MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Management of Opioid Substitution Therapy (OST) for people with an opioid addiction

Opioid dependence is a chronic disease with relapse rates greater than 90% in untreated people. In 2018-19 around 9% of adults aged 16-59 years had taken an illicit drug with 3.5% taking Class A drugs.

Opioid dependence develops after a period of regular use of opioids. The time taken for dependence to occur varies between individuals.

The mortality risk of people dependent on heroin is approximately 12 times greater than the general population. Co-existing mental health problems or cognitive impairment are associated with a poorer prognosis and effective management requires medical, social and psychological treatment provided by a multidisciplinary team.

Complications of opioid dependence include overdose, infection (including hepatitis B and C, HIV, TB), DVT and PEs, together with complex social and psychological problems.

Opioid substitution therapy (OST)

Patients who are physically dependent on opioids may require substitute (replacement) prescribing to:

- Relieve the distressing symptoms of opioid withdrawal
- Minimise/stop injecting behaviour and therefore promote harm reduction
- Minimise/stop the use of illicit opioids
- Encourage positive treatment outcomes

Opioid withdrawal is not a life-threatening condition whereas opioid toxicity is. Inappropriate prescribing of opioids for withdrawal prevention can be potentially fatal. Withdrawal can be both distressing and uncomfortable for patients and may increase the risk of self-discharge. Careful consideration of this patient group is necessary as there is an increased risk of medication error and patient harm when a patient is transferred from one sector of care to another.

In England, OST (usually methadone and buprenorphine) is routinely prescribed by community addiction services and some GPs on an FP10MDA prescription in accordance with the Misuse of Drugs Regulations 2001. Most prescriptions are for supervised daily consumptions to minimise the risk of overdose and diversion (consumed by another individual). Daily instalments can only be authorised for up to 14 days and supplies can only be made on the date specified on the prescription.

Oxfordshire Community Addiction Services are provided by Turning Point Roads to Recovery. There are 4 Hubs based in Oxford, Banbury, Witney and Didcot. The service should be contacted if any patients currently registered with them are admitted or if a newly initiated Oxfordshire patient is started on OST in hospital. They can also be contacted for advice on patient management.

To contact Oxfordshire Turning Point: either phone directly Oxford hub (01865 261690); Banbury hub (01295 225544); Didcot hub (01235 513360); Witney hub (01993 849405) or email turningpoint.oxon@nhs.net This e-mail address can be used to communicate clinical information. Emails are reviewed regularly and directed to the relevant TP hub or GP shared care practice.

Turning Point will contact the patient directly following referral

Patients can go to open access clinics without a prior appointment (Oxford hub Mon –Thurs 12.30 to 14.00: For other hubs see website for timetable).

A limited number of Oxfordshire GPs still provide substitution therapy directly - liaise with GP surgery for these patients.

This MIL highlights the procedure for

- **recreational (illicit) opioid addiction (refer to pain team if medical use of prescribed opioids)**
- **assessing and/or verifying doses of opioid substitution therapy in patients admitted to OUH**
- **appropriate prescribing during admission**
- **ensuring continuity of supply (if needed) on discharge for patients already on opioid substitution therapy *or* requiring opioid substitution therapy**
- **liaison with community addiction services**

Other OUH guidance for substance misuse
Advice regarding the ***management of acute pain relief in patients with opioid dependence can be found at*** The Management of Acute Pain in the Opioid Addicted Patient guideline

And also on the Oxford PainGuide on the MicroGuide app:
Microguide from an internet browser
Microguide from App store

Advice regarding the management of acute alcohol withdrawal can be found at Acute Alcohol Withdrawal MIL

Advice regarding nicotine replacement therapy for smoking cessation can be found at Smoking Cessation MIL

Methadone
Methadone hydrochloride is a long-acting synthetic opioid agonist. It is usually administered once a day as an oral solution (1mg/ml) for opioid dependence. A typical maintenance daily dose is 60-120mg.

Patients with a long history of opioid misuse, those who typically abuse a variety of sedative drugs and alcohol, and those who experience anxiety during withdrawal of opioids often prefer methadone as it has a more pronounced sedative effect.

Due to its long half-life, plasma concentrations steadily rise during initial treatment even if the patient remains on the same daily dose. It takes 3-10 days to reach steady state and a dose tolerated on the first day of treatment may become a toxic dose on the third day as cumulative toxicity develops. Titration to the optimal dose maintenance treatment may take several weeks.

Methadone is extensively metabolised by the liver via the cytochrome P450 system and blood levels can be affected by the concurrent use of drugs that either inhibit or induce liver enzymes.
Drugs that may **increase** blood levels of methadone include SSRIs, broad spectrum anti-fungals, macrolides, ciprofloxacin.

