

METHADONE & BUPRENORPHINE in-patient prescribing guideline

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1. Aim of this document

The aim of this document is to provide guidance to doctors and other clinicians on the prescribing aspects of methadone or buprenorphine for patients admitted to medical or psychiatric wards and presenting with a history of opiate dependence.

This document focuses mostly on the prescribing aspects of Methadone as opioid substitute for opioid dependence. This is the most common scenario that clinicians are likely to face in medical wards where buprenorphine is considered clinically less suitable because of its potential interactions with other pain relief medications. However, in psychiatric wards patients could choose either opiate substitute.

2. Key points

While hospitalisation can offer an excellent opportunity to engage a patient in starting specialist treatment of dependence, hospital/psychiatric doctors are strongly encouraged only to initiate Methadone/Buprenorphine as part of, or with clear advice and support from, a specialist drug treatment team (either through any liaison service available or by contacting the relevant community drug service).

Appropriate communication between key professionals in hospital and in the community, particularly around time of entry to hospital and around discharge, is vital to ensure safe, effective and seamless care, including making appropriate plans for seamlessly and safely continuing Methadone/Buprenorphine prescribing in the community

Patients may withhold information for fear of being stigmatised, judged or inviting unwanted interference from outside services, such as the police or social services. Confidentiality issues should be addressed sensitively and clearly.

People who use drugs have the same entitlement as other patients to the services provided by the NHS, including access to adequate symptomatic and pain relief, and to proper discharge planning. It is the responsibility of all doctors and other clinicians to provide the appropriate care for both general health needs and for relevant drug related health problems, whether or not the patient is ready to stop using drugs.

3. Choosing an appropriate opioid substitute for heroin or other opioids dependence

Methadone and buprenorphine are both effective at achieving positive outcomes in heroin dependent individuals. Both are cost-effective and recommended, for example, by NICE, for the treatment and prevention of withdrawals from heroin and for maintenance programmes.

While there is accumulating evidence that buprenorphine is associated with reduced risk of fatal overdose in the first weeks of treatment initiation, there is also evidence that methadone is more effective in retaining patients in treatment and so may indirectly reduce risks longer term for those patients. Currently, there remains insufficient evidence to justify recommending one drug over the other.

Also, some patients hold strong views against starting buprenorphine and others against starting methadone. Because of the lack of decisive discriminating evidence of greater effectiveness or of better patient safety, and because other factors also affect preference, there is no simple formula that can be recommended to determine the suitable clinical choice of methadone or buprenorphine.

Unlike for heroin, there is insufficient evidence to give clear definitive advice on the specific substitute opioids to prescribe for cases of dependence following excessive or illicit use of other opioids. Alternative opioids other than buprenorphine or methadone are sometimes prescribed in

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such cases after taking careful account of a patient’s circumstances and preferences. Individual clinicians will take account of the potency of the problem opioids and context of use (such as over-the-counter codeine or prescribed dihydrocodeine), evidence of severity of dependence, risks involved such as injecting, other comorbid conditions (including pain management), patient acceptability, treatment goal and other factors.

The limits of the evidence base should be discussed and a clinical judgement made with the patient. When any such opioid is prescribed ‘off label’, local policies on the use of unlicensed and off label medicines will need to be followed and it requires clear advice and support from, a specialist drug treatment team (either through any liaison service available or by contacting the relevant community drug service).

4. Signs of opiate withdrawal

DO NOT PRESCRIBE METHADONE UNTIL A DRUG / ALCOHOL ASSESSMENT HAS BEEN COMPLETED.

A drug assessment should include history of drugs taken during the last four weeks (frequency of use, amount, route) – if intravenous drug user (IDU) ask about sharing of injection equipment, history of withdrawal or overdoses, previous drug history including period of abstinence and treatments, blood born viruses (BBV) Hep B, C and HIV screening/status. An assessment should include a physical examination, a urine drug screen and blood testing.

While each case must be judged on its merits, there will often be no need to prescribe methadone within the first 24 hours of an emergency admission. This will allow baseline observations to be made and will act as a safety device. The purity of ‘street’ drugs cannot be guaranteed and the patient may or may not have taken any dose prescribed (if receiving treatment).

For safety, rely more on OBJECTIVE signs of opiate withdrawal	Do Not rely on what patient says, i.e. SUBJECTIVE signs of opiate withdrawal
<ul style="list-style-type: none"> • Yawning • Coughing • Sneezing • Running nose • Watering eyes • BP raised • Pulse increased • Dilated pupils • Cool/clammy skin • Diarrhoea • Nausea • Fine muscle tremor 	<ul style="list-style-type: none"> • Insomnia • Depression, • Drug craving • Abdominal cramps • Restlessness • Irritability • Anxiety

The Clinical Opiate Withdrawal Scale (COWS) is a validated tool which limits possibility of ‘pretended’ responses by combining subjective symptoms with objective signs (Appendix 3).

Prescribing symptomatically can reduce some of the physical effects of withdrawal, e.g.

- **Diarrhoea:** Loperamide 4mg stat followed by 2mg after each loose stool for up to five days; usual dose 6-8mg daily, max. 16mg daily.
- **Nausea and vomiting:** Domperidone 10mg up to three times per day or Metoclopramide 10mg eight-hourly or prochlorperazine 5mg ORALLY three times a day or 12.5mg IM 12-hourly.
- **Stomach cramps:** Mebeverine 135mg up to three times per day or Hyoscine N-butylbromide 20mg four times a day

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- **Agitation/anxiety and insomnia:** Diazepam (oral) up to 5-10mg THREE times daily when required or zopiclone 7.5mg at bedtime. **BE CAUTIOUS IF PATIENT ALREADY PRESCRIBED METHADONE AND AVOID CO-PRESCRIBING DURING INITIATION OF METHADONE** because possible interactions and risk of respiratory depression.
- **Muscular pains and headaches:** Non-steroidal anti-inflammatory drugs (Ibuprofen). Topical rubefacients, e.g. “Deep Heat” can be helpful for relieving muscle pain associated with methadone withdrawal.
- **Poor nutrition/malnourished:** Dietary supplementation including nutritional drinks.

5. Methadone

5.1 Patients already on Methadone treatment

For patients currently being prescribed methadone for treatment of opiate dependency, good communication between hospital and community is essential for safe patient care.

This should be a relatively straightforward matter of continuing the usual dose while in hospital, provided the safety notes described in these guidelines are observed. In addition, the doctor should ascertain by independent means (e.g. the patient’s Substance Misuse Service (SMS) doctor and/or pharmacist) the prescribed daily dose and, if possible, when the last dose of methadone was swallowed or, at least, when last script was issued and how many days have been supplied.

All patients would have a named key-worker from the local Substance Misuse service and an allocated community pharmacy from where they collect their prescriptions.

