Coventry & Warwickshire
Area Prescribing Committee
Resource Document
The APC approves this document as appropriate for use within the health economy by those clinicians, or group of clinicians, that choose to. This resource has not received the extensive scrutiny required for it to be designated as an APC clinical guideline.

Appendix 2: Methadone Induction - Illicit opiate (heroin) using patients

Commencement with opioid substitution therapy [OST] is not a criteria for admission in its own right. Accident and Emergency departments or assessment services would not routinely commence therapy. However patients who are physically dependent on opioids may need OST to relieve the distressing symptoms of opiate withdrawal whilst in hospital, and facilitate provision of their healthcare needs.

Opioid withdrawal typically starts 6 – 8 hours following cessation, peaking at 24 – 36 hours and lasting 5 – 7 days. Therefore consideration of starting OST should be considered for in-patients who are likely to be an in-patient for 12 hours or more, once admitted.

Where a stay in Accident and Emergency may exceed 12 hours, and the patient is not likely to be admitted consider prescribing short term dihydrocodeine oral up to 60 mg four times a day (unlicensed use) to limit short term withdrawal.

Opiate dependency identified → No → Do not prescribe

Yes ↓

Prescribing arrangements after discharge confirmed by community drugs service
(see Appendix 8 for contact details)
→ No → Short term in-patient use to prevent withdrawal and patient retention for duration of healthcare intervention may still be considered, **but OST will not be continued post discharge**

Yes ↓

Methadone Mixture SF 1mg/1ml Induction Procedure:
(SEE PRECAUTIONS AND INDICATIONS IN BOXES BELOW AND OVERLEAF)

If opiate withdrawal is apparent the dose of methadone is titrated against presenting physical symptoms.
Always clinically assess if patient appears intoxicated prior to administration of methadone.
Supervise all consumption

Day	**Typical dosing****. Morning dosing, minimises nocturnal overdose. PRN doses 2-4 hours later if initial dose not sufficient to relieve withdrawal
Day 1	5-10 mg PRN 2-4 hourly. Max 30 mg in 24 hours
Day 2	Day 1 total as a single dose + additional 5-10 mg PRN. Max 40mg in 24 hours
Day 3	Day 2 total as a single dose + additional 5-10 mg PRN. Max 50mg in 24 hours
Day 4	Day 3 total as a single dose + additional 5-10 mg PRN. Max 60mg in 24 hours
Day 5-7	Total dose no more than 30 mg above day 1's dose. Max 60 mg in 24 hours
Day >7	Once at steady state, once daily methadone should maintain the patient in an asymptomatic state for 24 hours. Dose adjustments require great care, rising in increments of 5 to 10 mg every 3 to 5 days (according to symptoms of withdrawal or sedation). Normal optimal doses typically 60-120 mg per day.

** Consider lower doses in those over 60 years, Recently using benzodiazepines or other sedating drugs (unless long term stable users on normal doses. Using sedating drugs (e.g. antipsychotics, sedating antidepressants), especially if newly started or on moderate to high doses. Respiratory disorders. Interacting medication that increases methadone levels (Consult BNF but includes fluconazole, voriconizole, ciprofloxacin, clarithromycin, fluoxetine, fluvoxamine, amitriptyline, quetiapine, sertraline, lidocaine or progesterone).
Note that some Interacting medication decreases methadone levels (Consult BNF but includes nevirapine and ritonavir (HIV medications), phenytoin, phenobarbital, carbamazepine, St John's Wort and cocaine). Seek advice.

Methadone Precautions
- Poly drug use – alcohol, benzodiazepines
- Respiratory insufficiency
- Severe hepatic dysfunction
- Renal impairment
- QTc elongation* see Appendix 5

Methadone Contraindications
- Acute respiratory depression
- Raised intracranial pressure
- Comatose patient

Methadone induction presents a potential risk of respiratory depression, and should be undertaken with care. The risk of death during methadone initiation is nearly seven times greater than that upon entering treatment. This is due to methadone's long half-life and accumulation.

