Therapeutics Advisory Group

Improving lives together
Norfolk and Waveney Integrated Care System

Prescribing Guidance Update

Methadone for use in pain management on advice from The Pain Management Service

November 2023 version 3.1

Norfolk and Waveney TAG recommends the prescribing of Methadone for Pain Management as 'Prescribe on Advice', which means that it is suitable for prescribing in primary care following specialist advice from a Pain Management Service for the treatment of:

- refractory neuropathic pain,
- severe, iatrogenic opioid dependence patients
- patients with chronic pain response to doses of strong opioid

ADVICE - Specialist advice required from primary or secondary care clinician with relevant expertise prior to primary care initiation.

Key Message

Patients will have been assessed by a specialist Pain Management Service and full holistic assessment of their pain completed. Their suitability for methadone prescribing will have been assessed by a Pain Consultant or experienced independent non-medical prescriber in 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 who require a stabilisation phase prior to rotation to a different opioid or preferably 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

Introduction

- Your patient has been identified as being suitable to receive methadone in accordance with the indications detailed above. 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.
- This document should be considered alongside the NHS Norfolk and Waveney Integrated Care Board (ICB) Opioid Deprescribing Toolkit. Where possible, patients' opioid reduction should be supported using resources available in the Deprescribing Toolkit.
- 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, some of which include opioids as an option.

Drug, Form and Dose

- Methadone tablet 5mg / Methadone oral solution 1mg/1ml
- 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 and stabilised by the Pain Management Service.
- The normal dosage range for patients prescribed methadone from the pain clinic is 15-60mg per day.
- Methadone oral solution will be considered where patients are unable to take tablets and occasionally when patients are using methadone for opiate reduction. This allows for slower downward titration, with the intention of minimising opiate withdrawal symptoms.
- 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.

Monitoring recommendations

- Prior to the initiation of methadone, patients will require a baseline ECG and blood tests (U&Es and LFTs). This will be undertaken in primary care.
- Methadone can lead to QTc interval prolongation, it is therefore contra-indicated in patient with QT prolongation including congenital QT prolongation.
- A list of other drugs that prolong QT interval can be found at www.crediblemeds.org.

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 always considered. 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. Under the care of the pain specialist, they will then be switched/rotated to alternative opioids if opioid responsive, or weaned off opioids altogether.

Contraindications

- 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.
- It is not recommended 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.
- Please refer to the British National Formulary (BNF) or summary of product characteristics (SPC) for a complete list of contraindications

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
- 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 advised by the 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)
- Please refer to the British National Formulary (BNF) or summary of product characteristics (SPC) for a complete list of warnings and cautions, and seek advice from specialist if there are further concerns.

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 with benzodiazpines, if co-prescription is considered necessary, utilise the lowest effective dose for the shortest period of time – seeking 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. See Netformulary for formulary options.

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).

Prescribing Advice in Primary Care

- A full, individualised plan will be agreed with the patient and communicated with the GP before prescribing can commence in primary care.
- Patients will be reviewed by the Pain Management Service within 2-4 weeks of commencing on methadone and will be reviewed regularly at least annually until the methadone dose is considered stable or has been discontinued.
- 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.

Adapted from Prescribing Support document – Methadone tablets in pain management – produced by Pan Mersey APC. Accessed 14/8/2023 and 23/10/2023

Title	Primary Care Prescribing Guidance - Methadone for use in pain management
Description of policy	*To inform healthcare professionals*
Scope	*Norfolk and Waveney Integrated Care System*
Prepared by	Norfolk and Waveney ICB Medicines Optimisation Team
Impact Assessment (Equalities and Environmental)	*Please indicate impact assessment outcome:* *Positive impact* *Adverse impact - low - action plan completed as per guidance* *Adverse impact - medium - action plan completed as per guidance* *Adverse impact - high - action plan completed as per guidance* *No impact* ***No policy will be approved without a completed equality impact assessment***
Other relevant approved documents	
Evidence base / Legislation	Level of Evidence: *A. based on national research-based evidence and is considered best evidence* ***B. mix of national and local consensus*** *C. based on local good practice and consensus in the absence of national research based information.*
Dissemination	Is there any reason why any part of this document should not be available on the public web site? ☐ Yes / No ☒
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2.0	Updates by Jen Carroll, TAG Lead, NWICB	Updated following comments from pain team. To submit final version to TAG for discussion and approval	Nov 2023
3.0	Updates by Jen Carroll, TAG Lead, NWICB	Updated following comments from pain team. To submit final version to TAG for discussion and approval	Nov 2023
3.1	Updates by Marion Sully, Head of Interface and Formulary, NWICB	Commissioning recommedation box at top updated	Nov 2023 – agreed by TAG and D+TC. Ratified by Planned Care and Medicines Management working group