- Patients should not bring methadone into hospital with them; therefore, it is not necessary for a SMS to bulk-prescribe for a patient in advance of admission to hospital.
- Contacting the prescriber will help ensure that relevant information is communicated and that arrangements can be put in place for smooth discharge.
- If the patient claims to have been receiving methadone under supervision in a community pharmacy prior to admission ALWAYS confirm this with the community pharmacist before prescribing any methadone.
- Contacting the patient’s key-worker (via the substance misuse service) is strongly advised, as they will be able to provide advice and background to the patient. This will greatly facilitate the assessment process and the procedure on discharge.
- On occasions patients may wish to take the opportunity of a hospital admission to reduce or detoxify 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, which exposes the patient to a substantial risk of overdose. This should be explained to the patient to ensure they are able to give properly informed consent to their decision to detoxify in these circumstances.

5.2 Patients NOT previously prescribed Methadone

Do NOT prescribe methadone until a drug/alcohol assessment has been completed. If you do, the patient may suffer a respiratory arrest from an overdose, which may be deceptively slow in onset.

In most circumstances, it should not be necessary to prescribe opiates or other controlled drugs to treat opiate withdrawal in a drug misuser in the A & E Department or within 24 hours of admission.

A decision to prescribe methadone for patients not previously prescribed methadone should only be taken senior medical advice (Consultant) .This is not only because of the risks associated with initiation of Methadone but because the patient will need a named substance misuse service key-worker before a SMS doctor/ Non-Medical Prescriber (NMP) will be willing to take on the

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management, treatment and prescribing of methadone once the patient is discharged from hospital. Liaising with the substance misuse service while the patient is in hospital will not guarantee that the SMS doctor/ NMP will be willing to take on the patient but may facilitate the process and is therefore strongly advised.

5.3 Initial methadone dosing schedule for Opiate Dependent Patients admitted to Hospital

SAFETY FIRST: Do not give in to pressure to prescribe immediately. Take time to assess.

- Polydrug users and alcohol misusers may develop multiple withdrawal syndromes and you will need to differentiate. Methadone may mask alcohol and benzodiazepine withdrawal symptoms.
- Do not try to match your prescription with the dose of an opiate an individual claims to have been taking.
- Do NOT use tables of equivalent doses, as these can be misleading.
- TAKE GREAT CARE!!! Especially in cases of respiratory disease, head injury and liver diseases.
- Be extremely careful when giving other analgesics or sedatives. Contact acute pain control team if available in your locality or with your Pharmacist for further advice on additional pain control.
- For pregnant patients please seek senior medical advice and liaise with Consultant and/or Addiction Consultant.
- Inappropriate dosing can result in overdosing in the first few days, cumulative toxicity develops to methadone. There is no uniquely fatal dose of methadone and deaths have occurred following doses as little as 20 mg.
- In general the initial dose will be in the range of 10-30 mg.
- After initial induction (over three to four days) allow time for methadone levels to reach steady-state (5-7 days) then reassess. DO NOT keep increasing dose over first week.
- Prescribe methadone in milligrams (not mls) of 1mg per ml mixture as wards may hold stocks of more concentrated strengths of methadone mixture. A 10-times error will be potentially fatal.
- Ensure the patient is observed swallowing the prescribed dose – by asking the patient to speak and/or drink water immediately afterwards.
- Signs of intoxication such as drowsiness, slurred speech or constricted pupils indicate a need to discontinue the drug or reduce dosage.
- BE AWARE OF ILLICIT DRUG USE ON THE WARD – this is not uncommon!

DAY	TIME	SUGGESTED DOSING	REMARKS
1	0	Do Not prescribe immediately	Take time to assess
2	24+	If COWS score >20 they should be given a starting dose of 10-20mgs (1mg=1ml).	Usual initial dose, and possibly all that will be needed on a daily basis thereafter
	28+ 32+	Additional 5-10 mg may be needed after four hours (and occasionally eight hours) if COWS score >20	Sometimes necessary if persistent OBJECTIVE withdrawal signs are evident
3 & 4	48+	Same as Day 2, total daily dose (=10 to 30 mg).	Be prepared to reduce even STOP the drug on day three

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		Maximum 3 rd day = 30 mg.	and/or day four. Give as single dose in the morning. Watch for signs of intoxication
5	96+	Previous dose +/- 5-10 mg Maximum 3 rd day = 30 mg.	Adjust dose up (if COWS score >20) or down (signs of intoxication) depending on the previous dose and the patient's response. Typical final required dose is 30-40 mg once daily (Do NOT exceed of 30mg without Consultant advice. Alternatively contact SMS Consultant)
6 & 7		Same as Day five	
8		Previous dose +/- 5-10 mg	Adjust dose up or down depending on the previous dose and the patient's response (COWS scoring)
Onwards			Do NOT increase further without close consultation with the local SMS service. Higher dose only used in severe cases and by experienced prescribers. Maximum increase per day is 10 mg. Maximum increase per week is 30 mg.

- **Always include naloxone on the prescription**, in case of overdose: dose 400micrograms SC/IM; if no response after 1 minute give 800 micrograms, and if still no response after another 1 minute, repeat dose of 800micrograms; if still no response give 2mg (4mg may be required in a seriously poisoned patient). See Trust guidance on [InTouch](#) (TEVV staff) or [Trust website](#) (other Trust staff) for further guidance. Use EWS to monitor vital signs and level of consciousness.
- In cases of overdose/suspected overdose, patient must be observed for a period of up to 72 hours because of long half-life of methadone. Be prepared to give repeated large doses of naloxone (see BNF or guidance linked above).

Pharmacists can provide advice on drug interactions for example rifampicin, phenytoin, phenobarbital and some antiviral drugs speed up elimination. Other drugs such as fluvoxamine and fluoxetine may have the opposite effect.

5.4 Risk factors for methadone

The risk factors for overdose during induction are:

- Low opioid tolerance
- Use of CNS depressant drugs, including alcohol
- Too high an initial dose
- Increases in dose that are too rapid
- Slow methadone clearance.

There is an increased risk of death during induction into methadone treatment and a consistent finding is that multiple drugs, particularly benzodiazepines and alcohol, are usually involved. Opioids induce respiratory depression and hypoventilation, and sedative drugs (including alcohol) potentiate this effect.

With methadone, toxicity is delayed, at least several hours after exposure, and often after several days of treatment. The reason for the delayed toxicity is methadone's long but

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variable half-life, measured at between 13 and 50 hours with chronic administration. Variation can occur between individuals and within an individual. The half-life can be affected by other factors such as alcohol consumption or other drugs taken. It takes five half-lives, or 3–10 days, for patients on a stable dose of methadone to reach steady state blood levels. The slower methadone is cleared, the longer it takes to reach steady state and the higher the steady state blood levels.