See additional notes overleaf

Precautions in new patients

- Do not give in to undue pressure to prescribe immediately. Take time to assess the patient. Remember a patient who is experiencing withdrawal symptoms may not be able to co-operate fully with medical or surgical treatment.
- A patient suffering from abstinence withdrawal will present with objective and subjective withdrawal. For safety's sake rely more on objective signs of opioid withdrawal. see Appendix 1
- Poly-drug and alcohol misusers may develop multiple withdrawal syndromes and hospital doctors will need to differentiate these to prioritise treatment. Methadone may initially mask alcohol and benzodiazepine withdrawal symptoms.
- Exercise particular care in cases of respiratory disease, head injury and liver disease.
- It is important to be extremely careful when prescribing additional drugs such as sedatives. It may be necessary, in some cases, to contact the relevant pain control team for further advice on improving pain control.
- If a urine test is negative for opioids and there is no evidence of opiate withdrawal symptoms, the drug misuser is very unlikely to be physically dependent on opiates and should be reassessed in the light of this.
- It is not appropriate to offer OST to patients who do not meet the diagnostic criteria for opioid dependency.
- If there is doubt about the degree of dependence it is advisable and safer to withhold prescribing of substitute medication initially and observe the patient until the physical manifestations of opioid withdrawal are evident
- Methadone may be a risk factor for QT prolongation and torsade de pointes with a possible dose-dependent action.
- The MHRA recommends monitoring for patients on high dose methadone (>100 mg daily) and with other QT interval prolongation risk factors where appropriate.
- Patients should be fully informed of the reasons for the clinical assessment and involved in the decision making process for their treatment.
- Screening before commencing methadone treatment is not currently advocated but may be considered.
- Any QT prolongation needs full investigation, consideration of specialist referral, identification of options for QT risk factor modification as well as ongoing ECG monitoring.

The following responses are indicators of optimal dosing[11].

- Prevention of opioid withdrawal for 24 hours or longer, including both early subjective symptoms and objective signs typical of abstinence
- Elimination of drug hunger or craving.
- Blockade of euphoric effects of self-administered opioids (this is not a true blockade like that achieved with an antagonist such as naltrexone, but reflects cross-tolerance to other opioids so that the desired sensations are attenuated or eliminated when illicit or prescription opioids are self-administered). The increasing purity of heroin and the wide availability of highly potent prescription opioids have made it increasingly difficult to achieve complete blockade in patients through cross-tolerance; consequently, some patients require doses larger than 120 mg/d to achieve this effect.
- Tolerance to the sedative effects of methadone, so that the patient can function normally without impairment of perception or physical or emotional response.

Risk factors – avoid overdose

- Over 20% of all methadone deaths take place within two weeks of starting treatment.
- Risk of overdose is increased by low opioid tolerance, too high an initial dose, too rapid increases and concurrent use of other drugs, particularly alcohol, benzodiazepines and CNS depressants.
- Patients in whom the first dose fully suppresses withdrawal completely for a full 24 hours may experience symptoms of toxicity as tissue stores accumulate.
- Methadone patients should be informed of the 'increasing effects' until a steady state is achieved, so that they do not excessively 'top up' with street drugs.
- A number of factors can alter methadone plasma levels, including gastric emptying, pregnancy and liver metabolism, which can increase risk of overdose.
- Warn the patient and where possible family members, about signs of impending toxicity. The ratio between a maximum therapeutic dose and potentially fatal dose is narrow.
- Overdose is marked by decreased alertness/consciousness, apnoea, respiratory failure, hypoxia, leading to coma, seizures, hypotension and death [11].
- Symptoms of overmedication may include unusual feelings of excess energy, with or without euphoria[11].

Vomited methadone doses[11]

Vomited methadone doses should not be replaced in full or part unless emesis has been directly observed.
The colour and volume of emesis should be noted. If only small amounts of mucus the dose does not need replacing.
Repeated dose replacements pose the risk of unexpected overdose, so great discretion is required.

Suggestions for replacing vomited doses, use discretion, include[11]	
Emesis occurs after xx minutes of dosing	Consider replacing xx % of full dose
< 15 minutes	50 to 75% (only 50% if on high doses near 120 mg)
15 – 30 minutes	25 to 50%
> 30 minutes	Do not replace dose