NHS Grampian

Guidance For Prescribing And Administration Of Buprenorphine Subcutaneous Injection (Buvidal®) For Treatment Of Opioid Dependence In Grampian

Co-ordinators:	Consultation Group:	Approver:
Specialist Pharmacist in Substance and Medicines Use	See relevant page	Medicine Guidelines and Policies Group

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		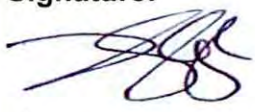

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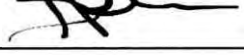
Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: 

Title: Guidance For Prescribing And Administration Of Buprenorphine Subcutaneous Injection (Buvidal®) For Treatment Of Opioid Dependence In Grampian

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Across NHS Boards	Organisation Wide	Directorate	Clinical Service	Sub Department Area

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Responsibilities for implementation:

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Corporate: Senior Managers
Departmental: Heads of Service/Clinical Leads
Area: Line Managers
Hospital/Interface services: Assistant General Managers and Group Clinical Directors
Operational Management Unit: Unit Operational Managers

Policy statement: It is the responsibility of all staff to ensure that they are working to the most up to date and relevant policies, protocols procedures.

Review: This policy will be reviewed in three years or sooner if current treatment recommendations change.

Responsibilities for review of this document:	Specialist Pharmacist in Substance and Medicines Use
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Jan 2024	Oct 2020	Amendments made throughout document to reflect patient choice and align with medication assisted treatment standards.	Throughout document
Jan 2024	Oct 2020	Reworded to remove reference to newly licensed product.	Section 1, Page 2
Jan 2024	Oct 2020	Added Buvidal® 160mg monthly dose.	Throughout document
Jan 2024	Oct 2020	Rationalised as duplication in Section 6.3.	Section 3.1, Page 5
Jan 2024	Oct 2020	Added statement to issue alert card.	Section 6, Page 7
Jan 2024	Oct 2020	Section added to highlight requirement to adhere to controlled drug prescription requirements.	Section 6.1, Page 7
Jan 2024	Oct 2020	Advice on 8mg injection added.	Section 6.2, Page 8
Jan 2024	Oct 2020	Advice on withdrawal symptoms expanded.	Section 6.3, Page 8
Jan 2024	Oct 2020	Point on change in clinical condition of patient added.	Section 6.4, Page 10
Jan 2024	Oct 2020	Rationalised information on supplemental dosing.	Section 6.4, Page 10

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Jan 2024	Oct 2020	Expanded information. in missed doses section	Section 6.5, Page 11
Jan 2024	Oct 2020	Clarified first bullet regarding reducing doses.	Section 6.7, Page 12
Jan 2024	Oct 2020	Bullet point with period of follow up for those who discontinue treatment added.	Section 6.7, Page 12
Jan 2024	Oct 2020	Added statement re transfer back to oral buprenorphine.	Section 6.8, Page 13
Jan 2024	Oct 2020	Additional information added to specific considerations section.	Section 8, Page 15
Jan 2024	Oct 2020	Side effects section added.	Section 8.1, Page 15
Jan 2024	Oct 2020	Liver section updated.	Section 8.2, Page 16
Jan 2024	Oct 2020	Driving section updated with latest DVLA advice.	Section 8.3, Page 17
Jan 2024	Oct 2020	Section on pregnancy and breastfeeding added.	Section 8.4, Page 17

* Changes marked should detail the section(s) of the document that have been amended, i.e. page number and section heading.

Guidance For Prescribing And Administration Of Buprenorphine Subcutaneous Injection (Buvidal®) For Treatment Of Opioid Dependence In Grampian

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Guidance For Prescribing And Administration Of Buprenorphine Subcutaneous Injection (Buvidal®) For Treatment Of Opioid Dependence In Grampian

1. Introduction

Buvidal® is a depot formulation of buprenorphine accepted for restricted use in NHS Scotland by the Scottish Medicines Consortium (SMC). Potential benefits of Buvidal® include improved dose stabilisation, reduction in opioid cravings and "on top" use, an improved quality of life and reduced risk of opioid related overdose. Overdose risk is lower than with full opioid agonists such as methadone but is still possible when combined with other medications, e.g. central nervous system (CNS) depressants.

Buvidal® administration is restricted to healthcare professionals. Take-home use or self-administration of the product by patients is not allowed. Appropriate precautions should be taken when prescribing and administering buprenorphine. This may include follow-up assessment and clinical monitoring according to the patient's needs, particularly in the early stages of treatment.

This guidance provides key information for prescribing and administering long-acting **subcutaneous** buprenorphine products to opioid dependent patients aged 16 years and over. Buvidal® is currently the only injectable product licensed in the UK for treatment of opioid dependence. Buvidal® is available in weekly and monthly depot injections with flexible dosing that can be increased or decreased. This facilitates individualised care.