During those 3–10 days, blood levels progressively rise even if patients remain on the same daily dose (Figure 1). A dose tolerated on day one may become a toxic dose on day three. Patients must therefore be carefully monitored and, if necessary, the dosage adjusted during the accumulation period. There are many factors affecting methadone metabolism and action, and most are not currently predictable on history and examination. They mean that patients can have markedly different responses to the same dose of methadone and their responses can vary over time.

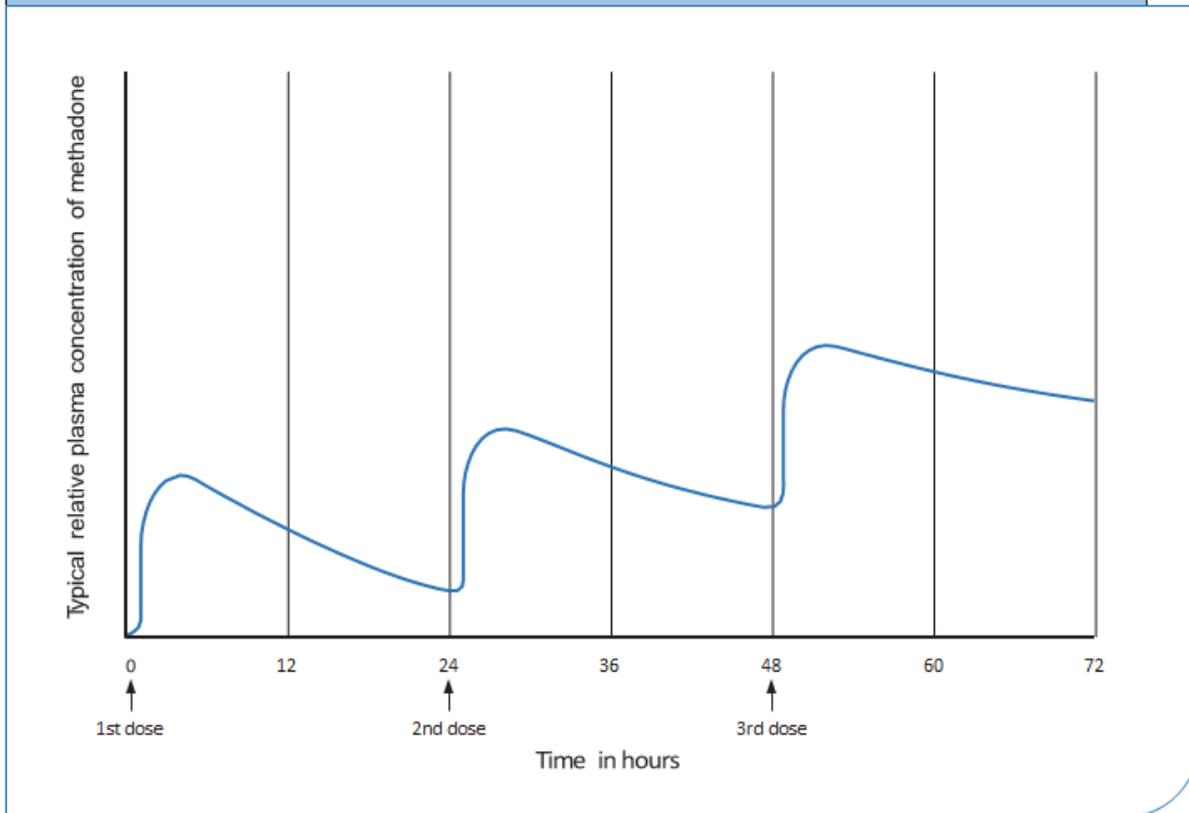
Drug interactions can slow or speed methadone metabolism, or can potentiate toxicity. See appendix 2 for more information, alternatively please use the following link http://fileserver.idpc.net/library/clinical_guidelines_2017.pdf. However, the critical factor in response to methadone is the degree of tolerance to opioids. It is in individuals with low tolerance that a starting dose that would be safe in the majority of patients can become a toxic dose.

Risks during induction can be minimised by:

- Careful initial assessment
- Identification of high-risk patients
- Avoiding too high starting doses
- Avoiding too rapid dose increases
- Frequent monitoring during induction
- Supervised consumption
- Alerting patients and carers to the early signs of overdose.
- High-risk cases require greater supervision.

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Figure 1. First three days of dispensing, for oral methadone, with once-daily dosing (doses at 0, 24, 48



5.5 Risks of QTc prolongation with methadone

Opioids including methadone can affect cardiac conductivity which could, in some cases, result in a prolonged QTc interval. Prolonged QTc interval has been shown to increase the risk of torsade de pointes and sudden cardiac death. This is thought to be a dose-related effect (i.e. higher opioid doses increase risk) but several factors, including age or co-prescribing, may exacerbate this risk.

Clinicians, either at initial assessment or prior to induction, can consider use of an ECG where they have concerns, in which case they can act in line with MHRA advice:

“... that patients with the following risk factors for QT interval prolongation are carefully monitored while 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. Further advice is included in the product information.” (MHRA 2006)

Clinicians must make a balanced judgement for each patient according to current relevant guidance. Monitoring will usually include checking other medications, general monitoring of cardiovascular disease (blood pressure and pulse), liver function tests and urea and electrolytes.

As the risk factors for QTc prolongation increase (such as with daily doses of methadone above 100mg or in the presence of multiple risk factors for QTc prolongation) clinicians will need to consider ECGs, and these may be carried out in some before induction onto methadone, and for others before increases in methadone dose (and then subsequently after stabilisation)

5.6 Patients already on methadone and presenting with missed doses or lost prescriptions

Missed doses can be associated with the emergence of an opioid withdrawal syndrome after two

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or three days, and it can take up to three days for blood levels to return to normal.

- If a person misses doses of methadone or buprenorphine:
- Do not replace the missed doses (i.e. do not give a double dose the next day).
- It may be appropriate to assess the person to find out why this occurred, especially if several doses have been missed.
- Ensure they are not intoxicated before prescribing.
- Assess for symptoms and signs of withdrawal.

1, 2, or 3 days: the usual dose may be given. If a patient on a daily dispensing regimen misses a pick-up from the pharmacy, the patient should resume the daily prescribed dose the next day as usual. The missed dose should not be replaced.

4 days: it may be appropriate to reduce the dose and titrate back up to the original dose as their tolerance may be reduced or lost. Often the person who uses drugs claims to have used street drugs, but this can never be verified or the purity known. If doses are missed for more than three days, then treatment should be reviewed to discover how the patient has managed without medication and to consider recommencing from a lower dose.

5 days or more: If doses are missed for five days or more, a re- assessment must be undertaken and consideration given to restarting the medication.

