Pharmaceutical services for opioid drug users

Annual Update Briefing. Issue 4 2022-24

Introduction

The aim of this Annual Update Briefing is to:

- Support the pharmacy in meeting the training requirements in the supervised consumption and naloxone (Prenoxad) supply service specifications.
- Update staff on the latest national guidance and local practice on substance misuse.

Pharmacy service specification 2022-23 training requirements

For both services:

- A lead pharmacist (or for the naloxone supply service only – a lead registered pharmacy technician) should be assured that all staff are adequately trained to meet the requirements of the service.
- All pharmacy staff involved in the service are expected to read this Annual Update Briefing and consider any further training needs.
- Staff are expected to keep up to date with guidance / service changes (via information circulated on PharmOutcomes) and to assess their competence on an ongoing basis.
- For 2022 – 23, each staff member who accesses the PharmOutcomes template will be required to enrol. This enrolment will ask for confirmation of information from the lead pharmacist / lead registered pharmacy technician as described in the service specification.

For the supervised consumption service:

The lead pharmacist providing this service should have completed the CPPE substance use and misuse e-course (or a previous equivalent CPPE course):[1]

- Unit 1 – Individual experience of substance use and misuse
- Unit 2 – Risks and challenges of substance use and misuse and associated harm reduction services
- Unit 3 – Recovery and treatment
- Unit 4 – Delivering holistic and seamless care

For the naloxone (Prenoxad) supply service:

Pharmacist / the lead registered pharmacy technician training

All pharmacists / the lead registered pharmacy technician intending to supply naloxone (Prenoxad) must view the following information on the Prenoxad website:

Read the brief information at:

- Use of naloxone in opioid overdose[2]
- When and how to give Prenoxad injection (6 sections)[3]

View the 5 videos (2-3 minutes each) at www.prenoxadinjection.com/drug/how-to.html.

And then complete the CPPE endorsed *Naloxone saves lives* e-assessment.[4]

Staff training

All staff intending to re-supply naloxone (Prenoxad) must read and view the information on the Prenoxad website (as above).

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[1] www.cppe.ac.uk/programmes/l/substance-e-02

[2] www.prenoxadinjection.com/drug/use_naloxone.html

[3] www.prenoxadinjection.com/drug/when_and_how.html

[4] www.ap-elearning.org.uk/

National guidance

The latest national guidance can be accessed at:

- Office for Health Improvement and Disparities[5] alcohol and drug misuse prevention and treatment guidance at www.gov.uk/government/collections/alcohol-and-drug-misuse-prevention-and-treatment-guidance (see Further Reading)
- Drug misuse and dependence: UK guidelines on clinical management. DHSC. Updated 15 Dec 2017 at www.gov.uk/government/publications/drug-misuse-and-dependence-uk-guidelines-on-clinical-management
- Drug misuse in over 16s: Opioid detoxification. NICE Guidance CG52. Published 25 Jul 2007 at https://www.nice.org.uk/guidance/cg52

The *Drug misuse and dependence: UK guidelines on clinical management* (commonly known as the Orange Guide) is the definitive national guidance. Key points in *Chapter 4: Pharmaceutical Interventions* include:

Choice of drug for opioid dependence

There is insufficient evidence to recommend one drug over the other. 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.

In the first weeks of methadone treatment there is an increased risk of death due to overdose. After around a month in treatment, the risk of death due to opioid overdose during maintenance treatment falls to very low levels.

Dose induction should aim carefully, as soon as possible, for a stable dose of opioid that avoids both intoxication and withdrawal. It may take two to four weeks (or more) to achieve an optimal dose with methadone. It usually takes less time with buprenorphine since induction with buprenorphine may be carried out more rapidly with less risk of overdose.