It is recommended that Buvidal® is initiated by local drug and alcohol teams.

1.1. Objectives

- Reduce harms associated with opioid dependence and addiction, including drug related death
- Provide an alternative treatment option to those currently available
- Encourage engagement with services
- Improve patient outcomes.

1.2. Definitions

For simplicity the word "oral" [buprenorphine] is used throughout the document to refer to both supralingual (Espranor®) and sublingual buprenorphine formulations.

1.3. Clinical Situations

Management of opioid dependence and/or addiction. This document outlines the pharmacological aspects of treatment. Administration processes should be covered by an accompanying Standard Operating Procedure (SOP). As with all opioid substitutes (OST), care must also include social and/or psychological support tailored to the person's needs.

2. Evidence Base

NICE evidence summary ES19 states 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.

The Scottish Medicines Consortium states: "Use in patients in whom methadone is not suitable and for whom the use of buprenorphine is considered appropriate".

"In a phase III study in patients with opioid dependence, subcutaneous buprenorphine was non-inferior to sublingual buprenorphine/naloxone for the mean percentage of urine samples with test results negative for illicit opioids".

In line with Medication Assisted Treatment (MAT) standards, patients should be supported to make an informed choice on treatment.

3. Pharmacology

Buprenorphine

⇒ Is a partial opioid agonist at opioid receptors, producing less euphoric or sedating effects than full opioid agonists such as heroin, morphine and methadone. It has enough opioid activity to reduce cravings and prevent or alleviate opioid withdrawal in opioid dependent patients.

⇒ Has a higher affinity for opioid receptors than heroin, methadone and many other opioid drugs. This means that:

- it can push other opioid drugs that are present off of opioid receptors taking their place. This may cause precipitated withdrawal (see below)
- at higher doses more opioid receptors will be occupied which can reduce the effect of other opioid drugs administered at the same time

- patients may be less likely to use additional opioids on top of their buprenorphine prescription as they will gain less effect from these
- analgesic effect can be less than expected if opioid pain relief is indicated

⇒ Has a ceiling effect. Continued dose increases above a certain point will not result in a proportionate increase in effect.

⇒ Has a lower risk of overdose than full agonists. Overdose can still occur, particularly with polysubstance use. The impact of prescribing other CNS depressant drugs alongside buprenorphine should be considered. Adverse effects such as sedation and respiratory depression should be monitored for and information on opioid overdose and a supply of naloxone given. Refer to NHS Grampian "Take-Home Naloxone" guidance for more information.

The pharmacology of buprenorphine in Buvidal® injections is similar to that of oral buprenorphine products. The key differences are the route and vehicle. Parenteral products have better bioavailability and the prolonged-release solution controls the rate of release allowing for reduced dose administration frequencies and steadier plasma levels.

Buvidal®

⇒ Has formulations which allow for either weekly or monthly administration-(for the purpose of this guidance one month is equivalent to 28 days).

⇒ Reaches peak plasma concentrations of buprenorphine approximately 24 hours after the weekly injection and 6-10 hours after the monthly injection. Buprenorphine plasma concentrations will then reduce slowly over time.

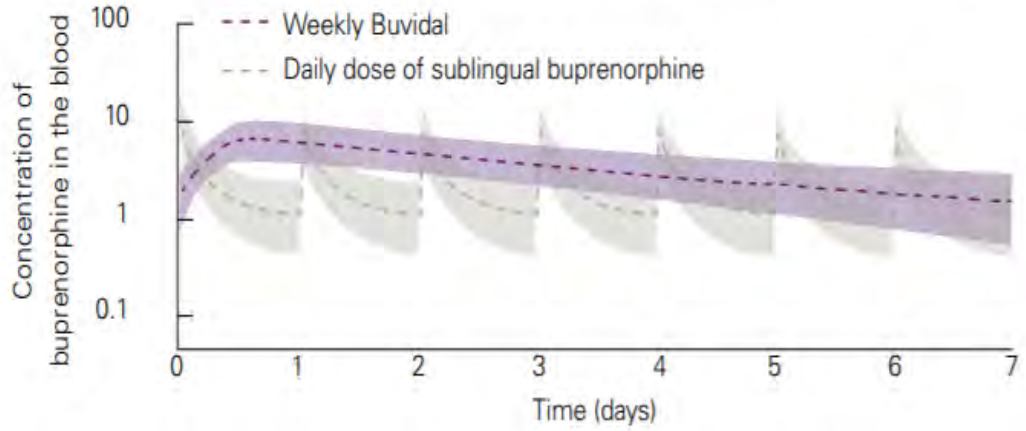
⇒ Produces an immediate effect but steady state will not be reached until around the 4th dose of either the weekly or monthly injection.