Patients admitted who have their methadone dispensed weekly should bring methadone to the ward where it should be secured or disposed of appropriately. A urine test must confirm compliance with this medication. If urine is negative for methadone and/or there are concerns with compliance with treatment patient should be commenced on symptomatic medication ONLY and consult SMS Team (SMS Consultant) for expert advice.

6. Buprenorphine

6.1 Patients already on Buprenorphine treatment.

For patients currently being prescribed buprenorphine for treatment of opiate dependency, good communication between hospital and community is essential for safe patient care.

This should be a relatively straightforward matter of continuing the usual dose while in hospital, provided the safety notes described in these guidelines are observed. In addition, the doctor should ascertain by independent means (e.g. the patient's Substance Misuse Service (SMS) doctor and/or pharmacist) the prescribed daily dose and, if possible, when the last dose of buprenorphine was taken or, at least, when last script was issued and how many days have been supplied.

All patients would have a named key-worker from the local Substance Misuse service and an allocated community pharmacy from where they collect their prescriptions.

- Patients should not bring buprenorphine into hospital with them; therefore, it is not necessary for a SMS to bulk-prescribe for a patient in advance of admission to hospital.
- Contacting the prescriber will help ensure that relevant information is communicated and that arrangements can be put in place for smooth discharge.
- If the patient claims to have been receiving buprenorphine under supervision in a community pharmacy prior to admission ALWAYS confirm this with the community pharmacist before prescribing any buprenorphine.

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- Contacting the patient’s key-worker (via the substance misuse service) is strongly advised, as they will be able to provide advice and background to the patient. This will greatly facilitate the assessment process and the procedure on discharge.
- On occasions patients may wish to take the opportunity of a hospital admission to reduce or detoxify 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, which exposes the patient to a substantial risk of overdose. This should be explained to the patient to ensure they are able to give properly informed consent to their decision to detoxify in these circumstances.

6.2 Patients NOT previously prescribed Buprenorphine

Do NOT prescribe buprenorphine until a drug/alcohol assessment has been completed.

In most circumstances, it should not be necessary to prescribe opiates or other controlled drugs to treat opiate withdrawal in a drug misuser in the A & E Department or within 24 hours of admission.

A decision to prescribe buprenorphine for patients not previously prescribed should only be taken senior medical advice (Consultant). This is not only because possible interactions with other opioids and likelihood of withdrawals but because the patient will need a named substance misuse service key- worker before a SMS doctor/ Non-Medical Prescriber (NMP) will be willing to take on the management, treatment and prescribing of buprenorphine once the patient is discharged from hospital. Liaising with the substance misuse service while the patient is in hospital will not guarantee that the SMS doctor/ NMP will be willing to take on the patient but may facilitate the process and is therefore strongly advised.

6.3 Initial buprenorphine dosing schedule for Opiate Dependent Patients admitted to Hospital (appendix 5)

SAFETY FIRST

- Do not give in to pressure to prescribe immediately. Take time to assess.
- Polydrug users and alcohol misusers may develop multiple withdrawal syndromes and you will need to differentiate. Buprenorphine withdrawal may mask alcohol and benzodiazepine withdrawal symptoms. .
- Do not try to match your prescription with the dose of an opiate an individual claims to have been taking.
- TAKE GREAT CARE!!! Especially in cases of respiratory disease, head injury and liver diseases.
- Be extremely careful when giving other analgesics or sedatives. Contact acute pain control team if available in your locality or with your Pharmacist for further advice on additional pain control.
- For pregnant patients please seek senior medical advice and liaise with Consultant and/or Addiction Consultant.

The guidance given here applies to patients within normal ranges of body weight, body mass index and liver and kidney function. Patients outside the normal ranges may need to have

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their dose adjusted up or down accordingly, although such variations are usually small and taken care of by normal induction flexibilities.

A cautious approach is to initiate treatment with 4mg on day one, then 8-16mg on day two and thereafter.

Dividing the daily dose may be useful as it may reduce precipitated withdrawal.

Effective maintenance treatment with buprenorphine involves doses in the range of 12-16mg for most patients dependent on heroin. It makes sense to work towards this dose rapidly, so long as this does not produce side-effects or precipitated withdrawal.

There is limited evidence for the effectiveness of adjunctive medications alongside the OST agent of choice, for the management of symptoms associated with withdrawal. The prescribing of other opioids, or any other respiratory depressant drugs, during induction onto buprenorphine treatment is therefore not recommended.

6.4 Buprenorphine-naloxone

A form of buprenorphine is available which includes the opioid antagonist naloxone (buprenorphine:naloxone 4:1) in a combined sublingual tablet. This form is for use at the same buprenorphine dose (the current 8mg sublingual buprenorphine being considered approximately as the same therapeutic dose as the combination of 8mg buprenorphine plus 2mg naloxone). The rationale is that, when taken sublingually as intended, the naloxone has very low bioavailability and has minimal effect and does not diminish the therapeutic effect of the buprenorphine. However, if injected, the naloxone has high bioavailability and is liable to precipitate withdrawal in an opiate-dependent patient, therefore discouraging further misuse by injection. Consequently, the combination tablet is expected to provide the same therapeutic benefit while reducing the liability for misuse. Clinical experience since its introduction suggests this formulation may add value when supervised dispensing is difficult to deliver or where there is concern about a patient's risk of reverting to injecting.

DAY	TIME	SUGGESTED DOSING	REMARKS
1	0	Do Not prescribe immediately	Take time to assess
2	24+	If COWS score >20 they should be given a starting dose of 2-4 mg buprenorphine or buprenorphine/naloxone	Buprenorphine: The total dose of buprenorphine monotherapy on day 1 must not exceed 4 mg Buprenorphine/naloxone: the BNF allows to give a second dose of 4 mg
3 onwards	28+ 32+	Buprenorphine: Increase by 2-4 mg per day until stable (max. 32 mg per day) Buprenorphine/naloxone: Increase by 2-8 mg per day until stable (max. 24 mg per day)	For doses higher than 16 mg please contact discuss with Consultant and/or contact with Specialist Substance Misuse Service
As soon as possible		Liaise with specialist addiction service and develop joint management plan Do not exceed previous community dose unless agreed with the addiction service	

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- In general the initial dose will be in the range of 8-16 mg.
- Ensure the patient is observed and that the tablet has dissolved sublingually.
- Signs of intoxication such as drowsiness, slurred speech will indicate a possible interactions with other substances i.e. benzodiazepines. In this case discontinue the drug or reduce dosage.
- BE AWARE OF ILLICIT DRUG USE ON THE WARD – this is not uncommon!
- Although the risk of overdose with buprenorphine is very low **always include naloxone on the prescription** because possible misuse of other opioids whilst in the ward, in case of overdose: dose 400micrograme SC/IM; if no response after 1 minute give 800 micrograms, and if still no response after another 1 minute, repeat dose of 800micrograms; if still no response give 2mg (4mg may be required in a seriously poisoned patient). See Trust guidance on [InTouch](#) (TEWV staff) or [Trust website](#) (other Trust staff) for further guidance. Use EWS to monitor vital signs and level of consciousness.