Signs of opiate withdrawal include

- Coughing, sneezing, runny nose, watering eyes
- Raised blood pressure, increased pulse
- Yawning, dilated pupils, cool and clammy skin, fine muscle tremor
- Diarrhoea, nausea
- Restlessness, irritability, anxiety

Methadone toxicity and risk of overdose

All staff working with service users who are taking methadone should be aware that there is a risk of death in early methadone treatment. This can be due to excessive initial doses, failing to recognise symptoms of cumulative effects, impaired liver function (due to chronic hepatitis), or failing to inform patients of the dangers of overdose if they are using other drugs (particularly benzodiazepines and alcohol) at the same time (since opioids induce respiratory depression, and sedative drugs potentiate this effect).

Signs and symptoms of methadone toxicity include:

- Drowsiness, slurred speech
- Slow and/or shallow breathing
- Constricted (pinpoint) pupils

[5] Previously Public Health England

- Disorientation/ confusion, dizziness/ feeling faint, balance/ coordination problems.

With methadone, toxicity is delayed at least several hours after exposure and this may only become apparent after several days of treatment. The reason for the delayed toxicity is methadone's long but variable half-life, of between 13 and 50 hours with chronic administration. It takes five half-lives, or 3-10 days, for patients on a stable dose of methadone to reach steady-state blood levels. During these 3-10 days, blood levels progressively rise even if patients remain on the same daily dose. A daily dose tolerated on day one may become a toxic dose on day three. Patients must therefore be carefully inducted on to methadone and then monitored, and if necessary, the dosage adjusted during this accumulation period.

Risk factors for buprenorphine

Buprenorphine is widely considered to cause less respiratory depression than methadone. At low doses, buprenorphine is a potent opioid agonist, producing morphine-like effects. However, due to its mixed agonist-antagonist properties, increasing doses become self-limiting and do not produce more intense opioid effects. This may be one reason some patients prefer methadone.

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.
- 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-acting opioid), or 24-48 hours after the last dose of low-dose methadone.
- Provide the anticipated day's doses, for the first day or two, in divided doses (typically using 2mg tablets) so that the speed of the induction can be managed.

Methadone dosing

In general, the initial daily dose will be in the range of 10-30mg.

- *First 7 days*: Where doses need to be increased during the first 7 days, the increment should be no more than 5-10mg on one day. In any event, a total weekly increase should not usually exceed 30mg above the starting day's dose. Patients should be alerted to the risk of over-sedation and the risks with ongoing illicit use.
- *Subsequent optimisation*: Following the first 7 days, doses can continue to be increased incrementally. A total target dose of 60-120mg a day, and occasionally more, may be required.

Buprenorphine sublingual dosing

Most dosing regimens involve starting with a low dose (4-8mg) that is rapidly increased. Effective maintenance treatment with buprenorphine involves doses in the range of 12-16mg for most patients dependent on heroin, with some needing up to 32mg. It makes sense to work towards this dose rapidly, so long as this does not produce side-effects or precipitated withdrawal. A cautious approach is to initiate treatment with 4mg on day one, then 8-16mg on day two and thereafter.

Supervised consumption service

Important reminders:

All daily doses of methadone should be dispensed in separate containers.

Medication should be withheld, and the recovery coordinator contacted if the client misses 3 or more doses consecutively.[6] If a client has missed 3 or more consecutive days of medication, they are likely to require a re-start appointment with the Service before any further medication is issued.

All service prescribers will, as a minimum, initial and date any handwritten changes to prescriptions. Any changes that are not amended in this way should be queried with the prescriber.[7]

Registered pharmacy technicians can now also provide the supervised consumption service.

In the event of any pharmacy service disruption, the pharmacy should contact the local Recovery Centre, and ring all affected clients to make suitable alternative arrangements e.g. asking clients to attend the pharmacy at a time when a pharmacist will be available. Pharmacies are required to confirm clients' telephone numbers once a month.

As part of contingency planning, pharmacies are also required to inform the Recovery Centre clinical lead if the pharmacy is reaching its capacity for a safe client list to see if any arrangements can be made to mitigate this, e.g. staggering of client supervision days.

Pharmacies will receive a payment of £2.50 ex VAT for each methadone supervised consumption per client visit to the pharmacy premises; and £3.50 ex VAT for each buprenorphine supervised consumption per client visit to the pharmacy premises. The fee per supervision is per client supervision (i.e. one supervision claim per client visit to the pharmacy) and not, for example, for each different strength of buprenorphine given to a client to make up a specific dose - therefore if a client has more than one prescription for buprenorphine (to make up a specific dose) only one of those prescriptions should then be entered onto PharmOutcomes in order to claim the supervision fee for that occasion.