⇒ Following administration of the last dose, for those that have reached steady state, it will take around 3 weeks for the weekly injection, or 3 months for the monthly injection for around 90% of the dose to be eliminated from the body.

⇒ Ensures that therapeutic plasma buprenorphine levels are maintained over an extended period which may improve compliance and effectiveness of the medication by preventing opioid withdrawal symptoms and reducing cravings.

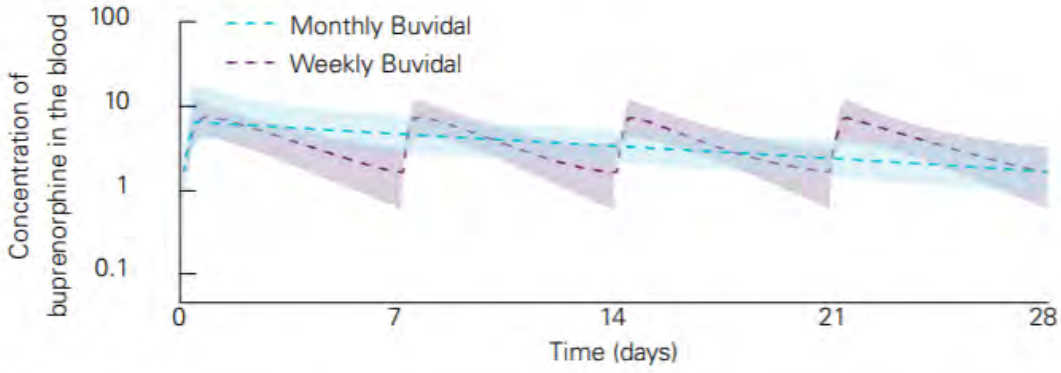
Weekly Buvidal compared with daily doses of sublingual buprenorphine[1]

The concentration of buprenorphine from weekly Buvidal is comparable with that achieved with daily doses of sublingual (under the tongue) buprenorphine.



Weekly Buvidal compared with monthly Buvidal over four weeks[1]

Monthly Buvidal provides a stable concentration of buprenorphine and is comparable with that achieved with weekly Buvidal.



Reference: 1. Abstract presented at the Annual Conference of the Society for the Study of Addiction, December 2018, https://www.addiction-ssa.org/symposium/presentation/cam-2038-a-new-liquid-lipid-crystal-depot-buprenorphine-a-dose-ranging-suit.

3.1. Precipitated Withdrawal

Because of its higher affinity for opioid receptors buprenorphine has the potential to precipitate symptoms of opioid withdrawal when starting treatment.

This risk is higher when administered to patients that still have full opioid agonists (e.g. methadone or heroin) in their systems. Buprenorphine pushes these full agonists off of opioid receptors leading to a drop in opioid effect which can precipitate symptoms of withdrawal in opioid-dependent patients.

4. Patients Who May Be Suitable For Treatment

Buprenorphine prolonged-release injection is accepted by Scottish Medicines Consortium for patients whom methadone is not suitable and for whom the use of buprenorphine is considered appropriate. Situations which may support its use are:

- In patients who state a preference for this treatment option (and is clinically appropriate).
- Where patients struggle with adhering to, or have been unable to stabilise on, other forms of OST.
- Where patients could benefit from a reduction of necessary pharmacy or clinic attendances, e.g. due to work, education or childcare commitments.
- If significant risk of overdose, treatment failure or treatment drop out is identified.
- Where there is a risk of diversion of OST. This may be by choice but also where pressure or risk of harm from others is identified.
- Where there are concerns about the safety of OST stored at home.
- In custodial settings and subsequent continuation in community settings where this is the preferred option on liberation.
- As a contingency management option, e.g. during pandemic situations.

5. Forms Of Buprenorphine Prolonged Release Injectable Solution (Buvidal®)

Buvidal® injections contain buprenorphine in a delivery system that when injected into subcutaneous tissue absorbs interstitial aqueous body fluid which transforms the injection from liquid to highly viscous liquid crystal (or gel-like) phases. This results in a slow and consistent release of buprenorphine. Excipients are described in the Summary of Product Characteristics (SmPC).

Buvidal® is available as:

- 8mg, 16mg, 24mg and 32mg doses for **WEEKLY** subcutaneous administration.
- 64mg, 96mg, 128mg and 160mg doses for **MONTHLY** subcutaneous administration.

The long-acting nature of Buvidal® allows some **flexibility** in administration schedule which reduces the risk of missing doses:

- The weekly dose can be administered up to 2 days before or 2 days after the next due date.
- The monthly dose can be administered up to 1 week before or 1 week after the next due date.

See Section 6.5 for advice on managing missed doses.