Drugs that may **decrease** blood levels of methadone include anti-epileptics, anti-tuberculosis medication.

Concurrent use of sedatives e.g. benzodiazepines, alcohol, antidepressants can increase the risk of respiratory depression and overdose.

There is an increased risk of ventricular arrhythmias when methadone is given with drugs known to prolong the QT interval, such as some antibiotics and benzodiazepines or if there are electrolyte imbalances - hypokalaemia or hypomagnesemia; or hepatic dysfunction.

Buprenorphine
Buprenorphine is a semi-synthetic opioid partial agonist. Formulations licenced for opioid dependence and on the OUH formulary are generic/Subutex/Suboxone sublingual tablets.

Espranor® oral lyophillisate (wafers which dissolve on the tongue), buprenorphine/naloxone combination tablet or Buvidal ®prolonged-release injection are also licenced for opioid dependence but are non-formulary within OUH.

These formulations are not interchangeable different buprenorphine products have different bioavailability and therefore the dose in mg can differ between products. Sublingual tablets must not be crushed. It is important to verify brand /formulation before prescribing. A typical maintenance daily dose is 12-16mg.

Buprenorphine is less sedating than methadone and therefore may be preferable in some patients. It also causes less respiratory depression due to its ceiling effect and therefore has a lower overdose potential.

As buprenorphine is a partial agonist it can displace opioids still in someone's system and precipitate an acute withdrawal syndrome. If initiating someone on buprenorphine they need to display objective signs of withdrawal before administration of buprenorphine to minimise this

risk. Symptoms develop within one hour, peaking at six hours.

If other opioids are likely to be needed for analgesia during the hospital admission, buprenorphine can be continued by dividing it into 2 or 3 smaller doses (i.e. bd or tds), providing the same total daily buprenorphine dose.

Buprenorphine is also extensively metabolised in the liver via the cytochrome P450 system but has fewer drug interactions than methadone.

NICE recommends that methadone should be used first line if both drugs are equally suitable. For maintenance doses, 50-80mg methadone is approximately equivalent to 12-16mg buprenorphine in terms of effectiveness**.**

Whilst methadone and buprenorphine are the most common treatments used for opioid dependence, occasionally other drugs such as morphine sulphate, dihydrocodeine and diamorphine are used.

Assessment on admission

Before prescribing any substitute medication, opioid dependence should first be confirmed by history and examination, including physical examination and by toxicology screening via urine or oral fluid swabs if available. The patient should also carefully be assessed in terms of possible current intoxication, and a history of recent drug use should be taken. Particular care should be given to use of any other sedative drugs (i.e. alcohol, benzos, GHB/GBL). There should be **objective** signs of opioid withdrawal before starting someone on a new OST, but not if you are continuing an existing OST prescription and have verified the dose and time of last administration.

All patients with an opioid addiction must be assessed for withdrawal using the Clinical Opioid Withdrawal Scale (COWS) accessed via www.mdcalc.com/cows-score-for-opiate-withdrawal. Symptoms of acute withdrawal from opioids include watering eyes, runny nose, yawning, sneezing, cool and clammy skin, dilated pupils, abdominal cramps, nausea, vomiting, diarrhoea, tremor, anxiety, irritability and hypertension. Symptoms of heroin withdrawal occur at 8 hours, with a peak at 36-72 hours. Withdrawal from methadone and buprenorphine occurs later, with longer lasting symptoms.

Treatment

Already on substitution therapy in community

If a person with an opioid addiction is admitted to hospital and known to be registered with community addiction treatment services and/or is being treated with substitution therapy (usually methadone or buprenorphine) by a GP, **the usual prescription for opioid replacement therapy should be given** provided there are no clinical contra-indications and the dose is verified as per the criteria below. A dose should be given within 24 hours of admission while the person remains an in-patient to avoid opioid withdrawal symptoms. Opioid withdrawal is an unpleasant state and is worsened by anxiety, often leading to challenging behaviour if there is a delay in its provision.

Verifying existing OST prescriptions

Addiction services and/or the GP and the community pharmacy must be contacted as soon as possible and certainly within 72 hours. This is to notify them of admission, to confirm current prescription details i.e. dose and formulation of OST, time and date of the last supply/administration and the total daily dose dispensed, and to ensure patient does not attempt to obtain supplies from both community and hospital. **Prescribers should not rely solely on the information given by the patient.** All information must be recorded in the medicines' reconciliation section on EPR together with the name and position of the person the information was obtained from.

There are some clinical situations where it may be necessary to stop, change or amend the dose of OST i.e.

