



Guidance on Drug (Substance) Misuse Management in the Adult Hospital Settings

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Why do we need this guidance?

“A 22-year-old heroin user was admitted to hospital for hand surgery following a fight. Post-operatively he became agitated, complaining of pain and requesting analgesia. When told his next scheduled dose of analgesia was not for several hours, he swore at the nurse and threatened her. The situation was only defused when the addictions nurse spoke with the patient, and arranged for methadone to be given. Once the patient was feeling better, the addictions nurse suggested to the patient that it would be diplomatic to apologise to the nurse he had abused. He agreed, and on a regular dose of methadone plus analgesia as needed, his remaining days in hospital were uneventful.”

This is an example of a situation that is all too common - a heroin user in hospital, withdrawing, and in pain, coming into conflict with nursing staff. Such situations are best prevented, and the key to prevention is anticipation, recognition and management of opioid withdrawal (and, indeed withdrawal from any drugs). This vignette highlights two important issues. Firstly, established opioid tolerance in current drug users means that doses of opioids required to control pain are higher than in non-tolerant individuals.

Secondly, withdrawal states - and pain - are associated with diminished control of behaviour. After surgery, or during acute illnesses, patients experience a stress response, characterised by a range of hormonal changes. Withdrawal states are also characterised by changes in neurotransmitters, including sympathetic nervous system over-activity and activation of the N-methyl-D-aspartate (NMDA) system. These changes contribute to stress and anxiety, which causes patients to be more fearful and distressed by pain. Sympathetic nervous system activation increases the post-operative stress response, and activation of the NMDA system intensifies pain. Good management of withdrawal reduces physical and emotional distress, and makes pain management easier.

It is hoped this guidance will support substance misusers to access acute care needs, whether physical or mental, preventing unintentional drug withdrawal (with potential adverse consequences, such as the risk that patients will prematurely self-discharge, or self-medicate with drugs of uncertain strength while unwell in hospital, or worse still self-discharge mid-medical treatment and suffer undue morbidity or mortality due to failed medical treatment and/or subsequent illicit drug overdose.

In individuals who are severely unwell, the priority in treatment is to ensure compliance with medical treatment. A secondary objective is to engage patients in treatment of their addiction post-hospital discharge.

The principles of treatment are:

- Minimise opioid withdrawal through administration of opioid substitution therapy
- In addition, administer other analgesia (oral, intramuscular or subcutaneous morphine depending on the severity of pain) titrated against analgesic response and against over-sedation.
- Over the duration of hospitalisation, switch injected analgesia to methadone or buprenorphine until at discharge the patient is on a daily dose of methadone or buprenorphine - with, if possible, arrangements made for treatment to be continued post-discharge.

The decision to prescribe Opioid Substitution Therapy [OST] should usually be made in discussion with the community drugs service ([see Appendix 8 for contact details](#)). In circumstances when these services are unavailable, e.g. out-of-hours, OST should be considered in accordance with these guidelines. This is particularly important when a patient is suffering withdrawal symptomatology which may mean their clinical condition is adversely affected or that they are unwilling or unlikely to remain in the healthcare setting and thus not receive the health input they need.

1. Introduction

These guidelines are intended as a resource in the management of patients with drug misuse issues, who are presenting and requiring full admission to an in-patient setting. For Accident & Emergency / Assessment Services [see section 6.8](#).

These guidelines particularly support substance misusers to access acute healthcare needs, preventing unintentional drug withdrawal (with potential adverse consequences, such as the risk that patients will prematurely self-discharge, or self-medicate with drugs of uncertain strength while unwell in hospital, or worse still self-discharge mid-medical treatment and suffer undue morbidity or mortality due to failed medical treatment and/or subsequent illicit drug overdose. [see Appendices 1-8 for quick access guidelines and contact details](#).

2. Duties and responsibilities

2.1. Doctors' responsibilities

Drug misusers have the same entitlement as other patients to the services provided by the National Health Service and it is the responsibility of all Doctors to provide care for both general health needs and drug-related problems, whether or not the patient is ready to withdraw from drugs¹.

All Doctors must provide medical care to a standard, which could be reasonably, expected of a clinician in their position. The focus for the clinician treating a drug misuser is on the patients themselves. However, the impact of their drug misuse on other individuals – especially dependent children – and on communities should be taken into consideration².

2.2. Prescribers' responsibilities (Doctor or Non-Medical Prescriber)

It is the responsibility of the prescriber to identify the purpose of prescribing, and ensure adequate assessment has been carried out prior to prescribing. [see section 5](#)

For continuity of community prescribing, confirmation of drug, dose and time last taken should be established and documented, and appropriate discharge arrangements for on-going prescription and supply should be put in place.

Where initiation of treatment is the goal, attention must be paid to the aim of treatment, namely;

- Stabilisation of the patient to allow provision of other health interventions
- Harm minimisation, whilst an in-patient and hopefully post discharge
- Detoxification, (used in exceptional circumstances due to high risks post-detoxification)

Wherever possible discharge to take home supplies should be avoided. If and when any discharge supplies of methadone or buprenorphine are prescribed this must only be done following liaison with the relevant community drug service ([see Appendix 8](#)), and confirmation/documentation of a plan for continuation of treatment upon discharge.

2.3. Nurses' responsibilities

It is the responsibility of nurses to ensure the safe administration of medicines as per local Trust medicines policy.

2.4. Pharmacy and medicines management responsibilities

Ensure that if and when any discharge supplies of methadone or buprenorphine are dispensed that assurance is gained that they have been prescribed following liaison with the community drug service ([see Appendix 8](#)), and that there is a plan for continuation of treatment upon discharge, including issuing the minimum length of supply to minimise risk.

2.5. Patient responsibilities

It is the patient's responsibility to provide details of any current community drug treatment and hand over any medications for safe storage.

All patients are expected to abstain from illicit drug use while in hospital.

2.6. Community Drugs Service responsibilities

The community drugs service provides telephone support for queries and advice in working hours. [see Appendix 8 for contact details](#). They also liaise with community teams/GPs, and community pharmacy to ensure continuity of treatment post discharge.

3. General guidance

3.1. Overview

Problematic drug users experience increased rates of morbidity and mortality due to their substance misuse³. Although drug misuse exists in every sector of society, it is most prevalent in areas of social deprivation where individuals are more likely to experience poorer health outcomes, independent of substance misuse.

Generally, there is a greater prevalence of certain illnesses amongst the drug-misusing population, including viral hepatitis, bacterial endocarditis, HIV, tuberculosis, septicaemia, pneumonia, deep vein thrombosis, pulmonary emboli, abscesses and dental disease². Mental health disorders are also more prevalent in the drug-misusing population.

3.2. General rationale for prescribing

For many people, prescribed treatment is an important part of their recovery journey. It is one component of a broader recovery-orientated system of health and social care⁴.

These guidelines particularly support substance misusers to access acute healthcare needs, preventing unintentional drug withdrawal (with potential adverse consequences, such as the risk that patients will prematurely self-discharge, or self-medicate with drugs of uncertain strength while unwell in hospital, or worse still self-discharge mid-medical treatment and suffer undue morbidity or mortality due to failed medical treatment and/or subsequent illicit drug overdose.

3.3. Treatment options fall broadly into three categories:

Opiate Substitution Therapy [OST], such as methadone, is the first choice option. It improves outcomes for most opioid dependent people. Treatment can reduce symptoms of dependence, and help to reduce associated difficulties.

OST allows people the time, space and platform to make meaningful choices. OST:

- Improves morbidity and mortality
- Improves the patients' health outcomes
- Within in-patient settings it allows patients to remain in receipt of healthcare
- Reduces harm to the individual and the wider community
- Prevents people dropping out of treatment
- Suppresses illicit use of heroin
- Reduces crime
- Reduces the risk of Blood Borne Virus [BBV] transmission
- Is cost effective

Coming off OST can lead to greater risk of relapse, BBVs and overdose; and treatment orientated to rapid abstinence produces worse outcomes than treatment initially orientated to maintenance⁵.

Detoxification as a "stand alone" treatment is associated with poor outcomes and can trigger renewed episodes of drug use and increased risk of death from overdose. Detoxification usually takes place following a reduction of substitution therapies and as part of a wider structured plan incorporating psychosocial and cognitive behavioural therapies.

Detoxification should only be considered in the acute hospital setting where there is a clinical need that prevents the use of opiate substitution therapy or the patient makes a specific choice. It must be done with support from the community drugs service including overdose training and naloxone provision (see [Appendix 8](#)). On occasions patients may wish to take the opportunity of a hospital admission to reduce or detox fully. While this may occasionally be useful, if unplanned and just in response to the admission, the patient is very likely to relapse on leaving hospital with a substantially increased risk of overdose. This should be explained to patients to support informed consent.

Relapse Prevention prescribing using opiate antagonist medication such as Naltrexone has become less common among community drug services but can be a useful stepping stone towards recovery as part of a structured program incorporating psychosocial and cognitive behavioural interventions.

4. Patient safety

4.1. Drug related deaths

Drug-related deaths among UK drug misusers are among the highest in Europe. Mortality rates amongst opiate users are 12 times higher than their non opiate using peers, and rise to 22 times higher for Intravenous drug users.

Drug-related deaths are especially high in the first weeks following release from prison⁷, and in the first few weeks of Methadone treatment⁸.