6. Prescribing Buvidal®

Services are required to have a Standard Operating Procedure (SOP) which outlines the process for prescribing, supply, administration and assessment of Buvidal®. Sample SOPs and Patient Specific Directions (PSDs) can be obtained by contacting the substance misuse pharmacy team gram.smspharmacists@nhs.scot.

Patients new to treatment of Buvidal® need to have:

- Been provided with a Buvidal® patient information leaflet along with discussion explaining key points. Leaflets can be obtained online from www.buvidal.co.uk/buvidal/buvidal-administration/ (website registration needed).
- Consented to having the treatment prescribed and administered.
- Be supplied with a Buvidal® alert card following administration of the first dose.

6.1. Requirements of Prescribers

Prescribers should:

- Provide a legal prescription **and** patient specific direction (PSD). All POMs require a legal prescription to allow supply. Prescribers will also need to provide a PSD to authorise administration. This is the authorisation and instruction from the prescriber to the healthcare professional who will administer Buvidal® (see Section 7.2).
- Agree who will administer the injection and on what day and supply an appropriate PSD which includes this information. If the administrating service is a community pharmacy the PSD should be supplied at the same time as the initial prescription. A new PSD should be supplied if there is a requirement for any dose changes, otherwise the PSD is valid for one year. gram.smspharmacists@nhs.scot can provide a list of community pharmacies authorised to administer Buvidal®.
- Ensure that prescriptions and PSD are written to allow flexibility in administration (as per Section 5). Producing individual prescriptions for each dose avoids the need for instalment dispensing directions and may allow more flexibility.
- Ensure that the service has a robust system in place for obtaining supply which is outlined in the service's SOP. Buvidal® **cannot** be collected by patients. If the prescription will be dispensed by a community pharmacy for collection by NHS staff it is recommended that the pharmacy are contacted to agree a plan. "For collection by NHSG staff" should be written on the prescription. The prescription should be supplied to the pharmacy a **minimum** of three working days in advance of intended collection date to allow time for stock to be ordered.
- Ensure controlled drug prescriptions requirements are adhered to, as Buvidal is a schedule 3 controlled drug.

6.2. Initiating Patients Currently Prescribed Oral Forms of Buprenorphine

Patients treated with oral forms of buprenorphine can be switched directly to weekly or monthly Buvidal®, starting on the day after the last oral daily dose, following confirmation of compliance at current oral dose. Weekly administration may be the preferred first step for patients to allow time to adapt to the new formulation and changes in plasma levels of buprenorphine that may be experienced moving form oral to depot formulations.

Note: Patients receiving 26-32mg sublingual buprenorphine can be transferred directly to 160mg monthly dose as a weekly equivalent is not available.

It is possible to use an 8mg weekly injection as a maintenance dose, however there is no equivalent monthly dose for patients requiring this dose. Therefore the patient would need to remain on weekly injections. The benefits and negative aspects of ongoing weekly administration should be carefully considered, discussed and agreed with medical staff or service pharmacist before initiation.

Table 1. Equivalent Doses of Buprenorphine Formulations

Daily dose of Espranor®	Daily dose of Sublingual buprenorphine product	WEEKLY dose of Buvidal®	MONTHLY dose of Buvidal®
2-4mg	2-6mg	8 mg	-
6mg-8mg	8mg-10mg	16mg	64mg
10-12mg	12mg-16mg	24mg	96mg
14mg -18mg	18mg-24mg	32mg	128mg
-	26-32mg	-	160mg

Closer review/monitoring of patients is recommended during the period of change from oral buprenorphine to Buvidal®. This may include follow up phone calls or appointments in the days after administration to assess impact and provide support.

6.3. Initiation to Buvidal® in Patients Not Already Receiving Buprenorphine

To avoid precipitated withdrawal (Section 3.1), clinicians should time the first administration of buprenorphine when symptoms of withdrawal are likely to occur. Consider the type of opioid used (long or short-acting), time since last opioid use and the degree of opioid dependence. See table below for further details. **This does not apply to transfers from oral buprenorphine** (see Section 6.2). A clinical opioid withdrawal scale (COWS) can be useful in assessing symptoms of withdrawal however other medications or drugs may reduce signs of withdrawal and patients may score lower than expected. Physical illness or withdrawal from other substances may also present in a similar manner to opioid withdrawal so any scale should be used alongside thorough clinical assessment and history taking.

Type of opioid	*Current dose*	*When to initiate*
Heroin	Any dose, any route of administration.	Wait for clear, objective, mild signs of withdrawal to appear, generally 6 hours or more after the last use of heroin.
Methadone	30mg daily or lower prior to transfer. Transfer from higher doses can precipitate withdrawal or lead to treatment failure if the opioid effect experienced is not enough to cover withdrawal symptoms so should only be performed with support and close supervision.	Wait for clear, objective, mild signs of withdrawal to appear, generally 24 hours or more after the last use of methadone.
Opioid Analgesics	Any dose, any route of administration.	Wait for clear, objective, mild signs of withdrawal to appear. Timing will depend on formulation of opioid, i.e. short or long acting.

