Humber Teaching
NHS Foundation Trust

EAST RIDING PARTNERSHIP BUVIDAL GUIDELINES

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CHANGE RECORD

Version	Date	Change details
1.0	*Sept 2020*	*New Guideline – Approved at DTG (30/07/2020).*
1.1	*Feb 2023*	*Review – Guideline formatted to Trust template and assigned reference code. Add any other amends to document content here. Approved at Drugs and Therapeutics Group (29 March 2023).*

Contents

1. Background

Methadone and buprenorphine are both effective medicines for maintenance treatment of opioid dependence, particularly when taken within the optimal dose range. The NICE technology appraisal on methadone and buprenorphine, for the management of opioid dependence, recommends that either of these drugs, as oral formulations, using flexible dosing regimens, are options for maintenance therapy in the management of opioid dependence (NICE 2017).

Supervised consumption should be available to all people to support induction onto opioid substitution therapy, and provided for a length of time appropriate to their individual needs and risks. Those on supervised consumption will often still have take-home medication for Sundays and some bank holidays (DoH 2017). Risks of providing take-home medication may include accidental ingestion of opioid substitution medicines by children and others, and risks of diversion. In some settings, such as custodial environments, supervised consumption of opioid substitution therapy is mandatory for the time the person is resident in the secure environment (NICE 2019).

2. Opioid Dependency Pathway

Currently, methadone and sublingual or oral buprenorphine (BPN) preparations e.g. Subutex, Suboxone, Espranor, are offered to all opioid dependent patients at the East Riding Partnership unless there are identified contraindications to either medication.

3. Buvidal®: Product overview

3.1. What is Buvidal®?

Buvidal® is a prolonged-release injection of buprenorphine used in opioid dependence. Buprenorphine is an opioid partial agonist/antagonist which binds to the mu and kappa opioid receptors in the brain. Its activity in opioid maintenance treatment is attributed to its slowly reversible properties with the mu opioid receptors which, over time, might minimise the need for illicit opioids for people with opioid dependence (Summary of Product Characteristics (SmPC), 2020).

Buprenorphine prolonged-release injection (Buvidal®) has a marketing authorisation for treating opioid dependence within a framework of medical, social and psychological treatment in adults and young people aged 16 years and over. (SmPC, 2020)

Buvidal® comes in weekly and monthly injections allowing for flexible dosing i.e. the dose can be increased or decreased.

3.2. Why include Buvidal® as a treatment option?

Buvidal® can offer similar benefits to sublingual buprenorphine i.e. suppression of withdrawal symptoms/ craving and opioid blockade if additional opioids are taken.

However, due to the sustained release of buprenorphine contributing to stable plasma concentrations either over a week or a month, it can address the daily peaks and troughs that some patients experience on daily buprenorphine medication (and other opioid substitutes).

3.3. Who might it be suitable for?

Patients that are working/studying or need to travel regularly (or have other commitments) may benefit from a weekly or monthly injection (depot) for convenience and to support them in becoming more independent. In contrast, those patients struggling with adherence to a daily medication regime could also benefit from the depot. For those patients requiring close monitoring and psychosocial support - the weekly depot may be preferable than the monthly.

3.4. Reduced diversion

There is expected to be reduced diversion with Buvidal® because the injection can only be administered by a Health Care Professional (HCP) and therefore a patient will never be in possession of their Buvidal® medication. Furthermore, with Buvidal®, there is a high level of assurance that every dose administered to a patient will be taken and this should significantly improve compliance in those patients that struggle to adhere to a daily drug regimen.

3.5. Other benefits

Buvidal® could potentially reduce clinic time and increase safety in managing and reconciling prescription requests, such as:

a) patients requesting change in their picks ups i.e. moving from supervised daily, daily to three times a week, three times to twice a week or to weekly
b) patients requesting holiday prescriptions and the time taken to establish if the host country permits export of controlled drugs
c) having to locate alternative pharmacies if the patient is traveling to another part of the country
d) if the patient loses their prescription/ medication and asks for a repeat

All the above scenarios can potentially contribute to a negative impact on the therapeutic relationship if the clinician refuses a change in a prescription request from a patient.

3.6. Exclusion criteria for Buvidal®

- Hypersensitivity to the active substance or to any excipients: Soybean phosphatidylcholine
- Glycerol dioleate
  Alcohol anhydrous
- severe hepatic impairment
- acute alcoholism or *delirium tremens*

3.7. Inclusion criteria for Buvidal®

Buvidal® should be considered for the following patients:

- On sublingual buprenorphine (SL BPN) who would prefer the convenience of a weekly/ monthly depot
- those travelling abroad
- those with work or study commitments
- on any opioid substitute that they are non-compliant with
- who infrequently attend at the pharmacy for supervised doses
- requiring frequent re-titration due to consecutively missing supervised doses
- continuing to use additional opioids on top of their current treatment
- experiencing withdrawals before their next daily dose
- with vulnerabilities

4. Prescriber review

East Riding Partnership's prescribing clinician may conduct a prescriber review either due to clinic protocols i.e. every three months or where there are concerns around the patient's compliance to existing treatment.