Pharmacist can provide advice on drug interactions with other opioids.

6.5 Risk factors for buprenorphine

High dose buprenorphine may cause changes in liver function in individuals with a history of liver disease. Ideally, such patients should have a liver function test (blood test) before commencing with follow-up investigations conducted 6–12 weeks after commencing.

Buprenorphine should not be given to any patient showing signs of intoxication.

Buprenorphine in combination with other sedative drugs can result in respiratory depression, sedation, coma and death.

6.6 Overdose with Buprenorphine

Buprenorphine as a single drug in overdose is generally regarded as safer than methadone and heroin because it causes less respiratory depression. However, in combination with other respiratory depressant drugs the effects may be harder to manage. Very high doses of naloxone (e.g. 10–15 mg) may be needed to reverse buprenorphine effects in addition to ventilator support.

6.7 Precipitated withdrawal

Precipitated withdrawal occurs when buprenorphine is first administered to an opiate-dependent person with circulating opioid agonist drugs present. In this situation, buprenorphine can inhibit the opioid actions of the full agonist without adequately replacing them, leading to the appearance of withdrawal signs and symptoms.

Precipitated withdrawal can be very unpleasant and may deter patients from continuing participation in treatment. There are three measures to minimise precipitated withdrawal:

- Administer the first dose of buprenorphine when the patient is exhibiting signs of withdrawal. The administering clinician/pharmacist needs to emphasise this point when supervising medication.
- If withdrawal is difficult for the patient to tolerate, delay the administration of buprenorphine until at least 6-12 hours after the last use of heroin (or other short-

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acting opioid), or 24-48 hours after the last dose of low-dose methadone.

- c) Provide the anticipated day's doses, for the first day or two, in divided amounts (typically using 2mg tablets) so the patient can manage the speed of the induction themselves.

In all cases, patients should be supported and encouraged, provided with information about precipitated withdrawal and informed that, if their discomfort is risking drop out of treatment, they could be seen for review early and treatment could be adjusted or could be changed to methadone.

6.8 Patients already on buprenorphine and presenting with missed doses or lost prescriptions

If a person misses doses of buprenorphine or buprenorphine:

- Do not replace the missed doses (i.e. do not give a double dose the next day).
- It may be appropriate to assess the person to find out why this occurred, especially if several doses have been missed.
- Ensure they are not intoxicated before prescribing.
- Assess for symptoms and signs of withdrawal.
 - **1, 2, or 3 days:** the usual dose may be given. If a patient on a daily dispensing regimen misses a pick-up from the pharmacy, the patient should resume the daily prescribed dose the next day as usual. The missed dose should not be replaced.
 - **4 days:** it may be appropriate to reduce the dose and titrate back up to the original dose as their tolerance may be reduced or lost. Often the person who uses drugs claims to have used street drugs, but this can never be verified or the purity known. If doses are missed for more than three days, then treatment should be reviewed to discover how the patient has managed without medication and to consider recommencing from a lower dose.
 - **5 days or more:** If doses are missed for five days or more, a re-assessment must be undertaken and consideration given to restarting the medication.

If buprenorphine is brought to the ward it should be secured or disposed of appropriately. A urine test must confirm compliance with this medication. If urine is negative for buprenorphine and/or there are concerns with compliance with treatment patient should be commenced on symptomatic medication ONLY and consult SMS Team (SMS Consultant) for expert advice

7. References

1. Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017) Drug misuse and dependence: UK guidelines on clinical management. London: Department of Health.
2. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). JPsychoactive Drugs. Taylor & Francis Group; 2003 Apr;35(2):253–9.

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3. Guidance for the use of methadone for the treatment of opioid dependence in primary care. London: Royal College of General Practitioners; 2011.
4. Group BSMP. Management and Treatment of Substance Misuse in Berkshire. 2001.
5. National Institute for Health, Clinical Excellence NICE. Methadone and buprenorphine for the management of opioid dependence. 2007 Jan.

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Appendix 1: Clinical Opiate Withdrawal Scale (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient Name:

Date:

Enter scores at time zero, 30min after first dose, 2 h after first dose, etc.

	Times:			
Resting Pulse Rate: (record beats per minute) Measured after patient is sitting or lying for one minute 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120				
Sweating: over past ½ hour not accounted for by room temperature or patient activity. 0 - no report of chills or flushing 1 - subjective report of chills or flushing 2 - flushed or observable moistness on face 3 - beads of sweat on brow or face 4 - sweat streaming off face				
Restlessness: Observation during assessment 0 - able to sit still 1 - reports difficulty sitting still, but is able to do so 3 - frequent shifting or extraneous movements of legs/arms 5 - Unable to sit still for more than a few seconds				
Pupil size 0 - pupils pinned or normal size for room light 1 - pupils possibly larger than normal for room light 2 - pupils moderately dilated 5 - pupils so dilated that only the rim of the iris is visible				
Bone or Joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored 0 - not present 1 - mild diffuse discomfort 2 - patient reports severe diffuse aching of joints/ muscles 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: Not accounted for by cold symptoms or allergies 0 - not present 1 - nasal stuffiness or unusually moist eyes 2 - nose running or tearing 4 - nose constantly running or tears streaming down cheeks				
GI Upset: over last ½ hour 0 - no GI symptoms 1 - stomach cramps 2 - nausea or loose stool 3 - vomiting or diarrhea 5 - Multiple episodes of diarrhea or vomiting				

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Tremor: observation of outstretched hands 0 - No tremor 1 - tremor can be felt, but not observed 2 - slight tremor observable 4 - gross tremor or muscle twitching				
Yawning: Observation during assessment 0 - no yawning 1 - yawning once or twice during assessment 2 - yawning three or more times during assessment 4 - yawning several times/minute				
Anxiety or Irritability 0 - none 1 - patient reports increasing irritability or anxiousness 2 - patient obviously irritable anxious 4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin 0 - skin is smooth 3 - piloerection of skin can be felt or hairs standing up on arms 5 - prominent piloerection				
Total scores with observer's initials				

Score:

5-12 = mild;

13-24 = moderate;