As a minimum, patients who have never been prescribed buprenorphine must receive **an oral dose of buprenorphine 4mg** and be observed for an hour before the first administration of weekly Buvidal®. This tests for adverse reactions, tolerability and acceptability of buprenorphine.

An alternative option is to stabilise patients on oral buprenorphine before starting Buvidal®. This may allow the patient more time to test the effects of buprenorphine before committing to a long acting formulation. Initiation of Buvidal® should then follow guidance in Section 6.2.

Ultimately the decision on how to initiate patients should be guided by clinical assessment of the individual's risk factors, type of opioid currently used, degree of dependence, preferences and circumstances.

Week 1

- The recommended starting dose is Buvidal® 16mg weekly injection.
- During the first week an additional **one or two 8mg doses** can be given at least 1 day apart, to a target dose of 24mg or 32mg (maximum) if the patient continues to experience opioid withdrawal, cravings or persistent additional opioid use.

Week 2 onwards

- The recommended dose for week 2 is the total dose administered during week 1, i.e. the starting dose plus any additional doses given.

- From week 2 onwards a maximum of **one** supplemental Buvidal® 8mg dose may be administered between regular weekly or monthly doses, based on patient response and prescriber judgement. Future weekly or monthly doses should be reviewed where additional doses have been needed.
- Patients can be transferred to monthly Buvidal® (see Table 1, Section 6.2) once stabilised on weekly treatment.

6.4. Maintenance Treatment and Dose Adjustments

- Following review, prescribers can increase or decrease doses or switch between weekly and monthly formulations according to clinical response and patient preference.
- Weekly dosing can continue if this is the most appropriate option. Drug costs are approximately equivalent.
- Stepwise increases to the next dose may be required where the patient continues to experience symptoms of withdrawal, craving or additional "on top" use.
- Decreases may be required if the patient is experiencing adverse effects including over-sedation.
- Changing between weekly and monthly dosing should occur on the date when the next dose is due
- Table 1 (Section 6.2) should be used to calculate equivalent doses when switching between weekly and monthly formulations.
- Close monitoring is recommended following dose changes or when switching between weekly and monthly formulations.
- The maximum total weekly dose of Buvidal® is 40mg and the total maximum monthly dose is 160mg.
- Patients on 160mg monthly Buvidal® cannot receive a supplementary 8mg dose.

In general, doses should be maintained if

- The patient is achieving key treatment goals, such as no reported opioid withdrawal or cravings and no additional use of opioids.
- There are no significant dose-related adverse events related to buprenorphine (e.g. sedation or lethargy, persistent headaches, nausea).
- The patient is satisfied and is requesting the dose be maintained.

Consider whether dose reduction is required where the patient:

- Reports dose-related buprenorphine adverse events.
- Is ready to reduce the dose with an ultimate goal of stopping OST.
- Reports the dose is too high and/or is seeking a dose reduction, and there are no significant concerns regarding deterioration in clinical condition (e.g. substance use, physical or mental health symptoms) that may arise with a dose reduction.
- Is using other CNS depressants to an extent where the combination is felt to increase risk of opioid overdose.

- The patient's clinical condition has changed which may mean that continuation of Buvidal® is no longer clinically appropriate.

Consider whether dose increase is required where the patient:

- Is not achieving desired treatment goals (e.g. ongoing opioid use, opioid withdrawal symptoms or cravings) and there are no reported adverse events.
- Reports their dose is too low and there are no significant clinical safety concerns in increasing it.

6.5. Missed doses

If a dose is missed, the patient should be reviewed and appropriateness of continuation of Buvidal® assessed as soon as practically possible. Factors to consider in the assessment include:

1) Reason for missed dose (e.g. forgot it was due, feeling fine/didn't feel they needed it, missed due to illness, thought they would try to come off, period of lapse, etc).
2) Changes in physical or mental health, or other medicines taken.
3) Current dose, how long prescribed, how long since last administration and administration history (i.e. has reached steady state or not – see Section 3) – how many doses missed.
4) Assess any recent substance use.
5) Assess for any adverse effects, signs of intoxication, symptoms of withdrawal, etc.
6) Is Buvidal® still the preferred treatment option.

Treatment Options include

1) Continue with current dose.
2) Consider dose reduction (top up dose available if needed).
3) Discuss and agree end of treatment plan if patient's goal is to discontinue treatment (see Section 6.7).
4) Revert back to oral buprenorphine, or methadone if this is the preferred option.

