PAN MERSEY APC

NHS Pan Mersey Area Prescribing Committee

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
APC BOARD DATE: 28 NOV 2018

METHADONE tablets (Physeptone®)

AMBER

The Pan Mersey Area Prescribing Committee recommends the prescribing of methadone tablets (Physeptone®) in adults following initiation by a consultant in pain medicine in a tertiary centre

PATIENT RETAINED BY SPECIALIST

This statement does not apply to the prescribing of methadone in palliative care

The Pan Mersey Area Prescribing Committee recommends the prescribing of METHADONE tablets 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
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 a low dose of methadone.

Methadone is a synthetic opioid acting as an agonist at Mu and delta receptors, and has been shown to demonstrate N-methyl-D-aspartate (NMDA) receptor antagonism in animal models.[1] The tablets are licensed for the management of moderate to severe pain.[2] Following oral administration, methadone tablets have a high bioavailability (>80%)[2] compared to other oral opioids[1] and have a long elimination half-life. It is metabolised in the liver by the cytochrome P-450 system and does not produce active/toxic metabolites.[3] It is these properties that suggest methadone may have different efficacy and safety profiles compared to other opioids[1] and is a good option for chronic pain.[4] It is thought that activation of NMDA receptors can lead to development of neuropathic pain.[1] Methadone's antagonist properties make it an alternative choice in the treatment of neuropathic pain[3,4] especially in those who have had a positive response to oral ketamine, which is also an NMDA receptor antagonist.[5]

Patients taking high doses of opioids often have symptoms of opioid induced hyperalgesia that is managed by changing to an alternative opioid such as methadone to provide a stabilisation phase before weaning or rotation. Opioid rotation should be considered for patients on chronic opioid therapy that experience adverse effects or fail to achieve adequate benefit despite dose increases.[6] Due to incomplete cross-tolerance across opioids and individual variation in response to different opioids, rotation may improve benefit to harm ratio.[6] Methadone can be an option in these patients at doses lower than equivalent morphine doses.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

METHADONE tablets (Physeptone®)

EFFECTIVENESS	SAFETY
Methadone tablets are licensed for moderate to severe pain. It is an opioid receptor agonist and a NMDA receptor antagonist. A 2017 Cochrane review looked at 3 randomised, double-blinded studies comparing methadone with either placebo or other active treatment. These were the only relevant studies from a literature search of 1673 records. The studies included a total of 105 participants, 55 of which received oral methadone 10-80mg/day.[1] As these studies provide limited data in terms of participants and quality, the review concluded there was no good evidence to support or reject the use of methadone in neuropathic pain.[1] Further studies are needed.	Methadone tablets are contra-indicated in respiratory depression, obstructive airway disease, severe liver impairment, acute alcoholism, head injury, raised intracranial pressure, obstetrics and patients with QT prolongation.[2] Concurrent administration of methadone with other CNS depressants, MAOi and within 2 weeks of MAOi is contraindicated. Tolerance and dependence may occur. Cases of QT interval prolongation and torsades de pointes have occurred, particularly at high doses (>100mg/day).[2] The most common side effects are constipation, nausea and vomiting, fluid retention, euphoria and hallucinations, sedation, blurred vision, vertigo, fatigue, rash and sweating.[2] For full details refer to the summary of product characteristics. Tablets should not be stopped abruptly[7] due to risk of opioid abstinence symptoms (headache, myalgia, fatigue, irritability).
COST	**PATIENT FACTORS**
One-year cost at recommended doses: Methadone £63 - £187[8] Expected patient numbers: No more than 40 in the Pan Mersey area.	ECG monitoring is recommended prior to prescribing and at dose stabilisation in patients with recognised risk factors for QT prolongation or concomitant drug treatment with potential to cause QT prolongation.[2] Use with caution in elderly patients and patients with renal and hepatic impairment.[2]

PRESCRIBING INFORMATION

The normal dose range for patients prescribed methadone from tertiary centre pain clinics is 15-45mg per day. Best analgesic effect is usually achieved with dosing in three divided doses.[4]
Patients will have a baseline ECG and baseline U&Es and LFTs prior to initiation.
The pain clinic should be contacted if patients suffer from any adverse effects or if they wish to discontinue therapy. Telephone support will be given whilst awaiting clinic appointment.
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.

IMPLEMENTATION NOTES

Initial dosing, titration and stabilising of a maintenance dose will be achieved by the pain clinic (consultant or specialist nurse) before transfer of prescribing responsibilities to primary care, subject to agreement by the GP. Dose alterations will only occur after outpatient pain clinic review and will be communicated in writing using the template letter. Patients will be reviewed in the pain clinic monthly during initiation then yearly once stable. Further support is available via specialist nurses.

REFERENCES

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3. Rajan J, Scott-Warren J. The clinical use of methadone in cancer and chronic pain medicine. *BJA Education*. 2016, 16(3) 102-106
4. Lynch ME. A review of the use of methadone for the treatment of chronic noncancer pain. *Pain Res Manage*. 2005, 10(3) 133-144
5. Pai A, Heining M. Ketamine. *Continuing Education in Anaesthesia, Critical Care & Pain*. 2007, 7, 59-63
6. Chou R, Fanciullo GJ, Perry GF, Adler JA et al. Clinical guidelines for use of chronic opioid therapy in chronic noncancer pain. *The Journal of Pain*. 2009, 10(2), 113-130
7. Electronic British National Formulary – Methadone. Accessed on 21/8/18 at https://www.medicinescomplete.com/#/content/bnf/_632459504?hspl=methadone#content%2Fbnf%2F_632459504%23pot-treatmentCessation
8. Drug Tariff. August 2018. Accessed on 17/8/18 at https://www.nhsbsa.nhs.uk/sites/default/files/2018-07/Drug%20Tariff%20August%202018.pdf