Drug-related overdose deaths are most commonly caused by opioid drugs but often they will involve the use of other depressant drugs such as alcohol, benzodiazepines and more recently pregabalin.

Initiation of methadone carries both benefits and risks. [see section 10 / Appendices 2-6](#)

4.2. Reducing drug related deaths²

Clinicians can help to reduce drug-related deaths in their patient's by:

- Identifying and assessing patients at greatest risk of drug-related death
- Providing education and training to drug misusers and their families on the risks of overdose and how to respond effectively advising drug misusers of the dangers of combining drugs, especially alcohol and benzodiazepines
- Educating drug misusers that the use of methadone, outside its medical purpose, is extremely dangerous
- Educating new patients starting on methadone and buprenorphine on the risks of loss of tolerance
- Supervised consumption especially in the early stages of methadone and buprenorphine treatment
- Adjusting dispensing frequency according to risks
- Requiring that patients moving on to take home methadone and buprenorphine provide details of satisfactory home storage arrangements and recording these in the patient's notes, especially when children are in the home
- Conducting or arranging for mental health assessments in patients who present a suicide risk
- Making use of local specialist support and referral in complex cases, such as cases of polypharmacy requiring specialist review
- Contributing to effective care pathways between hospital and community services
- Liaison with the community drug service who can also provide naloxone kits to family or contemporaries of the patient as well as to the patient themselves as part of an overarching strategy to reduce drug related deaths

4.3. Opiate intoxication

The ability to identify and respond to acute opiate intoxication is key to maintaining patient safety². Prior to OST dose administration nursing staff should consider if the patient appears intoxicated.

Where patients appear intoxicated carry out basic nursing observations and if appropriate seek medical advice.

If intoxication is mild the dose may be delayed and given once intoxication wears off.

If intoxication is severe the dose may be omitted.

Potential Signs of Intoxication	
SIGNS	SYMPTOMS
<ul style="list-style-type: none">• Euphoria/Relaxation• Constricted pupils (pinned)• Drowsiness• Slurred speech• Unsteady gait• Smell (alcohol)	<ul style="list-style-type: none">• Feelings of well-being• Poor attention/concentration• Slurred speech

4.4. Opiate overdose

In cases of opiate overdose, with respiration rates less than 8 and conscious levels being either P or U (responding to pain or unresponsive):

- Administer 100% oxygen
- Summon a crash response
- Administer naloxone 0-4 – 2.0 mg (IV / IM / SC), repeated as required after 2-3 minutes, max dose 10 mg
- Basic Life support Measures

At 60 minutes, the half-life of naloxone is much shorter than the effects of most opioid drugs / medications.

Once naloxone wears off the patient may be at risk of further opiate sedation and associated respiratory depression which could be life threatening.

Patients may attempt to leave hospital while experiencing Naloxone precipitated withdrawal symptoms. They should be discouraged from doing so and the risk of re-emerging overdose explained.

4.5. Illicit drug use

Patients who are dependent on illicit drugs may attempt to continue to use illicit drugs throughout their hospital admission either to prevent physical withdrawal, relief of psychological distress or simply for pleasure.

Steps should be taken to assist patients in abstaining from illicit drugs during their in-patient stay.

- Optimising the dose of substitution therapy
- Adequate assessment
- Maintaining Community Substitution Therapies - [see section 8 / Appendix 3](#)
- Initiating Substitution Therapy - [see sections 9,10 & 11 / Appendix 2](#)
- Dose Titration and optimising medication to the most effective dose - [see Appendix 2](#)
- Offering detoxification, if applicable - [see section 12](#)
- Prescribing appropriate analgesia - [see section 7](#)
- Treatment of insomnia - [see section 6.2](#)

Despite taking these steps some patients will continue to use illicit drugs, often in chaotic and dangerous ways, in these instances steps to reduce risk should be taken including:

- Supervised consumption of medication
- Morning administration of substitution therapy (methadone / buprenorphine)
- Urinalysis – full drug screen
- Discuss and document concerns with the patient.

5. Assessment

5.1. Overview

Assessment should balance the needs of the patient with those of the healthcare practitioner. The prescriber must ensure that an adequate assessment has been made before prescribing, and no prescriber should feel pressurised into prescribing until they feel an appropriate assessment has been completed².

5.2. Triage Assessment

A triage assessment aims to identify the immediate risks / medical complications that might arise from the intoxicating effects of drug use, the risk of further drug use and the risk of acute withdrawal.

Triage assessment can be sufficient to initiate prescribing where a full assessment is not possible or appropriate, for example where a patient has been admitted for a medical reason and where a lack of substitute medication may result in undue distress and poor compliance with continued health care.

Where it is not possible to obtain a history directly from the patient collateral history from the community drug service, partners, family can aid the decision making process.

[see Appendix 8.](#)

Triage assessment domains include:

- Drug of abuse type, is drug type usual or new to patient
- Frequency of use
- Amount used, typical or new to patient.
- Route of administration, typical or new to patient
- Time of last use
- Physical complications
- Blood borne virus status
- Evidence of Opiate Intoxication – [see section 4.3](#)
- Evidence of Opiate Withdrawal – [see Appendix 1](#)
- Maintenance of community drugs treatment [see section 8 / Appendix 3](#)

5.3. Comprehensive assessment

Comprehensive assessment aims to deliver a fuller and informed understanding of the person's wishes, substance use, and the severity and complexity of clinical and other problems: and it needs to identify their strengths and key obstacles to their recovery⁴. It is of particular use when longer term on-going treatment is anticipated post hospital-discharge. This is generally performed by community drug services.

A comprehensive assessment should consider both drug use and resources for recovery and include:

- treating the emergency or acute problem
- assessing the degree of dependence – [see section 5.5 and Appendix 1](#)
- assessing physical and mental health complications
- identifying social assets, including housing, employment, education and support networks
- assessing risk behaviour including domestic violence and offending
- safeguarding – [see section 5.6](#)
- determining the person's expectations of treatment and desire to change
- determining the need for substitute medication

5.4. Urine screening

Urine analysis should be regarded as an adjunct to the history and examination; it should be obtained before prescribing and randomly throughout treatment.

Results should always be interpreted in the light of clinical findings, as false negatives and positives can occur. Detection times are only approximate and highly dependent upon dose, frequency, route of administration and urine excretion and concentration.

Drug or Its Metabolite(s)	Duration of Detectability
Amphetamine/amfetamines, including methylamphetamine and methylenedioxy-methamphetamine (MDMA)	2 days
Benzodiazepines <ul style="list-style-type: none"> • Ultra-short-acting [half-life 2h] [e.g. midazolam] • Short-acting [half-life 2-6h] [e.g. triazolam] • Intermediate-acting [half-life 6-24h] [e.g. temazepam, chlordiazepoxide] • Long-acting [half-life 24h] [e.g. diazepam, nitrazepam] 	12 hours 24 hours 2-5 days 7 days or more
Buprenorphine and metabolites	8 days
Cocaine metabolite	2-3 days
Methadone [maintenance dosing]	7-9 days
Codeine, dihydrocodeine, morphine, propoxyphene [heroin is detected in urine as the metabolite morphine]	48 hours
Cannabinoids <ul style="list-style-type: none"> • Single use • Moderate use [three times a week] • Heavy use [daily] • Chronic heavy use [more than three times a day] 	3-4 days 5-6 days 20 days up to 45 days

5.5. Opiate withdrawal syndrome

The onset of physical withdrawal symptoms is a key characteristic of opiate dependency and their presence is required to establish a diagnosis.

Typically starting 6 – 8 hours following cessation, peaking at 24 – 36 hours and lasting 5 – 7 days the opiate withdrawal syndrome is often accompanied by increased levels of anxiety. [see Appendix 1](#)

The use of certain medications, naloxone, and buprenorphine can precipitate withdrawal symptoms in otherwise stable patients receiving opiate substitution therapies.

Unlike alcohol withdrawal acute opiate withdrawal is not associated with life threatening seizures.

5.6. Safeguarding considerations

A third of drug misusers in treatment have child care responsibilities⁶. Clearly, not all parents or carers with drug problems cause harm to their children, but for some substance misuse can significantly reduce their capacity to provide practical and emotional care¹⁰.

The risk of harm to a child or young person can come directly through exposure to substances, the effect of intoxication or withdrawal on the parent, exposure to and normalisation of criminal activity to fund drug use.

The following child protection issues must be taken into consideration:

- Effect of drug misuse on functioning, for example, intoxication, agitation
- Effect of drug seeking behaviour, for example, leaving children unsupervised, contact with unsuitable characters
- Impact of parent's physical and mental health on parenting
- How drug use is funded, for example, sex working, diversion of family income.
- Emotional availability to children
- Effects on family routines, for example, getting children to school on time
- Other support networks, for example, family support
- Ability to access professional support
- Storage of illicit drugs, prescribed medication and drug-using paraphernalia

If risk of significant harm to a child or young person is found or suspected, involve other professionals according to local safeguarding requirements. Link with local hospital/trust leads.

NB The above safeguarding considerations are also applicable where drug users may be caring for vulnerable adults. It is also important to ensure the individual themselves are safeguarded appropriately, as they may be a vulnerable adult.