Note: For people stable on weekly doses, buprenorphine will take in the region of 3 weeks or more to leave the body completely, for monthly doses it can be 3 months or more, which will help inform decision making. As a rule of thumb, for patients who have been receiving regular doses and have reached steady state (see Section 3), Australian guidance suggests that re-induction may be required if more than 14 days has elapsed between Buvidal® weekly doses, or more than 8 weeks between monthly doses. Where there is uncertainty in continuation please contact medical staff or service pharmacists for advice.

6.6. Transfer of Patients Between Services

Transitions between services such as prison and community based services or discharge from hospital are associated with risks such as default from services overdose and drug related death. Collaboration between services can help reduce these risks. Key points to consider include:

- Product prescribed and current dose
- Date of last administration date/date next dose is due
- Ensuring that the patient has an appointment for ongoing care before transfer.

This process should take place as soon as admission, transfer, discharge or release dates are known in order that logistical considerations such as arranging a competent healthcare professional (and venue) to prescribe, order and administer the product can take place.

6.7. Stopping Treatment With Buvidal®

Buvidal® will leave the body slowly over a number of weeks or months. For the monthly product it could be 3 months or more after last administration before the body clears buprenorphine reserves completely. Symptoms of withdrawal may not be an issue however there may be a delay in them presenting. Clinicians should assess each patient individually and collaboratively decide on the most suitable intervention.

- Stopping from a monthly dose of Buvidal® will provide a more gradual reduction in buprenorphine blood levels than stopping from a weekly dose. It is recommended that patients prescribed Buvidal® monthly are transferred to the lowest monthly dose before stopping the product, e.g. for patients prescribed Buvidal® 128mg transfer from 128mg to 96mg to 64mg before stopping.
- Prescribing each of the lower doses in turn for around 3 months before reducing can allow the body to adapt to each dose reduction before further reductions are made although there is no set guidance on how quickly to withdraw Buvidal®.
- More rapid reduction will result in a quicker reduction of buprenorphine blood plasma levels.
- The patient should be involved in each stage of planning.
- Patients and treatment plans should be reviewed regularly, include additional psychological support to maintain motivation, cope with cravings, withdrawal and the risk of relapse.
- If symptoms of withdrawal appear, there may be a role for symptomatic treatment however caution should be applied when considering extended use (beyond a few days) of sedative or hypnotic medication.
- Patients should be provided with overdose awareness information and naloxone.
- Due to the delayed nature of possible withdrawal symptoms patients should be monitored and supported for a minimum of 3 months following their last Buvidal® injection. Need for ongoing support and relapse prevention should be assessed and arranged as appropriate.

6.8. Transfer from Buvidal® to Other Forms of Opioid Substitution Treatment

If a switch back to an oral form of OST is requested or required, the transfer should occur on the date when the next dose of Buvidal® is due, i.e. one week or one month after the last dose depending on the formulation.

Transfer to an oral buprenorphine product. Use the conversion tables in Section 6.2 and restart on the equivalent dose, or lower dose as agreed with patient, on the date the next Buvidal® was due.

Where methadone is the preferred option, a cautious approach to titration will be required due to the long period of time Buvidal® can remain in the body. It should be initiated as per national guidance. That is a starting dose of 10-30mg daily and titrating by a maximum of 5-10mg daily and 30mg per week as clinically indicated for symptoms of withdrawal, illicit opioid use or craving. As buprenorphine has a higher affinity for opioid receptors it could be some time before the full effects of methadone become apparent. If titration occurs too quickly, overdose is a risk.

7. Administering Buvidal®

Administration of Buvidal® should be undertaken by appropriately trained healthcare professionals who have been approved by their professional manager as competent.

Healthcare Professionals must:

- Be trained in the administration of subcutaneous injections.
- Demonstrate competence in the use and administration of the Buvidal® injecting device.
- Have completed annual basic life support training.
- Have undertaken NHS e-anaphylaxis training or equivalent (including annual updates) which covers all aspects of the identification and management of anaphylaxis.
- Maintain their skills, knowledge and their own professional level of competence in this area according to their individual Code of Professional Conduct.
- Have knowledge of and familiarity with the service specific Standard Operating Procedure (SOP) and Summary of Medicinal Product Characteristics (SmPC) for Buvidal®.
- Be competent in assessing the patient's capacity to consent to the administration of Buvidal®.
- Be able to discuss issues associated with administration of Buvidal® with the patient.
- Be competent in the handling and storage of controlled drugs.

Professional manager(s) will be responsible for;

- Ensuring that the service has a SOP for prescribing, obtaining, storing and administering medication tailored to their service.

- Ensuring that the current SOP is available to all staff.
- Ensuring that staff have received adequate training and meet the requirements above.
- Maintaining an up-to-date record of all staff authorised to administer Buvidal®.