In this review, the clinician is reviewing the patient's treatment plan (Care Plan)/Risk Assessment and is considering the full range of treatment options (Psychosocial and Pharmacological) including Buvidal® alongside any physical or mental health conditions.

Buvidal® agreed by patient and clinician

Where the clinician and patient decide on Buvidal® as the most clinically effective treatment option, the clinician should provide the patient with the following:

- patient safety information booklet
- patient alert card (informing healthcare professionals that the patient is receiving a depot of buprenorphine and this could have implications on acute medical management and provides details of the addiction services prescribing clinician)

The clinician should explain the principle of a depot and how it differs from standard SL BPN or daily opioid substitution therapy (OST). The clinician should explain that administration will involve a subcutaneous injection (under the skin) which will be administered either weekly or monthly and their rationale for agreeing on either the weekly or monthly depot. They should also explain potential side effects (which are the same as SL BPN) but with the additional injection site reactions.

The clinician should explain how they will initiate Buvidal® i.e. when the patient should take the last dose of their current medication or if using illicit opioids (heroin) and the importance of presenting in objective withdrawal in order to avoid

precipitated withdrawal. They should explain the symptoms of precipitated withdrawal and how these could be managed if they occur.

Patient's current opioid	Length of time since last dose of opioid
Heroin	At least 6 hours
Methadone	At least 24 hours
Buprenorphine	The day after their last dose

Time also needs to be factored for ordering in Buvidal®. The Pharmacy (if this is how the patient will receive their medication) should be informed about the patient commencing on Buvidal® **and that their existing Prescription (PXN) will need to be cancelled from x date.**

5. Controlled Drug License

Buvidal® contains buprenorphine and this is categorised as a schedule 3 drug in the UK except for the Channel Islands where it is schedule 2.

The Drug service must act in accordance to the regulations stipulated by the UK Home Office Controlled Drug Licensing Units (Home Office 2014) when administering Buvidal onsite and any queries should be directed to:

Drugs and Firearms
Licensing Unit 2 Marsham
Street
London
SW1P
4DF

Email: dflu.dom@homeoffice.gov.uk

Telephone number: 020 7035 8972

Initiating Buvidal®

Checklist

Patient Safety Information Booklet given	☐
Patient Alert Card given	☐
Precipitated withdrawal explained	☐
Signed waiver from patient permitting clinic to collect Buvidal and destroy if necessary	☐
Buvidal® ordered from Pharmacy	☐
Registered staff onsite to administer Buvidal or agreement with Pharmacist to administer Buvidal®	☐
BPN naïve patients given 4mgs SL BPN	☐
Treatment Outcome Profile/ Outcome Monitoring Tool administered	☐

The following section is taken directly from the Summary of Product Characteristics (SmPC 2020)

5.1. Initiation of treatment in patients not already receiving buprenorphine

Patients not previously exposed to buprenorphine should receive a sublingual buprenorphine 4 mg dose and be observed for an hour before the first administration of weekly Buvidal® to confirm tolerability to buprenorphine.

The recommended starting dose of Buvidal® is 16 mg, with one or two additional 8 mg doses at least 1 day apart, to a target dose of 24 mg or 32 mg during the first treatment week. The recommended dose for the second treatment week is the total dose administered during the week of initiation.

Treatment with monthly Buvidal® can be started after treatment initiation with weekly Buvidal®, in accordance with the dose conversion in Table 2 and once patients have been stabilised on weekly treatment (four weeks or more, where practical).

5.2. Switching from sublingual buprenorphine products to Buvidal®

Patients treated with sublingual buprenorphine may be switched directly to weekly or monthly Buvidal®, starting on the day after the last daily buprenorphine sublingual treatment dose in accordance with the dosing recommendations in Table 1. Closer monitoring of patients is recommended during the dosing period after the switch.

Table 1. Conventional sublingual buprenorphine daily treatment doses and recommended corresponding doses of weekly and monthly Buvidal®

Dose of daily sublingual buprenorphine	Dose of weekly Buvidal®	Dose of monthly Buvidal®
2-6mg	8mg	
8-10mg	16mg	64mg
12-16mg	24mg	96mg
18-24mg	32mg	128mg

The dose of buprenorphine in mg can differ between sublingual products, which needs to be taken into consideration on a product-by-product basis. The pharmacokinetic properties of Buvidal® are described in section 5.2 (SmPC 2020).

5.3. Maintenance treatment and dose adjustments

Buvidal® can be administered weekly or monthly. Doses may be increased or decreased and patients can be switched between weekly and monthly products according to individual patient's needs and treating physician's clinical judgement as per recommendations in Table 2. Following switching, patients may need closer monitoring. Assessment of long-term treatment is based on 48-week data.

