Substitute Prescribing for Opioid Dependence

This article summarises the guidance on substitute prescribing for opioid dependence from the drug misuse and dependence guidelines jointly produced by the Department of Health, the Scottish Government, the Welsh Assembly Government and the Northern Ireland Executive. The guidelines were last updated in September 2007.[1]

Further information has been added from the guidance on the pharmacological management of substance abuse released by the British Association for Psychopharmacology, published in 2012.[2]

This article should be read in conjunction with the separate overview article Drug Misuse and Dependence: UK Guidelines.

Methadone and buprenorphine are both approved by the National Institute for Health and Clinical Excellence (NICE) for the treatment and prevention of withdrawals from opioids and for maintenance programmes.[3]

Aims and benefits of treatment

The aims of prescribing for opioid dependence are to:

- Reduce or prevent withdrawal symptoms.
- Provide an opportunity to stabilise drug intake and lifestyle while breaking with illicit drug use and associated unhealthy risk behaviours.
- Promote a process of change in drug taking and risk behaviour.
- Help to maintain contact and offer an opportunity to work with the patient.

Drug treatment using substitute prescribing helps to protect against a number of harms including:

- Risk of overdose
- Blood-borne infections
- Risk of offending

Before starting treatment

Before deciding to prescribe, a full assessment should be undertaken (see separate article Assessment of Drug Dependence) and a care or treatment plan should be drawn up with the patient.

The responsibility for prescribing lies with the person signing the prescription.

Consider substitute medication only if:

- Opiates are being taken on a regular basis (usually daily).
- There is evidence of current dependence.
- Patients are motivated to change some aspects of their drug misuse.
- Assessment has shown the need for treatment (eg, history, examination, drug testing).
- You are satisfied that the patient will comply with the prescribing regimen.
- The patient is not receiving a prescription from another clinician.

The patient must be fully informed before starting treatment, including:
• Understanding the rationale for treatment.
• Understanding the expectations of them (e.g., daily attendance, supervised consumption).
• Knowledge of the risks during induction.
• Knowledge of the dangers of concomitant use of central nervous system (CNS) depressants.
• Understanding the importance of keeping medication away from children.

See separate article Controlled Drugs, which includes details on their prescribing and on record keeping.

The GP's role[4]

In 2011, the Royal College of General Practitioners produced guidance for the use of substitute prescribing in the treatment of opioid dependence in primary care. The main points are as follows:

- All GPs have a duty to provide basic medical services to people who are dependent on opioids and they should screen patients for drug misuse.
- If detoxification and/or substitute prescribing are requested, after an initial assessment, GPs can refer to local specialist community drug services and there are usually locally agreed shared care guidelines. A care plan between the drug misuser and the service provider can then be drawn up.
- A GP may have a special clinical interest in the management of substance misuse in primary care and may be able to take more responsibility in the treatment of patients, particularly in complex cases.
- A multidisciplinary approach to care is needed.
- Strict practice policies surrounding the care of drug misusers are advised.
- The UK guidelines for drug misuse and dependence should be followed by all GPs.

Methadone or buprenorphine?

Consider the following factors when choosing which opiate substitute to use:

- Patient experience and preference.
- Prescriber’s experience with the medications.
- Safety, e.g., overdose risk (buprenorphine may have a lower risk of overdose - see below under the ‘Buprenorphine’ heading).
- Level of current opioid use.
- Any drug interactions if taking other drugs or medication.
- According to evidence, methadone is more likely to retain patients in treatment.
- People dependent on codeine preparations may benefit from buprenorphine.

NICE recommends that, if both drugs are equally suitable, methadone should be prescribed as first choice.[3]

Induction on to methadone and buprenorphine treatment

It can take 2-4 weeks, or more, to achieve an optimal dose with methadone, less with buprenorphine.

Induction should be monitored by a doctor or trained nurse.[3] The aim is to achieve a dose that will mean that patients experience minimal intoxication and minimal withdrawal symptoms.

Methadone

There is a risk of overdose during induction on methadone, highest during the first two weeks. This risk is increased if:

- There is low opioid tolerance.
- Other CNS depressants, including alcohol and benzodiazepines, are also used.
- The initial dose is too high.
- The increases in dose are too rapid.
- There is slow methadone clearance (a dose tolerated on day 1 may become toxic on day 3).

The risk of toxicity can be reduced by:
• Careful assessment beforehand.
• Identification of high-risk patients.
• Avoiding too high starting doses.
• Avoiding rapid dose increases.
• Frequent monitoring during induction.
• Supervised consumption.
• Explaining early signs of overdose to patient and carers.

Other considerations:

- Some antidepressants may interact with methadone (particularly tricyclics and fluvoxamine).
- Antipsychotics may increase the risk of toxicity and potentiate the hypotensive and sedative effects of methadone.
- Extreme caution and expert opinion are needed before starting methadone in end-stage liver disease.
- There may be interaction with HIV medications. Discuss with the specialist prescribing these.