7.1. Patient Specific Directions for Administration

Where the prescriber is authorising another healthcare professional to administer medication a Patient Specific Direction (PSD) is required. The NHSG "Prescription and Administration Record" and Prison "Prescription Sheet" are examples of PSDs. If a prescription has been dispensed by a community pharmacy a separate PSD for administration is required. The prescription for supply of medication does not fulfil this requirement.

As a minimum a PSD for administration should include:

- Name of patient and/or other individual patient identifiers (CHI, address) including age if a child.
- Name, form and strength of medicine (generic or brand name where appropriate)
- Route of administration.
- Dose and frequency of administration.
- Date of treatment, total number of doses and date treatment ends as applicable.
- Signature of the prescriber.

7.2. Administration of Buvidal®

Buvidal® is intended for subcutaneous administration only:

- Inject slowly and completely into the subcutaneous tissue of different areas (buttock, thigh, abdomen, or upper arm) at a 90-degree angle.
- Each area can have multiple injection sites.
- Injection sites should be rotated for both weekly and monthly injections.
- A minimum of 8 weeks should be left before re-injecting a previously used injection site (although the same area can be used).
- The dose should be administered as a single injection and not divided.
- A video and instruction leaflet covering administration can be accessed on the Buvidal® site www.buvidal.co.uk/buvidal-administration/ (website registration needed).

Buvidal® administration should be recorded clearly in the patient's record and as a minimum include:

- Name, address and CHI of the person having the dose administered.
- Name, formulation and strength of the controlled drug administered.
- Dose of the controlled drug administered.
- Date and time of administration.

- Location of site injected (the same site should not be used for 8 weeks).
- Name and signature or initials of the person who administered the dose.
- Name and signature or initials of any witness to administration.
- The batch number and expiry date of the dose.

8. Contraindications And Cautions To Use

Consult the SmPC for full product information.

Manufacturer listed contra-indications to use are as follows:

- Allergy or sensitivity to any of the excipients of Buvidal® (buprenorphine, soybean, glycerol dioleate, N-Methylpyrrolidone, Ethanol anhydrous (weekly formulations).
- Severe respiratory insufficiency.
- Severe hepatic impairment.
- Acute alcoholism or delirium tremens.

The following groups require specific consideration before prescribing which may require discussion with other specialty areas. They include:

- Elderly patients >65 years.
- Patients with moderate hepatic impairment (see Section 8.2).
- Patients with severe renal impairment (creatinine clearance <30mL/min).
- Children and adolescents <16 years of age (unlicensed).
- Pregnant women.
- Patients who require pain management where opioid analgesia is indicated.
- Patients with severe respiratory or cardiac disease.
- Patients prescribed co-concomitant medications, especially medications with serotonergic or central nervous system depressant properties.

8.1. Side effects

Consult the SmPC for full product information.

Injection site reactions can occur following administration of Buvidal®. These are usually mild or moderate in severity and mostly short lived. Injection site pain, injection site pruritus, injection site erythema, injection site swelling, injection site induration and injection site mass are common, whereas cellulitis, bruising and urticaria less so. There are some post-marketing reports of serious injection site-related adverse reactions of abscess, ulceration and necrosis.

Patients should be advised to monitor their injection site for any reactions. Mild redness, pain or swelling are likely to subside. Any reactions that are worsening or not classed as mild should be reviewed and assessed if treatment is required.

8.2. Hepatitis, Hepatic Events and Liver Disease

There are rare case reports of liver injury in patients prescribed buprenorphine, usually arising within 2-20 weeks of starting buprenorphine. This led drug companies to recommend routine liver function tests (LFTs). Current available evidence suggests the majority of reports occurred in patients with a diagnosis of hepatitis B or C or following injection of buprenorphine sublingual tablets. It suggests the risk is no greater for buprenorphine than for methadone.

Laboratory results, Trakcare and GP records (if accessible) should be checked for any evidence of previous/current liver issues before starting buprenorphine. Due to the long acting nature of Buvidal® recent LFTs would be preferable, however if this is not possible then clinicians should highlight the rare risk of liver injury with buprenorphine to patients in order to support an informed, shared decision on prescribing and necessity of LFTs prior to commencing Buvidal® .

Regular review of blood borne virus (BBV) status and BBV testing is recommended for all patients and will help identify those who may be at higher risk. LFTs should therefore be considered for patients with a diagnosis of hepatitis or evidence of hepatic dysfunction.

All patients should be offered BBV testing and discussion regarding vaccination status in the early stages of treatment. Details on how to access vaccination in each HSCP area can be via: www.grampianvax.com/professional-referrals/

Where a patient is identified as having clinically relevant liver disease (more than a mild elevation of LFTs) but not severe hepatic impairment, (which is a contraindication to Buvidal® treatment) then an extended period of treatment with oral buprenorphine (e.g. one-to-three months) may be an option. This allows for monitoring of liver function to ensure that buprenorphine does not worsen hepatic function, and for titration of dose, prior to initiating Buvidal® treatment. If Buvidal® is administered in preference to oral buprenorphine for a patient with moderate hepatic impairment then a weekly formulation would be a pragmatic choice due to its quicker washout period as compared to the monthly prolonged-release formulation.