Table 2. Recommended dose conversion when switching from weekly to monthly dosing or from monthly to weekly dosing

Weekly dose of Buvidal®	Monthly dose of Buvidal®
16 mg	64 mg
24 mg	96 mg
32 mg	128 mg

5.4. Supplemental dosing

A maximum of one supplemental Buvidal® 8 mg dose may be administered at an unscheduled visit between regular weekly and monthly doses, based on individual patient's temporary needs.

The maximum dose per week for patients who are on weekly Buvidal® treatment is 32 mg with an additional 8 mg dose. The maximum dose per month for patients who are on monthly Buvidal® treatment is 128 mg with an additional 8 mg dose.

5.5. Missed doses

To avoid missed doses, the weekly dose may be administered up to 2 days before or after the weekly time point, and the monthly dose may be administered up to 1 week before or after the monthly time point.

If a dose is missed, the next dose should be administered as soon as practically possible.

5.6. Termination of treatment

If Buvidal® treatment is discontinued, its prolonged-release characteristics and any withdrawal symptoms experienced by the patient must be considered, see section 4.4 SmPC (2020). If the patient is switched to treatment with sublingual buprenorphine, this should be done one week after the last weekly dose or one month after the last monthly dose of Buvidal® according to the recommendations in Table 1.

6. Overdose

6.1. Symptoms

Respiratory depression, as a result of central nervous system depression, is the primary symptom requiring intervention in the case of buprenorphine overdose because it may lead to respiratory arrest and death. Preliminary symptoms of overdose may also include excessive sweating, somnolence, amblyopia, miosis, hypotension, nausea, vomiting and / or speech disorders.

6.2. Treatment

General supportive measures should be instituted, including close monitoring of respiratory and cardiac status of the patient. Symptomatic treatment of respiratory depression, following standard intensive care measures, should be instituted. A patent airway and assisted or controlled ventilation must be assured. The patient should be transferred to an environment within which full resuscitation facilities are available. If the patient vomits, precautions must be taken to prevent aspiration. 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 Buvidal®, 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.

7. Formulary

The Addictions Consultant and Humber's Lead Pharmacist will progress the drug being included on the relevant formulary. Camurus will support this process by supplying the necessary information.

8. Costs

The NICE summary table below (NICE 2019) Buprenorphine is available as a prolonged-release injection in weekly strengths of 8 mg, 16 mg, 24 mg, and 32 mg; and monthly strengths of 64 mg, 96 mg and 128 mg. The cost for a 30-day supply, irrespective of the strength prescribed is £239.70. The drug acquisition cost of buprenorphine prolonged-release injection compared with other medicines for opioid dependence can be seen in the table below:

Medicine	Usual dose[a]	30-day cost excluding VAT[b]
Buprenorphine prolonged-release injection	8–32 mg weekly 64–128 mg monthly	£239.70[c]
Buprenorphine sublingual tablets sugar free	12–24 mg daily	£139.41 to £246.73[d]
Buprenorphine-naloxone sublingual tablets sugar free	12–24 mg daily	£137.44 to £247.37[d]
Buprenorphine oral lyophilisate (Espranor)	8–18 mg daily	£81.64 to £190.50[d]
Methadone oral solution 1 mg/ml sugar free	60–120 mg daily	£14.76 to £29.52[d]
Methadone oral solution 1 mg/ml	60–120 mg daily	£14.94 to £29.88[d]

[a] Doses shown do not represent the full range that can be used and do not imply therapeutic equivalence. Taken from the BNF or relevant summaries of product characteristics, or based on specialist opinion.
[b] Costs shown are for the drug acquisition cost only and do not include additional costs associated with dispensing, supervised consumption or administration of injections where these are necessary.
[c] Buprenorphine prolonged-release injections will be priced at an equivalent cost of £7.99 per day irrespective of strength (Camurus: personal communication 2018).
[d] Costs based on Drug Tariff, February 2019; excluding VAT.

1 NICE Methadone and buprenorphine for the management of opioid dependence. TA114, 2007
https://www.nice.org.uk/guidance/TA114/chapter/1-Guidance

2 DoH Drug misuse and dependence: UK guidelines on clinical management. 2017
https://www.gov.uk/government/publications/drug-misuse-and-dependence-uk-guidelines-on-clinical-management

3 NICE Evidence Summary: Opioid dependence: buprenorphine prolonged release injection (Buividal) 2019
https://www.nice.org.uk/advice/es19/evidence

4 BuvidalSmPC https://www.medicines.org.uk/emc/product/9706/smpc 2020

5 https://www.gov.uk/government/publications/domestic-controlled-drug-licensing-in-healthcare-settings Home office, 2014

6 NICE Evidence Summary: Opioid dependence: buprenorphine prolonged release injection (Buvidal) 2019
https://www.nice.org.uk/advice/es19/evidence/evidence-review-pdf-6666819661