25-36 = moderately severe;

more than 36 = severe withdrawal

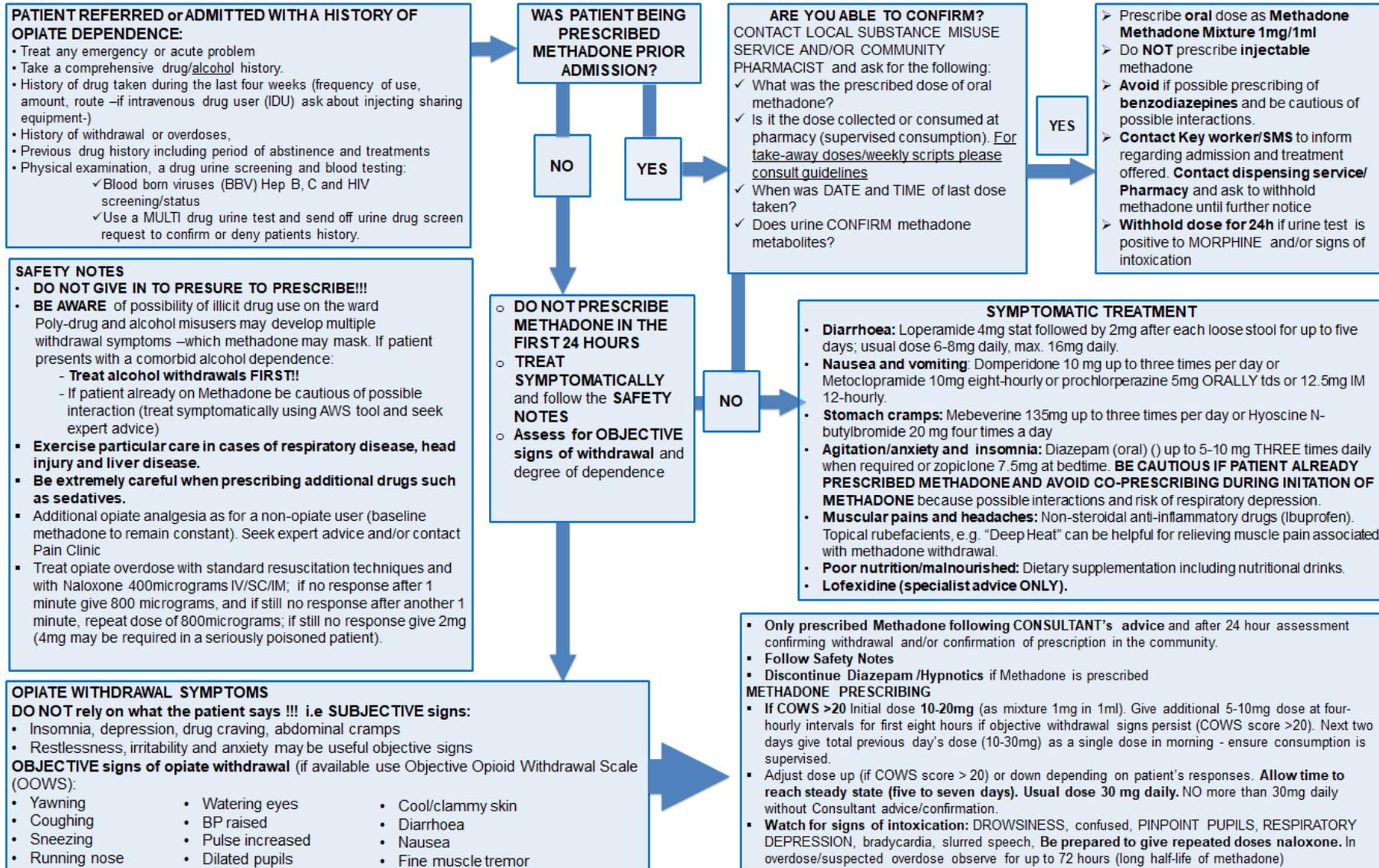
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Appendix 2: Drug Interactions

Opioid interaction	Examples	Opioids affected	Mechanism	Effect
Other medicines (and substances) that depress the CNS	Other opioids Benzodiazepines Tricyclic antidepressants Antipsychotics Older antihistamines Alcohol	All	Increased CNS depression	Additive effect – potentiation of respiratory depression
Medicines that increase opioid levels	Cimetidine Ciprofloxacin Erythromycin Clarithromycin Fluconazole Ketoconazole SSRIs: fluoxetine, fluvoxamine, paroxetine and sertraline.	Methadone Buprenorphine	Increased blood levels of methadone or buprenorphine by inhibition of the enzyme CYP3A4	Dose of methadone or buprenorphine may need to be decreased to prevent toxicity or overdose AND may need to be increased to prevent withdrawal symptoms when the enzyme inhibitor is stopped
Medicines that decrease opioid levels	Anticonvulsants (e.g. barbiturates, carbamazepine, phenytoin) HIV medicines (e.g. efavirenz, nevirapine) Rifampicin Spironolactone St John's Wort	Methadone Buprenorphine	Decreased blood levels of methadone or buprenorphine by induction of enzyme CYP3A4	Dose of methadone or buprenorphine may need to be increased to prevent withdrawal symptoms AND decreased to prevent overdose when the enzyme inducer is stopped
Opioids that act as partial agonists	Buprenorphine and other partial opioid agonists	Methadone Diamorphine Other full agonists	Buprenorphine is a partial agonist and displaces other opioids from receptor sites	Can precipitate withdrawal symptoms – advise waiting until opioid is excreted (confirmed by presence of withdrawal symptoms) before taking buprenorphine
Opioid antagonists	Naltrexone (active orally) Naloxone (active by injection – IV, IM and SC)	All	Naltrexone and naloxone are full antagonists and displace other opioids from receptor sites	Will precipitate withdrawal symptoms if taken when agonist or partial agonists have recently been taken
Medicines affecting QTc interval	Tricyclic antidepressants Antipsychotic medicines	Methadone	Prolongation of QTc interval	Can cause torsades de pointes. Use cautiously with methadone – see section 3.5 and annex A2
Medicines affecting urine pH	Vitamin C Sodium bicarbonate (antacids)	Methadone	Affects excretion of methadone – increased excretion in acidic urine, decreased excretion in alkaline urine	Increased excretion may cause withdrawal Decreased excretion may cause toxicity

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Appendix 3: Prescribing METHADONE for patients with opiate dependence in Psychiatric or Medical Wards