5.7. Cardiac Assessment - Methadone and QTc prolongation *(for more information see Appendix 5)*

Cases of QTc interval prolongation and torsades de pointes have been reported during treatment with methadone, particularly at high doses above 100mg per day.

Therefore methadone should be administered with caution to patients at risk for development of prolonged QTc interval, e.g. in case of:

history of cardiac conduction abnormalities, advanced heart disease or ischaemic heart disease, liver disease, family history of sudden death, electrolyte abnormalities, i.e. hypokalaemia, hypomagnesaemia, concomitant treatment with drugs that have a potential for QTc-prolongation, concomitant treatment with drugs which may cause electrolyte abnormalities, concomitant treatment with cytochrome P450 CYP3A4 inhibitors.

Clinicians should make a balanced judgment for each patient and as the risk factors for the QTc interval prolongation increase, e.g. high methadone dose or multiple risk; clinicians will need to consider ECGs. In particular ECG monitoring (before dose titration and seven days after titration) is recommended with doses over 100 mg per day and in those with substantial risk.

6. General management

Whilst substance misuse patients can be a particularly challenging group of patients, it is unfair to assume that all patients with substance misuse issues will be challenging. Like most patients they will have anxiety, discomfort and pain caused by the presenting condition. Unlike most patients they belong to one of the most stigmatised and disadvantaged groups in society.

Patients with substance misuse issues may have had previous negative experiences of health care systems. If patients do not feel confident that their misuse issues will be managed appropriately in hospital they may avoid admission / be less likely to engage with any medical / surgical plan. This lack of engagement may place them at a greater risk of medical or surgical complications.

6.1. Ward management

- Provide reassurance that any existing community treatment will be continued on admission, unless there is a medical reason not to
- The standard practice risk assessment procedures should be sufficient to determine and manage any risks to patient, staff, public and the environment
- Supervised consumption should be undertaken
- Urine samples should be taken
- Some opioid users may abuse other drugs and/or alcohol. Consider steps to manage concurrent withdrawal. [see section 14](#)
- Pain Team Review - It is well recognised that long term opiate misuse affect pain receptors so as to lower pain thresholds
- Ensure that safeguarding (of children and adults, including the service user themselves) is considered and appropriately acted upon. [see section 5.6](#)

6.2. Insomnia

Insomnia through opioid withdrawal can be a trigger for illicit drug or alcohol use. Short term use of hypnotic medication may be of benefit whilst an inpatient. Hypnotic medication should only be prescribed on a PRN basis, and whenever possible not be continued on discharge.

6.3. Pregnancy¹⁰

A large proportion of new presentations to treatment are women, and many are in their child-bearing years. Long term outcomes for pregnant women and the neonate are improved by entering substance misuse services, including oral substitution therapy. Any patient found to be pregnant and misusing drugs will require a sensitive approach and every opportunity taken to encourage them into mainstream service. Appropriate safeguarding action should be taken in relation to the unborn child. [see section 5.6](#)

- Sudden withdrawal of opioids should not be encouraged during pregnancy, or following miscarriage, or termination, because of the risks to the mother and/or baby.
- Advised take the lowest amount of drug needed to avoid withdrawal, in the safest way [e.g. smoke rather than inject]
- Offer urgent referral to community drug services / specialist midwife if available.

6.4. Substitute prescribing in pregnancy¹⁰

- Substitute prescribing can occur at any time in pregnancy and carries a lower risk that continuing illicit use. The general principles outlined in these guidelines should be followed, and a maintenance dose be prescribed that stops or minimises illicit drug use
- Many mothers who become pregnant whilst on methadone may request detoxification, although during the first trimester the patient should normally be stabilised as there is an increased risk of spontaneous abortion. Cautious detoxification in the second trimester may be considered as a potential option, as long as illicit opiate use is not continuing
- Detoxification should generally not be undertaken in the third trimester as maternal withdrawal, even if mild, may be associated with fetal distress and even stillbirth
- Whilst methadone or buprenorphine are both potential options for use in pregnant women, there is a lack of formal evidence to inform choice. Methadone has amassed the greatest level of experience so by consensus may be judged the safer of the two. However experience with buprenorphine is encouraging
- Pregnant new starters should not be expected to commence initiation of methadone whilst in significant withdrawal. The aim is to safely observe doses and allow safe rapid dose incrementation
- Twice daily dosing of methadone may be preferred by some patients to minimise nausea and vomiting, but avoid evening doses due to the association with nocturnal dosing
- Methadone tablets may minimise nausea and vomiting, but must only be used if risk of injecting, or diversion is low
- Transfer to buprenorphine during pregnancy is not advised because of the risk of precipitated withdrawal and the risk of inducing withdrawal in the fetus.
- Suboxone™ (buprenorphine / naloxone) is not suitable for treatment during pregnancy

6.5. Effects of drugs of misuse on the fetus and baby¹⁰

The effects of different drugs of misuse during pregnancy are broadly similar and are largely non-drug specific. Intra-uterine growth retardation and pre-term deliveries contribute to increased rates of low birth rates and increased perinatal mortality rates.

Maternal cocaine use is associated with higher rates of early pregnancy loss, third-trimester abruptions, stillbirth, neonatal death, and sudden infant death syndrome.

Maternal heroin use is associated with a higher rate of small-for-date babies and pre-term delivery.

There appears to be a correlation between methadone dose and severity of neonatal abstinence syndrome, but this is not always the case. There is also some evidence of delayed visual development in methadone exposed foetuses.

6.6. Breastfeeding¹⁰

Breastfeeding should be encouraged, even if the mother continues to use drugs, except where she uses cocaine, crack cocaine, or high dose benzodiazepines.

Methadone or buprenorphine treatment is not a contraindication to breastfeeding. Breastfeeding may reduce the intensity and length of neonatal abstinence syndrome and has been shown to improve outcomes.

6.7. Mental capacity / mental health act

A history of illicit drug misuse is not in itself evidence of reduced capacity.

Staff should consider that acute intoxication or an altered state brought about through acute withdrawal may result in temporary impairment of capacity to an extent that it prevents the patient from making informed decisions.

The misuse of alcohol or drugs is not considered to be a mental disorder within the Mental Health Act in its own right. There are no grounds for detaining a person in hospital for the sole treatment of their alcohol or drug dependence. However, whilst 'dependence on alcohol or drugs' is excluded from the provisions of the Act this exclusion does not rule out the possibility of a person being detained on the grounds of a mental disorder arising from, or suspected to arise from, alcohol or drug dependence. In other words if a person is suffering from a mental disorder, which pre-exists, or is prompted by, the use of alcohol or drugs, he/she should be assessed in the usual way. Drug and alcohol use can contribute to both acute and chronic mental health problems.

Those with coexisting mental health and substance use problems have poorer prognoses, greater levels of unmet need, higher rates of relapse, increased hospitalisation, housing instability, poorer levels of social functioning such as poverty, greater risk of being either a victim and/or perpetrator of violence, greater involvement with criminality and marginalisation, less compliance with medication and treatment, greater service utilisation, higher costs to services, high rates of suicide in drug dependent patients, high rates of history of drug misuse in those psychiatric patients who subsequently commit suicide or homicide and severe and multiple disadvantage (substance misuse, homelessness and criminal justice involvement).

It is important that individuals are not turned away from either drug and alcohol treatment services or mental health services due to their coexisting illness but rather that such services should aim to be perceived by service users and their carers as supportive with 'no wrong door' through which to enter services (whether based on levels of alcohol and/or drug dependence or on presence or absence of specific diagnoses of mental health).

6.8. Accident and Emergency (A & E) / Assessment Services

Where patients receive care in outpatient or emergency departments **and do not require full admission to hospital**, it is inappropriate to initiate new treatment.

Where a stay in A & E may exceed 12 hours, and the patient is not likely to be admitted consideration of prescribing short term dihydrocodeine oral up to 60 mg four times a day (unlicensed use).

Existing community treatment (methadone / buprenorphine) can be given providing the dose confirmation checks have been completed and the community pharmacy is aware that the dose has been given.

Attendance at A&E may present a window of opportunity to put drug misusers in touch with other services and consider their drug misuse².

On discharge, wherever possible, the following information should be offered:

- Contacts for further help (such as needle exchange services, community drug service or self-help groups) (see Appendix 8 for contact details)
- Advice on preventing overdose
- Advice on reducing the risk of blood-borne virus infection and its consequences (including support for hepatitis B vaccination). This information is available from the local community service. (please see section 8 for contact details)

6.9. Driving and notification to the DVLA

Full compliance with an oral methadone maintenance programme supervised by a consultant specialist or an appropriate health care practitioner may allow driving licensing subject to favourable assessment and, usually, annual medical review. Similar criteria may apply for an oral buprenorphine programme. There should be no evidence of continued use of other substances, including cannabis.

The patient should notify the DVLA if they are taking drugs of abuse.

7. Pain management

Pain is subjective and person defined. Pain in people who use drugs is common, complex and often forgotten and poorly treated. Up to 25% of people who use opioids say they started using opiates because of pain.

Chronic pain affects between 10 – 15% of the general population rising to between 30 and 50% of substance misusers. Under-treatment is common and is often based on misconceptions. Involve Trust pain teams in decisions.

