptoms
- Individuals with QT prolongation, including congenital long QT syndrome (precautions see above)
- As with all opioid analgesics, methadone 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 ( $\geq 1/10$ ):** Nausea, vomiting

**Common ( $\geq 1/100$  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 for complete list

## Interactions 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.

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

### **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)).

### **General 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 specialist for advice if necessary.

### **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

### **Signposting**

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 at: <https://academic.oup.com/bjaed/article/16/3/102/2897756>