Methadone dosing (NB: these doses apply to patients with normal body weight, body mass index, liver and renal function):

- Methadone should be prescribed as 1 mg in 1 ml oral solution.
- The initial daily dose is usually 10-30 mg but may be 10-20 mg if tolerance is low or uncertain.
- Experienced and competent clinicians with patients who are tolerant and heavily dependent may use up to 40 mg daily as a first dose.
- A supplementary dose on the same day may be considered if there is evidence of persistent opioid withdrawal.
- Follow up the patient frequently at the beginning of treatment.
- If dose adjustment is needed in the first week, do not increase by more than 5 to 10 mg on any one day. A total weekly increase should not usually exceed 30 mg above the starting day's dose.
- Doses can then be increased incrementally after the first week, up to a total of 60-120 mg a day (occasionally more is needed).
- Leave a few days between each dose increase.
- It may take several weeks to reach the desired dose so that the patient feels comfortable and is no longer using heroin.

Buprenorphine

- The risk of overdose in the induction phase is less with buprenorphine. This is because, at low doses, it works as a potent opioid agonist but, at increasing doses, it has mixed agonist-antagonist properties. This means that increasing doses do not produce more intense opioid effects. However, there is still a risk of overdose in people with low opioid tolerance and those who are also using CNS depressants such as alcohol.
- Withdrawal may also be precipitated if insufficient time is left between the last use of an opioid and the administration of buprenorphine (see below).
- There is more of a risk that buprenorphine can be misused by injection or intranasally.
- Extreme caution and expert opinion are needed before starting buprenorphine in end-stage liver disease.
- There may be interaction with HIV medications. Discuss with the specialist prescribing these.

Buprenorphine dosing (NB: these doses apply to patients with normal body weight, body mass index, liver and renal function):

- One suggested regime is to start at a low dose of 4 mg on day 1 and increase to 8-16 mg on day 2 and thereafter.
- 12-16 mg daily is the usual dose needed but some patients may need up to 32 mg.
- Regular assessment and review should be undertaken.
- When buprenorphine is given to an opiate-dependent person who still has circulating opioid agonist drugs present, precipitated withdrawal can occur. This is because the buprenorphine inhibits the agonist. To avoid this:
  - Wait until there are signs of withdrawal before the first dose is given.
  - If this is not possible, wait until 6-12 hours after the last use of heroin (or other short-acting opioid) or 24-48 hours after the last dose of methadone. If patients are taking >30 mg methadone daily, they are less likely to tolerate a transfer to buprenorphine.
Buprenorphine-naloxone

The opioid antagonist naloxone has recently become available in a combined sublingual tablet with buprenorphine (brand name Suboxone®). The idea behind this preparation is that it discourages misuse. If the tablet is crushed and injected, the naloxone has high bioavailability and is likely to precipitate withdrawal in an opioid-dependent person. The naloxone has low bioavailability when the tablet is taken sublingually. The tablet comes in two strengths - 2 mg buprenorphine/500 micrograms naloxone and 8 mg buprenorphine/2 mg naloxone. Expressed as buprenorphine, the dose is 2-4 mg daily initially with further increases according to patient response within the framework of the regimes recommended in the British National Formulary (BNF).

One study showed that both methadone and buprenorphine-naloxone combination were effective in reducing heroin use. In this, albeit small study, buprenorphine-naloxone combination yielded a larger magnitude reduction in heroin use days than methadone. [6] The BAP guidelines state that some specialists prefer the combination because of its better tolerability, adverse event profile and easier dose reduction to abstinence. [2]

The role of the pharmacist

- There should be a good relationship between the prescriber and the pharmacist issuing the prescription.
- The pharmacist must have capacity to take on a new patient, including supervised consumption if needed, and the patient should be introduced to them.
- The pharmacist should be able to feed back to the prescriber if there is failure to comply with treatment, or if they have concerns about the patient.

Supervised consumption

- Supervised consumption is usually by a community pharmacist. The person supervising consumption must be competent.
- The patient's privacy and dignity must be considered.
- Buprenorphine is less easy to supervise, as it is taken sublingually.
- The usual situation is that supervised consumption is carried out for three months. However, this can vary according to the patient's circumstances and level of compliance.
- Review the need for supervised consumption regularly.
- There may be local guidelines and protocols surrounding this.
- It can be useful to re-introduce supervised consumption if treatment is failing.
- Relaxation of supervised consumption can act as an incentive if progress is being made.
- The prescriber needs to be sure that compliance will be maintained before supervised consumption ceases.
- Do not stop supervised consumption if:
  - A stable dose has not been reached.
  - There is continued and unstable drug misuse, including alcohol.
  - There is significant unstable psychiatric illness or risk of self harm.
  - There are concerns about the safety of storage of medication at home where children are present.
  - There is concern that the medicine may be diverted or used inappropriately.

Reviewing treatment

Progress should be reviewed regularly, looking at response to treatment in the following areas:

- Drug and alcohol misuse.
- Physical and mental health.
- Social functioning.
- Offending and criminal justice.