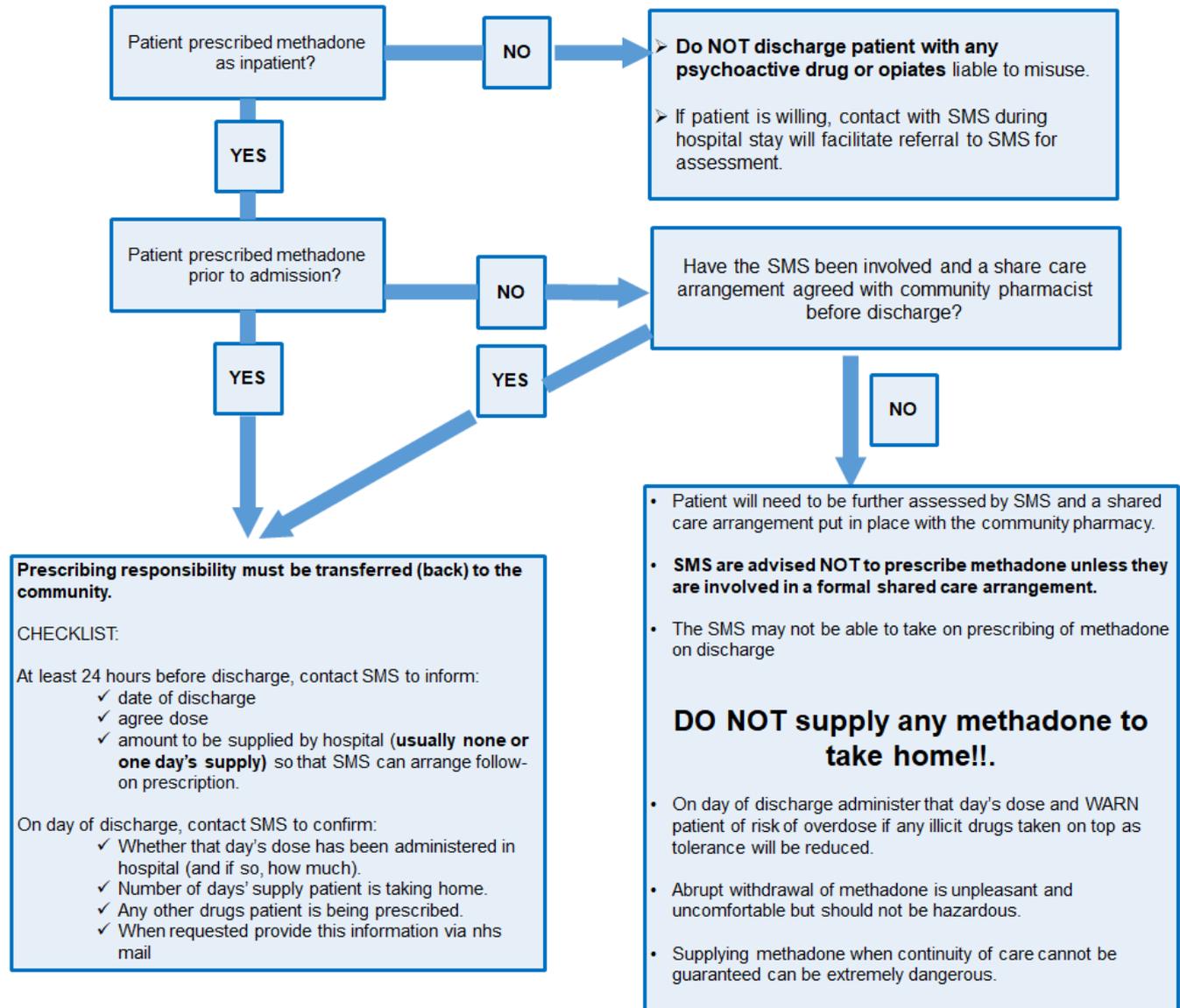


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Appendix 4: Methadone discharge procedure

While in Hospital:

- Maintain links with the substance misuse service - helps appropriate arrangements to be in place at discharge.
- Provide advice and information on:
 - Prevention of overdose (tolerance to opiates reduced rapidly). WARN patient of risks of returning to previous illicit/prescribed dose or using 'on top'.
 - Contacts for further help, e.g. substance misuse service (SMS), alcohol services, GUM clinic, HIV/Hepatitis B/C follow-up, needle exchange. Use opportunity for patient to link with other services.
 - Health promotion advice; Hepatitis B vaccination, HIV/Hepatitis C testing.
- For patients in Psychiatric wards having leave periods prior discharge:
 - Overnight leave (one/or two days) : Patient would have to come back to the ward for daily supervised consumption
 - Long leave periods: To consider daily supervised consumption at a local chemist close to patient's home. Contact SMS for advice regarding prescribing issues/requirements.



SAFETY NOTES

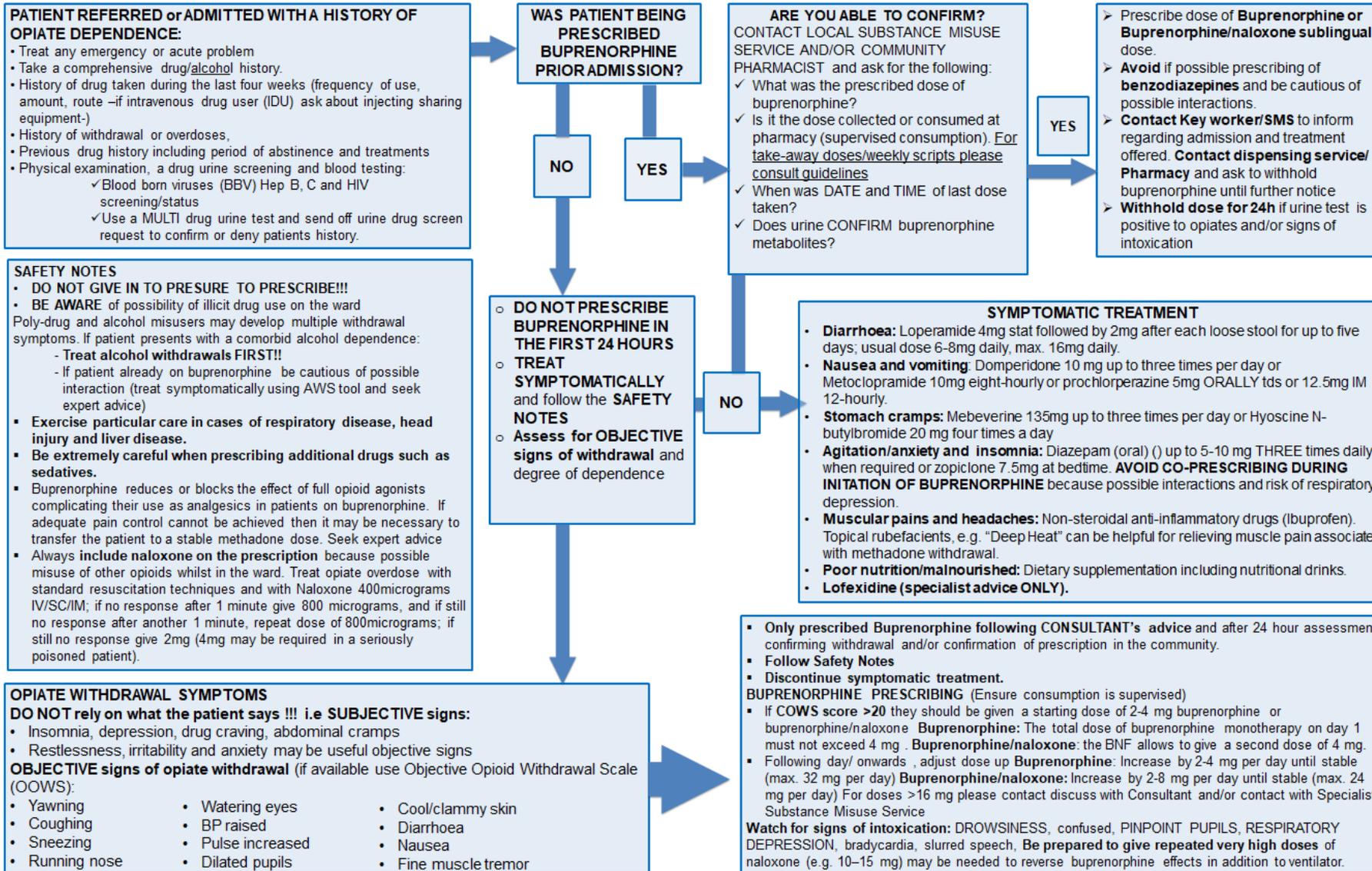
Aim to avoid risk of overdose by:

- ✓ Avoiding risk of patient receiving double dose on day of discharge.
- ✓ Warning patient of reduced tolerance if opiate use (illicit or prescribed) has reduced or stopped during hospital stay.
- ✓ Preventing patient from being in possession of large volumes of methadone which patient may be tempted to consume or pressured into handing over to someone else.

Aim to ensure continuity of treatment so patient is not tempted to obtain illicit supplies because doses are missed.

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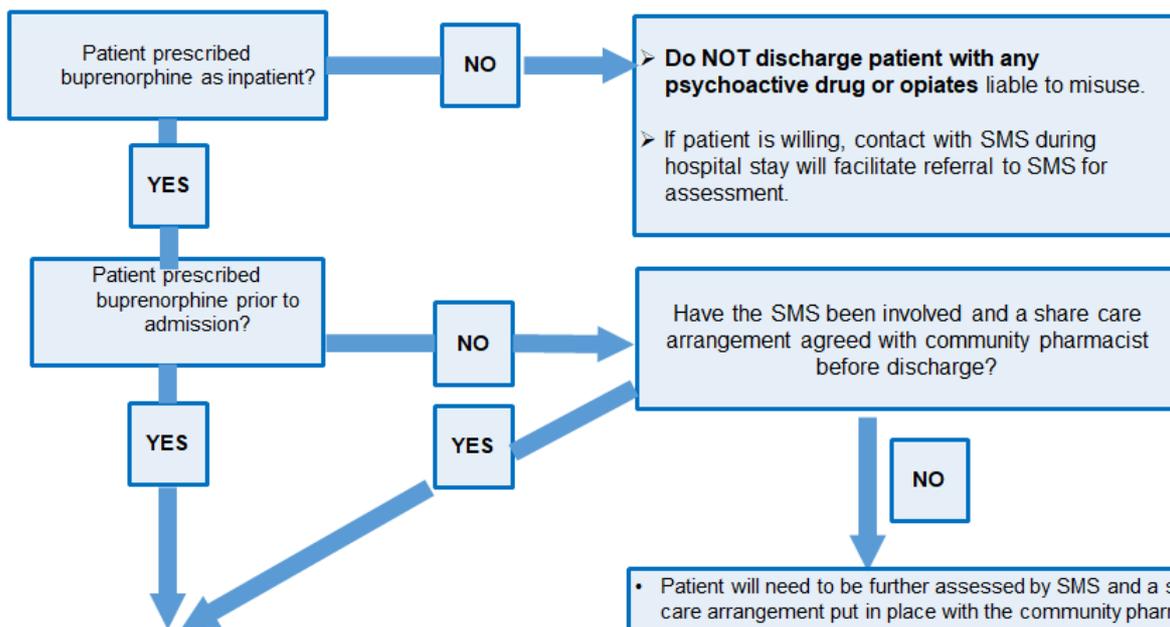
Appendix 5: Prescribing BUPRENORPHINE for patients with opiate dependence in Psychiatric or Medical Wards



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While in Hospital:

- Maintain links with the substance misuse service - helps appropriate arrangements to be in place at discharge.
- Provide advice and information on:
 - Prevention of overdose (tolerance to opiates reduced rapidly). WARN patient of risks of returning to previous illicit/prescribed dose or using 'on top'.
 - Contacts for further help, e.g. substance misuse service (SMS), alcohol services, GUM clinic, HIV/Hepatitis B/C follow-up, needle exchange. Use opportunity for patient to link with other services.
 - Health promotion advice; Hepatitis B vaccination, HIV/Hepatitis C testing.
- For patients in Psychiatric wards having leave periods prior discharge:
 - Overnight leave (one/or two days) : Patient would have to comeback to the ward for daily supervised consumption
 - Long leave periods: To consider daily supervised consumption at a local chemist close to patient's home. Contact SMS for advice regarding prescribing issues/requirements.



Prescribing responsibility must be transferred (back) to the community.

CHECKLIST:

At least 24 hours before discharge, contact SMS to inform:

- ✓ date of discharge
- ✓ agree dose
- ✓ amount to be supplied by hospital (**usually none or one day's supply**) so that SMS can arrange follow-on prescription.

On day of discharge, contact SMS to confirm:

- ✓ Whether that day's dose has been administered in hospital (and if so, how much).
- ✓ Number of days' supply patient is taking home.
- ✓ Any other drugs patient is being prescribed.
- ✓ When requested provide this information via nhs mail

- Patient will need to be further assessed by SMS and a shared care arrangement put in place with the community pharmacy.
- **SMS are advised NOT to prescribe buprenorphine unless they are involved in a formal shared care arrangement.**
- The SMS may not be able to take on prescribing of buprenorphine on discharge

DO NOT supply any buprenorphine to take home!!.

- On day of discharge administer that day's dose and WARN patient of risk of overdose if any illicit drugs taken on top as tolerance will be reduced.
- Abrupt withdrawal of buprenorphine is unpleasant and uncomfortable but should not be hazardous.
- Supplying buprenorphine when continuity of care cannot be guaranteed can be extremely dangerous.

SAFETY NOTES

Aim to avoid risk of overdose by:

- ✓ Avoiding risk of patient receiving double dose on day of discharge.
- ✓ Warning patient of reduced tolerance if opiate use (illicit or prescribed) has reduced or stopped during hospital stay.
- ✓ Preventing patient from being in possession of large amount of buprenorphine tablets which patient may be tempted to consume or pressured into handing over to someone else.

Aim to ensure continuity of treatment so patient is not tempted to obtain illicit supplies because doses are missed.

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