Monitoring of liver function may be considered for patients with mild to moderate liver disease and/or liver impairment after commencing treatment with Buvidal® (e.g. clinical examination, liver function blood tests and underlying causes, for example viral hepatitis, or alcohol use). Patients who develop moderate hepatic impairment while being treated with Buvidal® should be monitored for signs and symptoms of precipitated opioid withdrawal, toxicity or overdose caused by increased levels of buprenorphine as buprenorphine plasma exposure can be increased approximately 3-fold in people with severely impaired hepatic function. Sedation following the initial dose may occur with high doses, and the patient should be warned accordingly. Termination of Buvidal® treatment may be warranted if a patient's hepatic function significantly deteriorates. For patients who develop severe hepatic impairment, Buvidal® should be stopped and the patient switched to an alternative OST. The patient should continue to be monitored regularly following cessation of Buvidal®.

8.3. Driving

At the time of writing the DVLA guidance for Assessment of Fitness to Drive notes that subcutaneous long acting buprenorphine may be eligible for consideration. Patients should be reminded of their legal duty to inform the DVLA of any medical conditions. They should also be advised that buprenorphine may affect their ability to drive or use machinery, and that they should avoid doing so until fully aware of how they are affected by Buvidal®. Up to date information can be accessed from: Drug or alcohol misuse or dependence: assessing fitness to drive - GOV.UK (www.gov.uk)

8.4. Pregnancy and Breastfeeding

Specialist support should be sought when treating pregnant patients.

It is recommended that Buvidal® may be used in pregnancy if the potential benefit outweighs the risk.

There is, however, more experience in using oral buprenorphine in pregnancy. UK clinical guidance states: "Research evidence demonstrates no difference in adverse effects between methadone and buprenorphine with both having no adverse effects on the pregnancy or neonatal outcomes, with incidence of Neonatal Abstinence Syndrome (NAS) similar to methadone exposure (Blandthorn, Forster & Love 2011, Jones et al 2010). However, there is some evidence that buprenorphine use results in NAS of lower severity."

Given this, switching to oral buprenorphine may be an option for those patients on Buvidal®. It is necessary for women and their clinicians to weigh up the risks and benefits to both mother and baby of not taking a specific treatment against those of initiating or continuing the treatment. This will vary from person to person and depend on the severity of the mother's condition and the complications that could arise if her treatment is altered.

The impact of Buvidal® on pain management plans during labour should be considered.

The manufacturer of Buvidal® recommended that Buvidal® should be used in caution in those breast-feeding as buprenorphine is excreted in breast milk.

For women stabilised on a buprenorphine product who wish to breastfeed, an individual risk-benefit analysis to inform decision making should be undertaken. Due to the lack of evidence of the effects of these drugs on breastfed infants, manufacturers' advice is to avoid, although expert consensus opinion states that the effects of these medications on the breastfed infants is likely to be minimal and that breastfeeding is not contraindicated.

UK Guidance states “Breastfeeding should be encouraged, even if the mother continues to use drugs, except where she uses cocaine or crack cocaine, or a very high dose of benzodiazepines. Specialist advice should be sought if she is HIV positive. Hepatitis C is not a contraindication to breast feeding (HIS 2013).

Methadone or buprenorphine treatment is not a contraindication to breastfeeding and breastfeeding may reduce the intensity and length of neonatal abstinence syndrome and has been shown to improve outcomes (Mayet et al 2008)”.

9. Consultation List

The document was sent to the following individuals/groups for consultation

Steven Beason	Associate Specialist in Addiction Psychiatry
Jack Bonnar	Community Mental Health Nurse/Team Lead, Kessock Clinic
Jennifer Brooks	Primary Care Clinical Pharmacist, AHSCP
Rhona Campbell	Community Mental Health Nurse/Team Lead, Timmermarket
Susanne Duncan	Pharmacist prescriber in substance misuse, Buchanhaven Pharmacy
Patrice Forget	Clinical Chair in Anaesthesia, University of Aberdeen, Honorary Consultant, NHS Grampian
Richard Legg	GP with Specialist Interest in Substance Use
Tracey Scorgie	Specialist Midwife, NHS Grampian
Lucy Skea	Specialist Pharmacist in Substance Use NHS Grampian
Michael Turner	Consultant Psychiatrist

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11. Distribution List

NHS Grampian Clinical staff in:

- Acute Services
- Grampian Drug and Alcohol Services
- HMP Grampian
- Mental Health Services
- Primary Care Pharmacy Teams
- Grampian Community Pharmacy and GP Distribution lists