- Dose cannot be verified

- Three or more consecutive days of treatment have been missed (e.g. after diarrhoea and vomiting)
- Intoxication (do not give)
- Decompensated liver disease (contact hepatology)

Dose cannot be verified
Do not rely on information from the patient. If the dose cannot be verified, prescribe as for patients not established on substitution therapy.

Missed doses of OST
Patients who miss 3 days or more of their regular prescribed dose of methadone are at risk of toxicity because of loss of tolerance. **Prescribe a maximum of 30mg (30ml) once daily dose of methadone 1mg/ml solution if usual dose is unconfirmed.** A lower dose should be considered if there is underlying hepatic decompensation.

Patient requires another opioid for pain relief
Refer to management of acute pain relief in patients with opioid dependence (link above) and/or liaise with OUH pain team.

Intoxication
Signs and symptoms of opioid intoxication include euphoria, constricted pupils, drowsiness, slurred speech, poor concentration/attention. If present, OST should not be given. Naloxone 400mcg as a single dose should be given if there is respiratory depression or reduced GCS.

Vomiting post OST dose
Vomiting after a dose of buprenorphine will not reduce its effect due to the way the formulations are absorbed.

If vomiting occurs more than 20 minutes after a dose of methadone, a replacement dose should not be given. If vomiting occurs within 20 minutes (and only if witnessed), consider giving 50% of the original prescribed dose.

OST in pregnancy and breastfeeding
Acute withdrawal of opioids should be avoided in pregnancy as it increases foetal mortality. OST is recommended as it carries a lower risk to the foetus than continued use of illicit drugs. Established OST should be continued as normal. Initiation of new OST should not be started without advice from community addiction services.

Doses of OST should be kept as low as possible in breastfeeding mothers. Babies should be monitored closely for signs of increased sedation, limpness or difficulties in breathing. If the mother has been on long-term, stable dose OST, she should be encouraged to breastfeed as the small doses of transferred opioid will help mitigate neonatal abstinence syndrome.

Treatment

Not established on substitution therapy in community

For those persons who are **not registered** with Community Addiction Treatment services and/or receiving OST via a GP but are showing objective signs of opioid withdrawal, methadone can be prescribed to alleviate withdrawals, once this has been discussed and agreed with the patient. Patients need to understand that they must engage with Turning Point (or Gp if outside Oxfordshire) on discharge to enable continuation of OST and to avoid experiencing withdrawal symptoms as a prescription will not be provided by the hospital.

The recommended starting dose is 20 -30mg (20-30ml) once daily of methadone 1mg/ml solution. Due to the time taken to reach steady state a dose increase should not occur within the first 3 days of initiation (unless advised by a senior doctor/addiction specialist). It is prudent to not consider more than two 10mg dose increases within a 7 day period. Advice on dose increases should be sought from an addiction specialist. Observe patient for signs of intoxication and do not increase if these occur.

At discharge

TTOs for opioid substitution therapy should only be given in **exceptional circumstances** i.e. when it is not possible to arrange a community pharmacy supply to start on discharge. In this case a **maximum of 48 hours** of methadone or buprenorphine can be prescribed and supplied.

The GP and/or Addiction Service and the community pharmacy must be informed about the patient's discharge including the dose and time administered in hospital and any supplies

made at discharge. This is to ensure continuity of supply (valid prescription available) and to prevent any duplication of the prescription.

For ALL patients newly initiated on OST in hospital, they must be referred to Turning Point (or their GP if they live outside Oxfordshire) for follow up.

Patients should be warned of the risk of accidental drug overdose on leaving hospital if they combine opiates with OST.

General prescribing information

Patients may request other drugs which may be abused (e.g. benzodiazepines). Do not prescribe these without checking whether the GP usually prescribes them.

Benzodiazepines may be prescribed if medically indicated (e.g. for alcohol withdrawal) but keep the duration of treatment to a minimum and do not prescribe a discharge supply. Avoid prescribing benzodiazepines prn.

DO NOT prescribe methadone dose as number of millilitres as there are two concentrations. Always prescribe in milligrams and specify the concentration (1mg/1ml)

References

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- **Wesson DR & Ling W (2003). The Clinical opiate Withdrawal scale (COWS). J Psychoactive Drugs. 35(2) 253-9.**
- **Drug Misuse and Dependence – Guidelines on Clinical Management. Department of Health. 2017 available from www.gov.uk**
- **Summary of Product characteristics available form www.medicines.org.uk**
- **Guidance for the use of substitute prescribing in the treatment of opioid dependence in primary care. Royal college of General Practitioners 2011. Available from rcgp.org.uk**

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