There are a number of reasons why individuals who are drug dependent may have greater than expected needs regarding pain relief:

- Chronic opiate misuse affects pain regulation mechanisms so as to result in lower pain thresholds and hyperalgesia
- Drug misusers have a low tolerance of non-pharmacological interventions to achieve pain control
- Virtually all forms of addiction are associated with sleep disturbance and this is a well-established exacerbating factor in chronic pain
- Depression and anxiety are common features in addiction and these have an important influence on the pain experience
- Drug misusers are more likely to suffer from accidental and non-accidental injury, and medical complications related to their drug use. This places them at high risk from physical problems that may require analgesia

7.1. Methadone and pain

Methadone is a full opiate agonist drug and is the most common substitution therapy for treatment of opiate dependency.

- Give the usual methadone maintenance dose
- Prescribe opioid analgesia where the condition warrants
- Morphine is the preferred opioid agonist
- It is not necessary to “rationalise” the patient’s entire opioid requirements to one drug
- Increased sensitivity to pain or cross tolerance will often necessitate higher or more frequent doses
- Avoid partial agonists (e.g. buprenorphine) and antagonist drugs (e.g. naltrexone) for patients receiving methadone as withdrawal may be precipitated
- If adequate pain control cannot be achieved, it may be necessary to transfer the patient to a stable methadone dose so that an opioid analgesic can be effectively used for pain management.

7.2. Buprenorphine and pain

Buprenorphine is an opioid-receptor partial agonist (it has opioid agonist and antagonist properties). Patients taking buprenorphine may experience opiate blockade effects.

Management steps:

- Try non-steroidal anti-inflammatory drugs and paracetamol.
- If this fails, seek further advice.

7.3. Naltrexone and pain

Naltrexone is an opiate antagonist “blocker” drug used in recovery from opiate dependency. Taken daily naltrexone blocks the effects of heroin and prevents the user getting “high”, with no reward the user is less likely to repeatedly use heroin and return to dependent use.

Naltrexone will also block the benefits of opiate analgesia, patients should be made aware of this potential problem.

- Discontinuation of naltrexone does not produce withdrawal symptoms
- Minor or intermediate elective surgery: manage the pain with non-opioid analgesics
- Major surgery with expected severe post-operative pain: naltrexone should be discontinued 72 hours beforehand. Expect a degree of resistance to opioid analgesics, although there may be increased sensitivity to pain
- If unexpected or severe pain should occur, then intravenous paracetamol, high dose nonsteroidal anti-inflammatory drugs, and local anaesthetics are potentially effective treatment options
- Seek specialist advice if non-opiate analgesia is ineffective/inadequate

7.4. Peri Operative Pain

Methadone may be given as per the patient’s usual requirements within 2 hours before surgery.

The anaesthetist will need informing of the amount and time of the last methadone dose given.

It may be necessary to omit or delay Buprenorphine dosing to prevent either opioid blockade or precipitated withdrawal effects.

8. Existing community patients (methadone, buprenorphine)

Unless there are valid grounds, established community Methadone / buprenorphine prescribing should be continued without interruption or dose alteration during inpatient admissions.

Good communication between the hospital, community drug service ([see Appendix 8 for contact details](#)) and community pharmacy is essential to ensure continuity of treatment and maintain patient safety.

See [Appendix 3](#) for further details on:

- how to confirm existing medication and dosing
- advice if out of hours
- dealing with any missed doses
- patients’ own supplies
- on-going supply considerations post discharge

9. New Patients: Illicit Opiate (Heroin) Using Patients

Commencement with OST is not a criteria for admission in its own right. Similarly 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.

As opioid withdrawal typically starts 6 – 8 hours following cessation, peaking at 24 – 36 hours and lasting 5 – 7 days, consideration of starting opioid substitution therapy 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 consideration of prescribing short term dihydrocodeine oral up to 60 mg four times a day (unlicensed use).

10. Methadone

Methadone is a Schedule 2 Controlled Drug. It is prescribed as “Methadone Mixture SF 1mg/1ml”. It is a full opioid agonist and can be substituted for opioid drugs such as diamorphine (Heroin) to prevent the

onset of physical withdrawal symptoms. It is itself addictive and should only be prescribed for those who are physically dependent on opioids.

See Appendix 2 for advice on methadone induction and Appendix 3 for methadone maintenance

11. Buprenorphine

Buprenorphine, a partial agonist and schedule 3 controlled drug, is licensed for the treatment of opioid dependence in individuals over the age of 16 years of age (if under the age of 16 please contact the community drugs service). Whilst it is of value in OST, buprenorphine is not prescribed until opioid withdrawal symptoms have settled. It is available as 0.4 mg, 2 mg, & 8 mg sub lingual tablets.

11.1. Buprenorphine precipitated withdrawal

Precipitated withdrawal occurs in someone commencing buprenorphine who has recently taken heroin (less than 6 hours previously) or methadone (less than 24 hours previously).

It is caused by the high affinity of buprenorphine displacing other opioids e.g. methadone, heroin from opioid receptors, but having less opioid activity (partial agonist). This rapid reduction in the opioid effects can be experienced as precipitated withdrawal, typically occurring 1 to 3 hours after the first buprenorphine dose, peaking in severity over the first 3 to 6 hours, the gradually subsiding.

If it occurs, reassure the patient and offer symptomatic treatment such as lofexidine e.g. 400 – 600 micrograms 8 hourly, as appropriate, if withdrawal symptoms are severe.

Buprenorphine standard & enhanced titration

Standard titration

Day 1 8 mg (4mg + 4 mg)
Day 2 12 mg (8 mg + 4 mg)
Day 3 16 mg (12mg + 4mg)

Where there are health concerns, lower doses of heroin use,
or previous history of precipitated withdrawals

Day 1 4 mg
Day 2 8 mg (4 mg+ 4 mg)
Day 3 12 mg (8 mg + 4 mg)

11.2. Precautions

Poly-drug use especially benzodiazepines

Chronic pain requiring opiate pain relief

Concomitant use of methadone and buprenorphine should be avoided due to the increased risk of opiate withdrawal.

11.3. Contraindications

Severe hepatic/respiratory disease

11.4. Risk factors for overdose

Low opioid tolerance,

Use of CNS depressant drugs, including alcohol

11.5. Buprenorphine or methadone?

The initial objective of the drug treatment of an opioid dependent patient admitted to hospital is to stabilise their opioid dose as quickly and safely as possible to avoid unnecessary distress and to stabilise the patient enough that they can be treated for any other medical conditions. Therefore in view of the initial objective and also the risk of precipitated withdrawal, it is recommended that prescribers do not choose buprenorphine as first line new treatment within an acute medical setting.

Before the commencement of buprenorphine, a full explanation should be given to the patient covering the properties of the drug, its effects, the induction period and the possible side effects. Understanding that the first 3 days are usually the worst is very helpful to the patient, especially when explaining precipitated withdrawal and the need for compliance to the treatment programme³.

If switching from methadone to buprenorphine, specialist advice should be sought from the substance misuse service or pain management team, as there is a risk of precipitated opiate withdrawal.

12. Opioid detoxification

Opioid detoxification should be a readily available treatment option for people who are opioid dependent and have rejected an offer of OST (methadone / buprenorphine) in favour of becoming opioid abstinent.

When any detoxification is considered, **it is essential** that this is done in liaison with the community drugs service, and not started without this advice. The community drugs service may also provide Naloxone training to the individual or those in close contact with them. The reasons for the requirement for detoxification to be undertaken in liaison with the community drugs service is that detoxification does carry higher risk, particularly if not part of a coherent aftercare plan. The patient should always be advised about the risk of overdose following detoxification and lowered opiate tolerance (there is a 6-8 times increase in the death rate from overdose in the weeks post detoxification).

There are a number of circumstances in which detoxification in hospital is appropriate, but it should always be done in liaison with the community drugs service.

Detoxification can be simple / symptomatic or complex / medically assisted.

12.1. Simple / symptomatic relief

Symptomatic relief using a range of “as required” based medication to tackle specific symptoms of withdrawal if and when they occur.

- Diarrhoea – **loperamide** 4 mg immediately followed by 2 mg after each loose stool for up to five days; usual dose 6 - 8 mg daily, maximum 16 mg daily
- Nausea, vomiting, may also be useful for stomach cramps – **metoclopramide** 10 mg eight hourly or **prochlorperazine** 5 mg three times a day or 12.5 mg intramuscularly 12-hourly
- Stomach cramps – **hyoscine butylbromide** 20 mgs four times a day
- Agitation and anxiety, sleeplessness – diazepam (oral) up to 5-10 mg three times daily when required (or zopiclone 7.5 mg at bedtime for patients who have been dependent on benzodiazepines). In severe cases of anxiety and agitation, obtain suitable psychiatric advice from an addiction psychiatrist or the on-call duty psychiatrist
 - Muscular pains and headaches – paracetamol or ibuprofen. Topical rubefacients can be helpful for relieving muscle pain associated with methadone withdrawal

12.2. Complex / medically assisted

Lofexidine is a non-opioid alpha-adrenergic agonist licensed for the management of symptoms of opioid withdrawal. It is not a controlled drug, it comes as a 200 microgram tablet and the effect lasts only a few hours

Lofexidine may be used in patients who:

- Have made an informed and clinically appropriate decision not to use methadone or buprenorphine
- Who have made an informed and clinically appropriate decision to detoxify within a short time period
- With mild or uncertain dependence (including young people)
- Where the patient cannot be made comfortable with symptomatic measures

The treatment course is between 7–10 days with doses starting at 800 micrograms daily and rising to a maximum of 2.4 mg in divided doses. The dose is then reduced over subsequent days.