Naloxone (Prenoxad) supply service

Naloxone is an emergency antidote to opioid overdose. In the event of a suspected opioid overdose, naloxone can temporarily reverse the life-threatening effects of an opioid overdose such as depressed breathing, for approximately 20-30 minutes.

With drug-related deaths continuing to increase, there continues to be a national focus on increasing the availability of naloxone:

- The 2021 RPS report *Improving care, reducing harm and preventing death in people who use drugs: Pharmacy's role*[8] recommends that: Naloxone must be available from every community pharmacy for supply to people who use drugs, family, healthcare professionals, and carers. Naloxone should also be kept in first aid boxes for

[6] If a client has not taken their regular prescribed dose of opioid, there is the possibility that their tolerance to the drug could have reduced, increasing risk of overdose if the usual dose of medication is then taken. A pharmacist should not dispense the fourth day's dose unless they have confirmed with the prescriber that it is appropriate to do so.

[7] To report CD incidents and concerns, such as prescription fraud see https://medicines.necsu.nhs.uk/controlled-drugs/destructions-and-reporting-incidents/

[8] https://www.rpharms.com/recognition/all-our-campaigns/policy-a-z/drug-deaths-and-the-role-of-the-pharmacy-team

emergency use in any clinical setting, and staff trained to use it, where people who use drugs attend. Pharmacy teams in those locations must be among the staff trained to use it.

- In 2021, the Government consulted on expanding access to naloxone by expanding the list of services and individuals that can give it out without a prescription or other written instruction (e.g. supply by homelessness or rough sleeping support services).[9]

For new supplies of naloxone made by a trained pharmacist or lead registered pharmacy technician, the person receiving the supply should receive a brief intervention on basic life support, signs and symptoms of opioid overdose, and how to assemble and safely administer naloxone (Prenoxad) using the training checklist on the customer new supply form. Re-supplies of naloxone can made by any trained member of staff, using the re-supply form. All customers should receive the *Prenoxad Injection Clients Guide*.[10]

Prolonged release buprenorphine injection

In this region, several drug and alcohol services are piloting the use of buprenorphine prolonged-release injection. In addition, buprenorphine prolonged-release injection is now a treatment option in the North-East prison system and discharge of a number of these patients on this preparation to community services will begin from April 2022.

As at March 2022, Buvidal® is the only licensed buprenorphine prolonged-release injection in the UK. Buvidal® is administered as a once weekly (8 mg, 16 mg, 24 mg, or 32 mg) or once monthly (64 mg, 96 mg,128 mg, or 160 mg) depot injection. It is indicated for the treatment of opioid dependence within a framework of medical, social and psychological treatment in patients aged 16 years or over.

National guidance

A NICE Evidence Summary *Opioid dependence: buprenorphine prolonged-release injection (Buvidal®)*[11] stated that:

- Buprenorphine prolonged-release injection may be an option where there is a risk of diversion of opioid substitution medicines or concerns about the safety of medicines stored at home. It may also be an option for people who have difficulties adhering to daily supervised opioid substitution medication, such as for people who are working or in education.
- Buprenorphine prolonged-release injection may have a place in treating opioid dependence in people in custodial settings, where the risk of diversion and time needed for supervised consumption currently leads to challenges in supplying supervised medicines safely.