Repeated risk assessment needs to be undertaken and any risks should be highlighted to the patient.

Drug testing can provide evidence of progress and can be built into the care programme.
What to do if treatment is failing

Aim to increase the intensity of the programme.

- Ensure medication is at an optimal level.
- Consider changing to a different substitute medication.
- Increase keyworking.
- Increase psychosocial interventions.
- Increase supervised consumption.
- If a relapse has occurred, try to discover what has triggered it and help to develop techniques to avoid this in the future.

If a patient has missed their daily pick-up of opioid for three days, they may have lost their tolerance to the drug and may be at risk of overdose when the next dose is taken. This is more likely with methadone than with buprenorphine. There should be a system in place so that the pharmacist alerts the prescriber if this has happened. This should instigate an urgent review of the patient by the prescriber before the pharmacist can issue the next dose.

Decisions to exclude a patient from a drug treatment service should not be taken lightly. It can put them at increased risk of overdose, offending and contracting a blood-borne infection. It may also increase risk to any dependent children or vulnerable adults in the home. Consideration should be taken about offering treatment at another local service or setting.

Maintenance prescribing for opioid dependence

- Some people are able to achieve abstinence quickly; others need long-term support and long-term opioid substitute prescribing. In some people it may take months or years for all illicit drug and alcohol misuse to stop.
- Maintenance is more appropriate in adults with a long history of drug dependence than in young people. The incidence of opioid use in young people is on the rise but the history of dependence is usually short so the aim should be substitution followed by detoxification and abstinence. [2]
- This needs regular review and needs to be part of a social and psychological support programme.
- Local protocols and guidelines should be drawn up.
- Patients usually need to be seen every two weeks initially and, if stable, may then be seen monthly. Sometimes they can be seen less frequently if very stable.
- Supervised consumption is usually needed and NICE recommends that methadone and buprenorphine should be administered daily, under supervision, for at least the first three months. [3]
- Random drug testing may be helpful, at least twice a year.
- Review should cover the same areas as outlined in the 'Reviewing treatment' section above.
- NICE recommends that methadone and buprenorphine may both be used in maintenance treatment and, if both drugs are equally suitable, methadone should be used as first choice. [3]

Methadone

- Dose induction and stabilisation are carried out first.
- Patients are usually maintained on methadone doses between 60 mg and 120 mg daily.
- Supervised consumption is usually needed.
- Reassessment is required if methadone is missed for three days or more. If this is five days or more, assessment of tolerance is needed before methadone is inducted again.

Buprenorphine

- Dose induction and stabilisation is carried out first.
- Daily doses between 12 mg and 16 mg (and may be up to 32 mg) are usually used for long-term prescribing.
- Alternate day dosing may suit some patients.
- Reassessment is required if buprenorphine is missed for three days or more. The dose may need to be reduced and re-titrated.
- If this is five days or more, assessment of opiate misuse is needed before buprenorphine is inducted again. This helps to avoid precipitating withdrawal.

Other oral opioids
Oral opioids other than methadone and buprenorphine, such as dihydrocodeine and slow-release oral morphine preparations, are not licensed in the UK for the treatment of opiate dependence. They should not normally be used in the community. They are occasionally used in some circumstances by specialist clinicians.

**Injectable opioid treatment** [7]
- This is less established and less accepted as a form of maintenance treatment, although some long-term patients are still receiving injectable opioids under what is referred to as the 'British System'.
- It is also known as heroin-assisted treatment (HAT).
- It is a second-line treatment that should only be considered, after specialist assessment, if methadone and buprenorphine treatment are not suitable or have not had the expected benefit.
- A Cochrane review found that oral therapy is superior to injectable treatment in reducing drug-related behaviours with a high risk of HIV transmission (but not sexual risk taking). [2]
- A new form of injectable opioid treatment is being introduced in some areas of the UK, modelled on Swiss and Dutch supervised injectable maintenance clinics, for patients who have failed to benefit from normal treatments.
- Smuggling and overdosing are the main concerns of staff working at HAT centres.

**Further reading & references**
- Drug misuse: opioid detoxification; NICE Clinical Guideline (July 2007)
- Drug misuse: psychosocial interventions; NICE Clinical Guideline (July 2007)

2. Evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP: British Association for Psychopharmacology (May 2012)
3. Methadone and buprenorphine for the management of opioid dependence; NICE Technology Appraisal Guidance, January 2007

**Disclaimer:** This article is for information only and should not be used for the diagnosis or treatment of medical conditions. EMIS has used all reasonable care in compiling the information but make no warranty as to its accuracy. Consult a doctor or other health care professional for diagnosis and treatment of medical conditions. For details see our [conditions](#).
Ask your doctor about Patient Access

- Book appointments
- Order repeat prescriptions
- View your medical record
- Create a personal health record (iOS only)

Simple, quick and convenient. Visit patient.info/patient-access or search ‘Patient Access’

© EMIS Group plc - all rights reserved.

Like us.
it’s good for you!

Like us on Facebook
fb.com/patient