Reported side effects of lofexidine are dry mouth and mild drowsiness. Patients sometimes complain of a metallic taste in their mouth and that their urine smells of yeast.

There is a risk of bradycardia and hypotension hence pulse and blood pressure need to be monitored. There is also a risk of rebound hypertension when treatment with lofexidine ends.

Sedation is increased with concomitant use of alcohol or central nervous system depressants and overdose can result in hypotension, bradycardia, sedation and coma.

Use lofexidine with caution in-patients with cardiac disease, cerebrovascular accidents, and chronic renal failure.

The safety in pregnant and breastfeeding women has not been established.

[See Appendix 7 for suggested lofexidine regimen](#)

12.3. Clonidine or dihydrocodeine

Neither clonidine nor dihydrocodeine should be used routinely for opioid detoxification. Note that dihydrocodeine is often used off-label to manage opiate withdrawal symptoms in A&E / Assessment Services where the patient is experiencing withdrawal, but the patient is unlikely to be admitted to an in-patient bedded unit.

13. Relapse prevention – naltrexone

Naltrexone is a long-term therapy and will need to be continued via a community drug service on discharge. Therefore consideration of prescribing within an in-patient setting should only occur in consultation with the community drugs service ([see Appendix 8 for contact details](#)). Appropriate arrangements for exit prescribing will need to be put into place to ensure a seamless transfer of care back into the community before the patient is discharged.

13.1. Benefits

Naltrexone is an oral opioid antagonist which, when taken regularly, blocks opiate receptors within the brain thus preventing a former opiate user from experiencing the effects of opioids. It can be helpful following detoxification in enabling a patient to maintain abstinence.

Before considering commencement of naltrexone, the patient needs to be fully informed of the effects, side effects and risks of naltrexone so that they are able to make an informed choice.

13.2. Risks

There is a risk of fatal overdose should the patient attempt to ‘override’ the opioid blockade with illicit drug use.

13.3. Investigations

Due to the potentially hepatotoxic nature of naltrexone, liver function tests should be conducted before and during naltrexone treatment.

13.4. Dosing

- Following a negative urine or oral fluid test for opioids the patient is given a single dose of naltrexone (25 mg) orally
- Observe the patient for any withdrawal or other ill effects
- If the patient does not experience any withdrawal a 50 mg. dose may be given the next day
- The usual maintenance dose is then 50 mg a day

13.5. Loss of tolerance

The patient should be warned of the risk of drug overdose on leaving hospital, due to loss of tolerance.

Accidental overdose is often due to reduction in tolerance after a period of abstinence (e.g. release from prison, discharge from rehabilitation or hospital).

Appropriate written support information should be given to the patient to refer to on discharge, alongside a good, effective explanation of the literature to ensure understanding and informed choice.

14. Other drugs of abuse

It is not possible to provide guidance on every substance or scenario that might arise. Here you will find general guidance on some of the more common substances of abuse.

<p>Over the counter [OTC] opiates: e.g. codeine. Patients regularly taking OTC codeine may display symptoms of opiate dependency i.e. increased tolerance, physical withdrawal. Patients may be unaware that they are dependent / withdrawing. A detailed history including the use of OTC medication is advised.</p> <p>Prescribing Options: In most cases, where pain is the trigger, continued prescribing, gradual withdrawal and analgesic review is sufficient. For a few patients, where the mood altering effects of opioids is attractive, specialist help from the community drug team may be required.</p>	<p>Benzodiazepines: Maintain any regular community prescriptions, with details confirmed via medicines reconciliation. Initiation of regular / repeat benzodiazepines for dependence should not routinely be undertaken in the acute hospital setting. If there is clear evidence of acute benzodiazepine withdrawal short term prescribing on a PRN basis may be considered.</p> <p>Prescribing option Diazepam as a consolidated dose of benzodiazepine at lowest dose: The use of benzodiazepines with other depressant drugs such as alcohol, heroin, methadone, or pregabalin increases the risk of overdose deaths. Wherever possible, take home prescribing of benzodiazepines should be minimised to 7 days.</p>
<p>Alcohol: Acute alcohol withdrawal syndrome is a medical emergency. It requires timely and appropriate intervention to prevent potentially life threatening complex symptoms. Combined alcohol and opiate dependency requires more specialist support.</p> <p>Prescribing options – Chlordiazepoxide, lorazepam, diazepam, idazepam. Check for local trust guidance.</p> <p>Involve community drug service (see Appendix 8 for contact details)</p>	<p>Amphetamine / cocaine: There are no licenced pharmacological treatments to eliminate the symptoms of withdrawal from stimulants. Dexamfetamine is not recommended, unless within specialist drug treatment settings.</p> <p>Prescribing Options: In the acute hospital setting short term symptomatic relief of agitation with anxiolytics may be considered i.e. diazepam / lorazepam. For psychosis short term management consider antipsychotics i.e. haloperidol, and seek support from mental health services.</p>
<p>Cannabis: There are no licenced pharmacological treatments to eliminate the symptoms of withdrawal from cannabis.</p> <p>Prescribing options: Short term symptomatic relief of agitation or insomnia with anxiolytics may be considered i.e. diazepam.</p>	<p>New psychoactive substances: Broadly split into two categories. 1. Stimulant type compounds mimicking the effects of drugs like ecstasy or amphetamine such as “MCAT” or 2. synthetic cannabinoids such as “SPICE”. There are also drugs mimicking opiates and benzodiazepines. There are some anecdotal reports of withdrawal symptoms associated with habitual use of synthetic cannabinoids, however, there are no substitute medications. Heavy intoxication can trigger seizures and result in overdose. The effects are increased when taken with other depressant drugs such as alcohol. Close monitoring and frequent physical observation is advisable with intoxicated patients.</p> <p>Prescribing Options: Consider symptomatic relief of agitation with low dose diazepam.</p>
<p>Pregabalin / gabapentin: Pregabalin and gabapentin misuse is common with users reporting euphoria, sociability, relaxation and calming effects. They also have CNS depressant effects causing drowsiness, sedation and respiratory depression. Taken in combination with other CNS depressants such as opiates, benzodiazepines or alcohol the depressant effects are additive and overdose may result.</p> <p>Prescribing Options: Gradual withdrawal of pregabalin (max rate 50-100 mg/week) or gabapentin (max rate 300 mg every four days). Anecdotal evidence of symptomatic relief of agitation with low dose diazepam².</p>	

15. Medication on discharge - planning and counselling

Take home supplies of methadone or buprenorphine, for substance misuse, should not routinely be given to patients upon hospital discharge. It is essential to liaise with the community drugs service as part of discharge planning to prevent either gaps in treatment or duplication of prescribing.
(see [Appendix 8](#))

Where this is not possible/practical then any take home doses should be kept to the absolute minimum to maintain prescription continuity, i.e. weekend cover only. The circumstances should be documented in the patient's notes.

15.1. To Take Home doses – new starters

Extra safeguards are required when discharging patients who are “New Starters” as mortality in the first few weeks of OST is significantly elevated⁸.

Every effort should be taken to minimise the need for take home dosing, and additional steps should be considered to prevent discharge at weekends or public holidays.

Arrangements for continued prescribing from the community drug service should be in place and the patient made aware of where to go / who to contact upon discharge. Their medication should be on a supervised consumption basis by a local community pharmacist.

On discharge be mindful that the community drugs service will counsel patients regarding on-going use, which includes the below storage and safety advice. Further examples of counselling points are available in [Appendix 6 – Example Methadone Safety Plan](#)

15.2. Storage Recommendations in Patients' Homes

Keep in a locked cupboard, out of access, reach and sight of children. Please note that the community drugs service are able to provide safe storage for patients. Example storage areas that methadone should **not** be kept in include;

- in the fridge
- under the bed
- in a car glove box
- accessible in a handbag

15.3. Inform the patient that:

- as little as 10 mg of Methadone can kill a child. Talk to children about the dangers of ALL medicines
- a mouthful can kill a teenager
- using heroin/other sedatives/alcohol greatly increases the risk of overdose
- most people who die from methadone poisoning have bought it from someone who is on a prescription
- inform the patient that their tolerance of heroin/opiates may have been affected and there is a higher risk of overdose if continuing to take illicit drugs.