In April 2021, on behalf of the Regional Medicines Optimisation Committee (RMOC) system, RMOC (South) published *Buprenorphine long-acting injection: considerations for opioid substitution treatment use in community settings and secure environments in England*.[12]

[9] https://www.gov.uk/government/consultations/consultation-on-expanding-access-to-naloxone/consultation-on-expanding-access-to-naloxone
[10] https://www.medicines.org.uk/emc/product/3054/rmms
[11] www.nice.org.uk/advice/es19/chapter/Key-messages
[12] https://www.sps.nhs.uk/articles/rmoc-buprenorphine-long-acting-injection-guidance/

Regional and local guidance
In September 2021, the Northern Treatment Advisory Group (NTAG) approved the use of buprenorphine prolonged-release injection for opioid dependence as an alternative option for the management of opioid dependence after oral methadone and/or oral buprenorphine by SMSPs.[13]
Area Prescribing Committees in the region have considered this NTAG decision for potential inclusion on to their area formularies as red drugs (i.e. specialist only provision by the drug and alcohol recovery services).

Clinical issues for wider stakeholders to consider include:

- **Being aware that a patient is being prescribed a buprenorphine prolonged-release injection**: Discharge guidance from the North-East prison system to community services states that services must inform the patient's GP as soon as possible so that the provision of a buprenorphine prolonged-release injection can be added to the Summary Care Record.[14] This can be added to the GP clinical system as a 'hospital issued drug (or equivalent)' so that other users of the Summary Care Record can see that the patient is being prescribed this treatment. Similarly prescribing notified by any community service should also be recorded on the patient record. For Buvidal®, a 'patient alert card' is also available for patients to carry in order to alert health professionals that they are in receipt of a buprenorphine prolonged-release injection.
- **The implications for pain management**:[15] Adequate analgesia may be difficult to achieve when administering a full opioid agonist in patients receiving buprenorphine. The potential for overdose also exists with a full agonist, especially when attempting to overcome buprenorphine partial agonist effects, or when buprenorphine plasma levels are declining. For management of acute pain, a combination of use of opioids with high mu-opioid receptor affinity (e.g. fentanyl), non-opioid analgesics and regional anaesthesia might be necessary. Titration of oral or intravenous short-acting opioid pain medicinal products (immediate-release morphine, oxycodone or fentanyl) to the desired analgesic effect in patients treated with buprenorphine prolonged-release injection might require higher doses.
- **The treatment of overdose**:[16] Use of an opioid antagonist (i.e. naloxone) is recommended, despite the modest effect it may have in reversing the respiratory symptoms of buprenorphine compared with its effects on full agonist opioids. The long duration of action of buprenorphine and the prolonged release from the injection should be taken into consideration when determining length of treatment needed to reverse the effects of an overdose. Naloxone can be cleared more rapidly than buprenorphine, allowing for a return of previously controlled buprenorphine overdose symptoms. This is unlikely to affect how emergency responders would manage an overdose but would be taken into consideration following transfer of the patient to a hospital setting.

[13] https://ntag.nhs.uk/recommendations/central-nervous-system-recommendations/
[14] In 2022, the North-East prison system will begin to use a GP2GP programme which will allow prisons, with a person's consent, to access and add to patients' medical records.
[15] Information adapted from: Buvidal prolonged-release solution for injection. Electronic medicines compendium. https://www.medicines.org.uk/emc/. Accessed 19.01.22
[16] Information adapted from: Buvidal prolonged-release solution for injection. Electronic medicines compendium. https://www.medicines.org.uk/emc/. Accessed 19.01.22

Further reading

Useful resources at www.gov.uk/government/collections/alcohol-and-drug-misuse-prevention-and-treatment-guidance include:

- Misuse of illicit drugs and medicines: Applying All Our Health. Evidence and guidance to help health professionals identify, prevent or reduce drug-related harm. Office for Health Improvement and Disparities. 23 Feb 2022 at www.gov.uk/government/publications/misuse-of-illicit-drugs-and-medicines-applying-all-our-health
- Opioid substitution treatment good practice resources. For example:
    1. The Best practice in Optimising Opioid Substitution Treatment (BOOST) elearning programme at https://www.e-lfh.org.uk/programmes/best-practice-in-optimising-opioid-substitution-treatment-boost/ which aims to provide drug treatment and recovery professionals with the information they need to deliver good quality opioid substitution treatment to service users.
    2. Opioid substitution treatment: Guide for keyworkers. PHE. 21 Jul 2021 at https://www.gov.uk/government/publications/opioid-substitution-treatment-guide-for-keyworkers