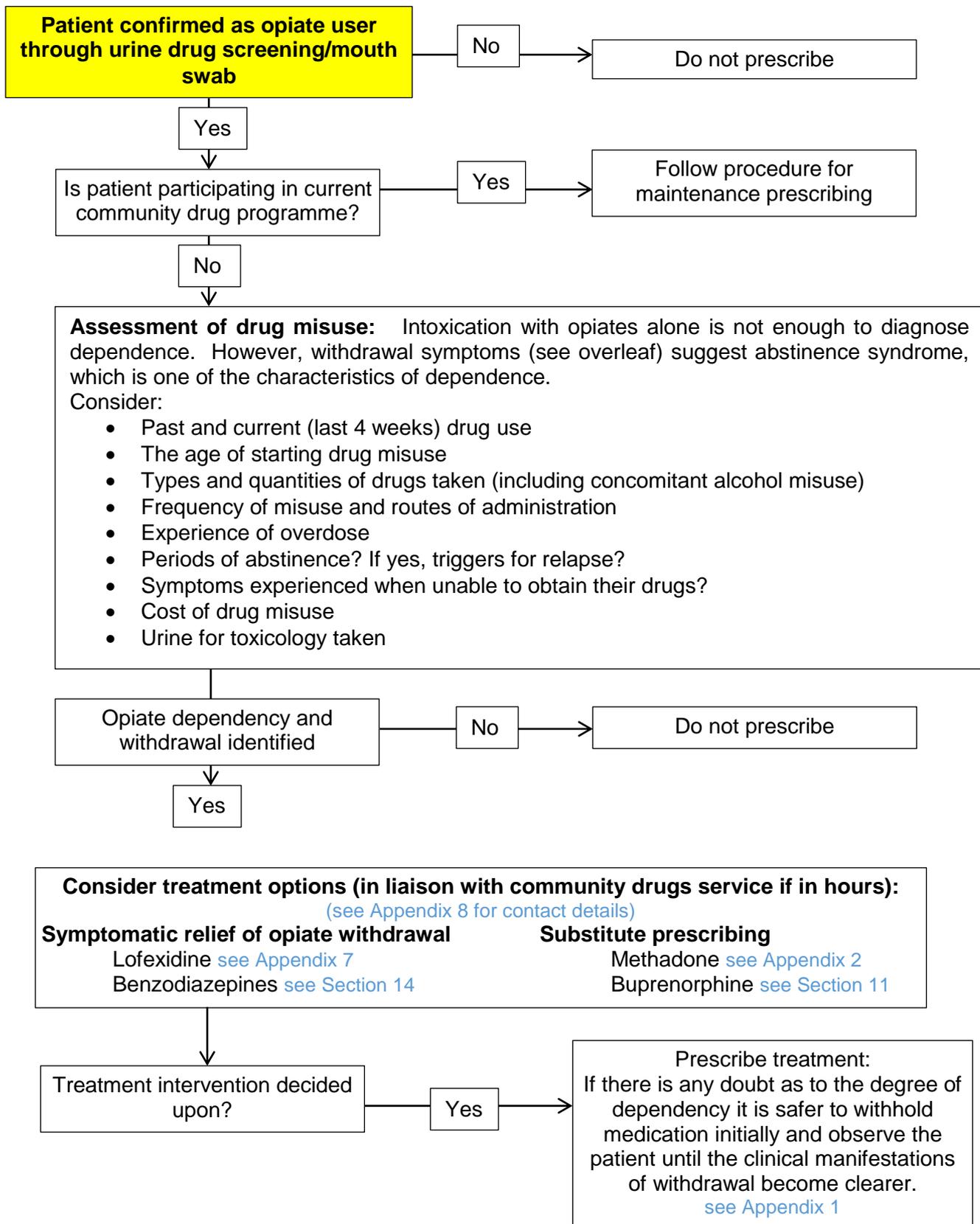
Upon discharge, if patient engagement with treatment with the Community Drugs Service is not agreed / secured then oral substitution therapy should not be continued post discharge. A Methadone safety care plan (see [Appendix 6](#)) should be undertaken prior to discharge.

Remember where there is no need for OST prescribing on discharge, and patients are misusing other substances, it is crucial to promote engagement with the community drugs service, and also to alert the patient to the fact that tolerance to drugs or alcohol may be affected/reduced, with a heightened risk of overdose.

16. References

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Appendix 1: Assessment of Opiate Dependency and Withdrawal Syndrome and Clinical Opiate Withdrawal Scale (COWS)



See overleaf for Opiate Withdrawal Syndrome & Assessment Scale

Opiate Withdrawal Syndrome¹³

Signs and Symptoms	Heroin	Methadone
Drug craving, anxiety, drug – seeking	6 hours	
Yawning, sweating, running nose, lacrimation	8 hours	34-48 hours
<i>Increase in above signs and:</i> Dilated pupils, goose-flesh, tremors, hot/cold flushes, aching bones/muscles, loss of appetite, abdominal cramps and irritability	12 hours	48-72 hours
<i>Increase in intensity of above and</i> Insomnia, increased blood pressure, low grade fever, increased respiration, increased pulse rate, restlessness, nausea and vomiting	18-24 hours	24-36 hours
Increase in intensity of above and Weight loss, diarrhoea, weakness, febrile, foetal position (curled up on a surface), increased blood sugar	36 hours - 4days	36 hours-4days

Objective signs of opiate withdrawal ²	Subjective signs of withdrawal ²
<ul style="list-style-type: none"> ● Yawning ● Coughing ● Sneezing ● Runny nose ● Lacrimation ● Raised blood pressure ● Increased pulse ● Dilated pupils ● Cool, clammy skin ● Diarrhoea ● Nausea ● Fine muscle tremor 	<ul style="list-style-type: none"> ● Restlessness ● Irritability ● Anxiety <p>[The signs above may also be useful objective signs]</p> <ul style="list-style-type: none"> ● Sleep disorders/depression ● Drug craving ● Abdominal cramps

A patient's subjective assessment of severe withdrawal symptoms may be comparatively low when compared to objective assessment. Therefore withdrawal should be assessed using the Clinical Opiate Withdrawal Score (COWS) as detailed below:

COWS Clinical Opiate Withdrawal Scale

For each criterion, document the number that best describes the patient's signs or symptoms at the time of each assessment.

Ensure scoring is based ONLY on the apparent relationship to opiate withdrawal e.g. if the patient is tachycardic because of sepsis, the increased pulse rate should NOT be added to the total COWS score.

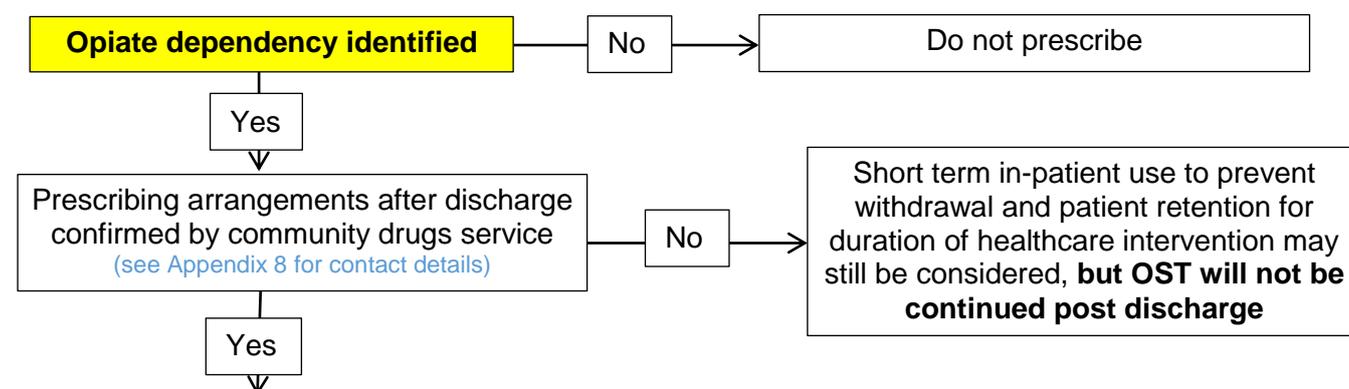
Patient Name:						
PiD/Hospital No:						
Enter scores at time zero, then every 4 -6 hour below.						
Date/ / /	Time:	:	:	:	:	:
Resting Heart Rate (beats per minute) measured after patient has been sitting or lying for 1 minute:						
Heart rate 80 or below	0					
Heart rate 81 – 100	1					
Heart rate 101 – 120	2					
Heart rate greater than 120	4					
Sweating over the last 30 minutes, not accounted for by room temperature or patient activity:						
No report of chills or flushing	0					
Subjective report of chills or flushing	1					
Flushed or observable moistness on face	2					
Beads of sweat on brow or face	3					

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.



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, voriconazole, 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 dosing¹¹.

- 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

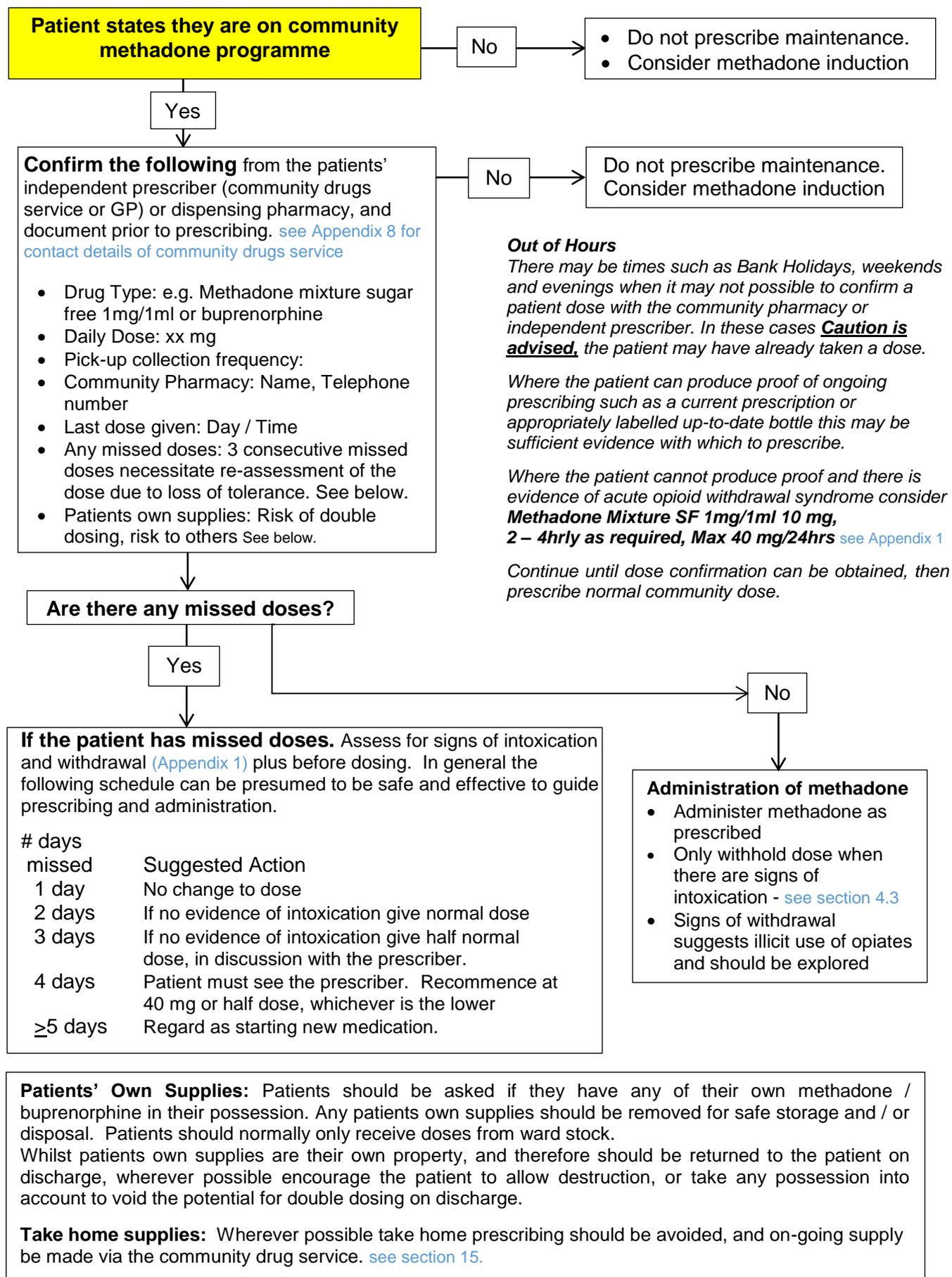
- Over 20% of all methadone deaths take place within two weeks of starting treatment.
- Risk of overdose is increased by low opioid tolerance, too high an initial dose, too rapid increases and concurrent use of other drugs, particularly alcohol, benzodiazepines and CNS depressants.
- Patients in whom 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 death¹¹.
- Symptoms of overmedication may include unusual feelings of excess energy, with or without euphoria¹¹.

Vomited methadone doses¹¹

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

Appendix 3: Methadone Maintenance – existing patients



Appendix 4: Methadone and buprenorphine pharmacology

	Methadone	Buprenorphine
Peak Plasma Conc	<ul style="list-style-type: none"> Four hours after regular oral administration (Range two to six hours) 	<ul style="list-style-type: none"> 90 to 150 minutes after regular sublingual administration.
Peak Clinical Effects	<ul style="list-style-type: none"> Two to six hours post oral dose (two to four hours first dose) Takes four to five days for methadone tissue plasma levels to stabilise, though accumulation continues beyond this, finally reaching a steady state after ten days. Once at steady state variations in blood concentrations are small. 	<ul style="list-style-type: none"> One to four hours post sublingual dose. It takes three to four days for buprenorphine plasma levels to stabilise.
Duration of action (half life)	<ul style="list-style-type: none"> The length of time it lasts in the body varies. Single dose; shorter half-life than maintenance dosing 12 – 18 hours means 15 hours. First few days between 13 and 112 hours mean 37 hours. Because of its cumulative effect until steady state is reached, methadone induction should be a cautious and gradual process. Elimination half-life is normally 20 – 37 hours but can range up to 91 hours for some individuals; its rate of clearance from the body can vary by a factor of almost 100. Optimal doses are usually between 24 – 36 hours. 	<ul style="list-style-type: none"> Related to dose. Low dose (e.g. 2 to 4 mg) may exert clinical effects for only a few hours, up to a maximum of 12 hours, because receptor occupancy will be minimal and plasma concentrations suboptimal. Higher doses (e.g. 16 to 32 mg) can exert effects for up to 48 to 72 hours. Optimal doses are usually between 24 and 36 hours. Elimination half-life is between 20 and 37 hours.
Metabolism	<ul style="list-style-type: none"> Well absorbed from the gastrointestinal tract into the blood stream Well distributed in body fats Metabolised through the liver via cytochrome P450 sub family of enzymes, thus susceptible to pharmacokinetic interactions with drugs that inhibit or induce liver enzymes. Binds well to plasma proteins and to lungs, liver and kidney tissues. Varies enormously in different people and widely different doses of methadone are needed to create the same serum methadone level. 	<ul style="list-style-type: none"> Principally in the liver via two hepatic pathways: glucuronide conjugation and N-dealkylation by the cytochrome P450 enzyme system. The tablets are administered sublingually because it has poor bioavailability. It is inactivated by gastric acid and has a high first pass metabolism.
Excretion	<ul style="list-style-type: none"> Excreted in the faeces and urine; urinalysis is useful only in confirming if being taken, but not establishing the dose. 	<ul style="list-style-type: none"> Excreted in the faeces and urine; urinalysis is useful only in confirming if being taken, but not establishing the dose.
Dosing	<ul style="list-style-type: none"> While research evidence suggests that optimal doses for most people lie between 60 and 120 mg some people will need more and some people will need less due to a range of individual factors such as size, gender, age, other health problems and metabolic clearance rates. Doses between 10 and 120 mg may exert clinical effects for 24 to 36 hours; low doses exert clinical effects for only a few hours. 	<ul style="list-style-type: none"> Maintenance is between 8 and 32 mg daily but the blockade dose (dose where the effects of additional opioids are markedly reduced) is maximal above 16mg daily.
Equivalence	<ul style="list-style-type: none"> Direct equivalence to street heroin is difficult to estimate, as purity of street heroin can vary (between 20 and 60%). One gram of street heroin is usually very roughly equivalent to 50 to 80 mg methadone. Direct equivalence of methadone and buprenorphine and vice versa is difficult to estimate, as the pharmacological properties of the two agents are not identical and it is not a linear relationship. When comparing the efficacy of maintenance doses, 50 to 80 mg methadone is approximately as effective as 12 to 16 mg buprenorphine in reducing heroin use and retaining patients in treatment. When comparing the equivalence of methadone to injectable pharmaceutical diamorphine, half-lives must be taken into consideration. This is not a linear relationship, so equivalence can vary from a methadone: diamorphine relationship of 1:3 (or even 1:1 for very low doses) to around 1:5 for high doses of diamorphine (e.g. 120mg methadone is equivalent to between 360 and 600mg of injectable diamorphine). 	<ul style="list-style-type: none"> Direct equivalence of methadone and buprenorphine and vice versa is difficult to estimate, as the pharmacological properties of the two agents are not identical and it is not a linear relationship. When comparing the efficacy of maintenance doses, 50 to 80 mg methadone is approximately as effective as 12 to 16 mg buprenorphine in reducing heroin use and retaining patients in treatment.
Tolerance	<ul style="list-style-type: none"> Develops at different speed in different individuals, can change in individuals over time and develops differently for different effects. With long term use, and in response to continued exposure of the brain to opiates, neuro adaptation occurs and involves changes in nerve and receptor function. Level of heroin use is not the only factor in determining the final dose of substitution that will be required. Patients react differently: some will need more and some will need less than others using the same amount of heroin. 	<ul style="list-style-type: none"> Develops at different speed in different individuals, can change in individuals over time and develops differently for different effects. With long term use, and in response to continued exposure of the brain to opiates, neuro adaptation occurs and involves changes in nerve and receptor function. Level of heroin use is not the only factor in determining the final dose of substitution that will be required. Patients react differently: some will need more and some will need less than others using the same amount of heroin

Drug-induced prolongation of the QTc interval

The QTc interval is measured on an ECG* from the beginning of the QRS complex (caused by contraction of the ventricular mass) until the end of the T wave (caused by the return of the ventricular mass to the resting state). The QT corrected (QTc) interval is the QT interval (in milliseconds) corrected for heart rate using a standard formula (for example, Bazett's formula: $QTc \text{ (ms)} = QT \text{ (ms)} / \sqrt{RR}$ – QT divided by the square root of the R-R interval). QTc calculators are available on the internet.

The QTc interval is a useful indicator of risk of polymorphic ventricular tachycardias, or torsade de pointes which can be fatal. QTc interval prolongation beyond normal limits (440 ms for men and 470 ms for women) is associated with increased risk of cardiac arrhythmias and sudden death, especially above 500 ms.

Various psychotropic medications have recently been identified as causing QT prolongation and sudden death. In the past decade, this has become the most common reason for a drug to be withdrawn from the market. In the drug treatment field, this was the reason for levacetylmethadol (LAAM or ORLAAM) being withdrawn in 2001.

Methadone and risk of QTc prolongation

Methadone may prolong the QTc interval and induce torsade de pointes. However increases in QTc interval following methadone induction may not exceed specified thresholds (440 ms in adult males and 470 ms adult females). Findings in relation to the effect of methadone dose have been varied but recently there have been a number of case reports of patients on high-dose methadone experiencing QT prolongation and torsade de pointes. Reducing or stopping methadone was followed by reduction in the QT interval.

Cocaine has been shown to increase QTc intervals acutely. Other confounding factors may be the use of antipsychotic and tricyclic antidepressants.

In summary, the evidence, as currently available, points towards methadone as a risk factor for QTc prolongation and torsade de pointes, with a possible dose-dependent action.

MHRA guidance 2006

In May 2006 the Medicines and Healthcare Products Regulatory Agency (MHRA) drew attention to reports in Europe and elsewhere which “highlighted the risk of QTc prolongation in patients taking methadone, especially at high doses”. The MHRA recommended that: “patients with the following risk factors for QTc interval prolongation are carefully monitored whilst taking methadone:

- heart or liver disease
- electrolyte abnormalities
- concomitant treatment with CYP 3A4 inhibitors
- or medicines with the potential to cause QT interval prolongation
- in addition any patient requiring more than 100 mg of methadone per day should be closely monitored.” (MHRA, 2006)

Patient consent and information

The patient should be fully informed of the available evidence, the reasons for the clinical assessment and fully involved in the decision making process for their treatment.

Clinical assessment of patients on methadone maintenance

A standard physical health assessment and physical examination should be carried out on all patients entering methadone maintenance treatment. For patients already in methadone treatment, the clinical assessment should cover assessment of heart or liver disease, concomitant treatment with CYP 3A4 inhibitors, other drugs with the potential to cause QT interval prolongation and the presence of electrolyte abnormalities.

Clinical assessment of patients when initiating methadone

At present, the decision to perform an ECG prior to commencing methadone treatment should be based on a risk-benefit analysis. A baseline ECG should be considered in patients with evidence of heart or liver disease, concomitant treatment with CYP 3A4 inhibitors, use of other QTc prolonging drugs or electrolyte abnormalities.

If QTc prolongation is detected, alternatives to methadone should be considered, and other QTc risk factors (such as cocaine use) should be reassessed. It is important that the patient is fully informed and involved in the decision making process.

Summary

- 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.

Appendix 6: Example Methadone Safety Care Plan

Methadone Safety Care Plan	Affix label here if applicable NHS Number Surname Forename(s) Address DOB.
Activity	Outcome
Initial Dose > Should stop you suffering withdrawal > We will not over sedate you	Initiation of methadone by ward? <input type="checkbox"/> Yes. If yes state starting dose
Stability > Best taken once a day in the morning, roughly at the same time each day > It takes 3-4 days for Methadone to take full effect	Stabilisation whilst an in-patient? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, final dosage.....
Drug Related Death Avoid Accidental Overdose > Beware of lost tolerance > Tolerance builds slowly; a few missed doses can raise the risk of overdose. > Patient needs to be honest about how much heroin they are using. > Persuading prescriber to give higher doses increases risk. > Patient needs to be warned of the dangers of using heroin, alcohol, other sedatives, e.g. diazepam/sleeping pills. Taking temazepam as well as methadone is dangerous and can cause overdose. > Risk is increased if patient has serious liver damage.	Confirmation. Prescribed methadone dose from prescriber? <input type="checkbox"/> Yes. Dosage Did patient pick up most recent supply of methadone from designated pharmacy? <input type="checkbox"/> Yes Name of pharmacy..... Date of pickup Supervised or non-supervised: <input type="checkbox"/> Supervised <input type="checkbox"/> Non-supervised Is there a history of accidental overdose? <input type="checkbox"/> Yes <input type="checkbox"/> No Is there a history of serious liver damage? <input type="checkbox"/> Yes <input type="checkbox"/> No
Alcohol > Methadone and alcohol boost each other's effect, which if a patient oversubscribes to either (or both), is much more likely to lead to overdose. Methadone and other drugs > If Naltrexone or Buprenorphine is taken by a patient whilst opiates are in their blood system, he/she will more than likely suffer withdrawal symptoms. Severity of symptoms will depend on the level of opiate within the blood system. > Inform patient that heroin may have a reduced effect, or none at all. > Trying to 'jump' the blockade increases the risk of overdose and fatality	
Storage Recommendations Keep in a locked cupboard. Talk to children about the dangers of all medicines. Make sure that Methadone Is never kept: > in the fridge > under the bed > in a car glove box.	How does the patient ensure safe storage at home? Are there any children at home or visiting?

<p>Inform the patient that:</p> <ul style="list-style-type: none"> ➤ as little as 10mg can kill a child ➤ a mouthful can kill a teenager ➤ using heroin/other sedatives/alcohol greatly increases the risk of overdose ➤ most people who die from methadone poisoning have bought it from someone who is on a prescription. 	
<p>Side-effects of Methadone Sweating, constipation, itching, small pupils</p> <p>Health Advice</p> <ul style="list-style-type: none"> ➤ Constipation: Eat plenty of fruit, vegetables and non-alcoholic drinks ➤ Oral hygiene: Do not share a toothbrush ➤ Loss of sex drive: Need for safer sex 	
<p>Women's Health</p> <ul style="list-style-type: none"> ➤ Amenorrhoea: Advice that absence of period does not prevent patient from getting pregnant 	
<p>Pregnancy - Inform</p> <ul style="list-style-type: none"> ➤ Stable Methadone use poses no risk to delivery of baby. ➤ Stopping taking Methadone suddenly can be dangerous both to patient and baby ➤ Being stable on Methadone is better for the patient and baby than being unstable on illicit drugs ➤ Doctor and midwife need to be informed that patient is on methadone (if this is not already known to them) ➤ If baby experiences withdrawal this may not start immediately after the birth ➤ Methadone detoxification should be a planned reduction with medical/psychological support during last six months, involving the Women's Services 	
<p>Driving - Inform</p> <ul style="list-style-type: none"> ➤ The Road Traffic Act requires the license holder (i.e. patient) to inform the DVLA that they are being prescribed methadone or using drugs. ➤ If the patient drives whilst on a prescription of methadone, he/she should be advised not to do so if they feel sedated or have had any alcohol. ➤ Insurance claims may be affected if accidents occur with a patient who is on a methadone prescription. ➤ Should the patient present in an intoxicated state and is known to be in charge of a vehicle, he/she will be requested by staff to hand over their vehicle keys and find an alternative method of travelling home. ➤ The keys will be handed over to a named responsible person or to the patient when he/she is deemed to be in a safe state to drive. ➤ Should the patient refuse to hand over their vehicle keys, he/she will be informed that in order to protect the public at large, they will be reported to the police as being a potential hazard on the road. 	

Appendix 7: Lofexidine regimen

Before commencing a patient on lofexidine, it is advisable to obtain a baseline blood pressure (BP) reading and pulse (P); then measure the BP and P prior to administration of medication. Lofexidine should be discontinued if the blood pressure drops significantly i.e. if diastolic falls below 60 and pulse rate fall below 55 beats per minute - see [Appendix 8 for contact details of community drugs service](#).

Procedure for induction of lofexidine

DAY 1	DAY 2	DAY 3 - 6	DAY 7
<ul style="list-style-type: none"> ● All opioids stopped, record withdrawal symptoms using COWS – Appendix 1 Check BP/Pulse ● Commence lofexidine regime as shown below ● Check BP/Pulse 30 minutes post dose ● If BP/Pulse stable continue lofexidine 0.2 mg four times a day ● If diastolic BP falls below 60, pulse rate falls below 55 beats per minute or if client develops physical symptoms e.g. dizziness or fainting then omit the next lofexidine dose and seek medical advice. 	<ul style="list-style-type: none"> ● Chart withdrawal symptoms ● Check BP/Pulse ● Lofexidine as per regime ● Symptomatic treatment as required 	As day 2	<ul style="list-style-type: none"> ● No further medication unless objective withdrawals present. If observed 0.2 mgs four times a day ● May be considered with a reduction of 1 tablet daily.

Lofexidine regime

Time / Day	08.00	14.00	18.00	22.00	TOTAL TABLETS (200 micrograms)
DAY 1	2	2	2	2	8
DAY 2	3	2	2	3	10
DAY 3	3	3	3	3	12
DAY 4	3	3	3	3	12
DAY 5	3	2	2	3	10
DAY 6	2	2	2	2	8
DAY 7	0	0	0	0	0

Additional short-term medication for symptoms such as stomach cramps and diarrhoea may be required. Withdrawal symptoms can be monitored using the Clinical Opiate Withdrawal Scale (COWS) as detailed in [Appendix 1](#), which provides a comparison over time.

Appendix 8: Community Drug Service contact details

Change Grow Live – Community Drug Service

Please note that the opening hours for all services below are 9am to 5pm.

CGL Coventry
1a Lamb street
Coventry
CV1 4AE
02476 010241

CGL Rugby
35-37 Albert Street
Rugby
CV21 2SG
01926 353513

CGL Nuneaton
112 Abbey Street
CV115BX.
Nuneaton
01926353513

CGL Leamington Spa
16 Court Street
Leamington Spa
CV 312BB
01926 353513