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Dear Colleagues

This guidance is currently under review by the author.

Guidance For Prescribing And Administration Of Buprenorphine Subcutaneous Injection (Buvidal®) For Treatment Of Opioid Dependence In Grampian – Version 1

This document has been risk assessed by the author and deemed appropriate to be used during this review period. A copy of the risk assessment can be provided on request.

If you have any queries regarding this, please do not hesitate to contact the Medicines Guidelines and Policy Group (MGPG) email at gram.mgpg@nhs.scot

Yours sincerely



Lesley Coyle
Chair of MGPG, NHSG

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

Co-ordinators: Specialist Pharmacists in Substance Misuse	Consultation Group: See relevant page	Approver: Medicine Guidelines and Policies Group
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Signature: 		Signature: 
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Uncontrolled when printed
Version 1

Executive Sign-Off

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

Signature:  _____

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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). Benefits of Buvidal® include dose stabilisation, reduction in cravings and “on top” use, an improved quality of life and reduced risk of opioid related overdose. Overdose risk is lower than with full opioids such as methadone but is still possible with other medications, e.g. CNS depressants.

Buvidal® administration is restricted to healthcare professionals only. 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. Take-home use or self-administration of the product by patients is not allowed.

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.

As a new formulation it is recommended that prescribing of Buvidal® is undertaken initially by specialist substance misuse teams and/or prescribers with experience in the use of buprenorphine for treatment of opioid dependence. This will be reviewed and updated as experience is gained. Suspected adverse drug reactions (ADRs) should be reported through the yellow card scheme www.yellowcard.mhra.gov.uk.

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. **Note:** [Section 8.1](#) is a direct transcription and contains the abbreviations “SL” and “BPN” referring to “sublingual” and “buprenorphine” respectively.

1.3. Clinical Situations

Management of opioid dependence and/or addiction. This document outlines the pharmacological aspects of treatment. Process 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 ES19¹ 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 Consortium² 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".

3. Pharmacology

Buprenorphine

- ⇒ Is a partial opioid agonist. This means it only partially activates opioid receptors producing a milder, less euphoric and less sedating effect than full opioid agonists such as heroin, morphine and methadone.
- ⇒ Has a higher affinity for opioid receptors than heroin, methadone and many other opioid drugs. This means that:
 - buprenorphine can push other opioid drugs that are present in the body off the opioid receptors and take their place which may cause precipitated withdrawal (see below)
 - at higher doses more opioid receptors will be occupied which can block or 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 little or no additional effect
 - if opioid pain relief is required the analgesic effect achieved can be significantly less than expected

- ⇒ Has a ceiling effect. Continued dose increases will not result in a proportionate increase in effect.
- ⇒ Possesses opioid activity which is usually enough to reduce cravings and prevent or alleviate opioid withdrawal in opioid dependent people despite only being a partial agonist of opioid receptors.
- ⇒ Has a lower risk of overdose than full agonists. Overdose can still occur particularly with poly drug 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.

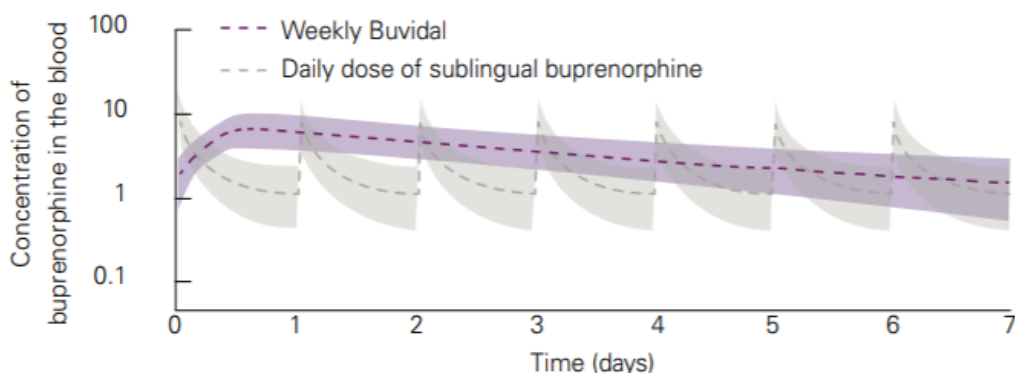
The pharmacology of buprenorphine in Buvidal® injections is similar to that of oral buprenorphine products. The key differences are the route and vehicle. Parenteral products have better bioavailability and the prolonged-release solution controls the rate of release allowing for reduced dose administration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

Buvidal®

- ⇒ Has formulations which allow for either weekly or monthly administration.
- ⇒ Reaches peak plasma concentrations of buprenorphine approximately 24 hours after the weekly injection and 6-10 hours after the monthly injection. Plasma buprenorphine concentrations will then decrease slowly over the dosing interval.
- ⇒ Produces an immediate effect but will take in the region of 4 weeks for the weekly product and 4 months for the monthly product to reach steady state in the body.
- ⇒ Following administration of the final dose similar time periods will be required to clear the product from the body.
- ⇒ Ensures that therapeutic plasma buprenorphine levels are maintained over an extended period improving compliance and effectiveness of the medication by preventing opioid withdrawal symptoms and reducing cravings.

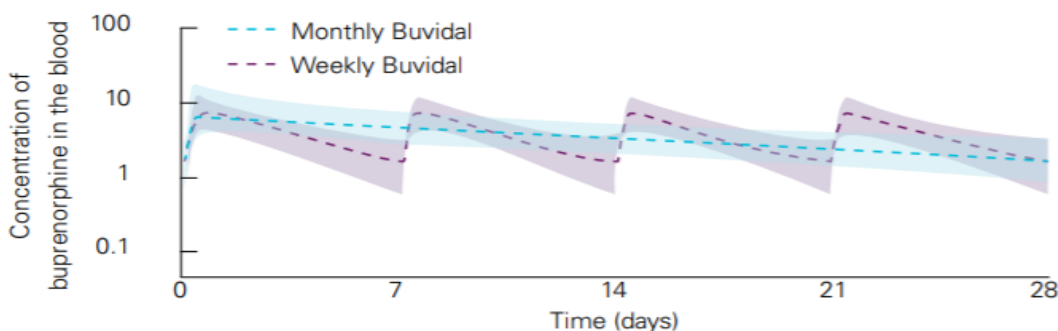
Weekly Buvidal compared with daily doses of sublingual buprenorphine¹

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 weeks¹

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 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.

To avoid precipitating withdrawal in patients new to buprenorphine, the first dose of buprenorphine should be taken when the patient shows objective signs of opioid withdrawal. Use of a [clinical opioid withdrawal scale](#) can help assess the extent of withdrawal.

4. Patients Who May be Suitable for Treatment

Buprenorphine prolonged-release injection may be a treatment option:

- 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 the active substance buprenorphine in delivery system compositions based on the proprietary FluidCrystal® injection depot technology, a lipid-based liquid. When injected into subcutaneous tissue the FluidCrystal® formulation absorbs interstitial aqueous body fluid and transforms from liquid to highly viscous liquid crystal (or gel-like) phases in situ, which effectively encapsulate the active substance. This results in a slow and consistent release of buprenorphine, which can be controlled for over a week or a month depending on the composition. 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 and 128mg 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.

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 PSDs (see below) 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.
- Consented to having the treatment prescribed and administered.

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 for 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 administering service is a community pharmacy the PSD should be supplied at the same time as the prescription. At time of writing a limited pilot of community pharmacy administration is in planning. This service is not currently available routinely from community pharmacy.
- Consider the timing of administration and ability to monitor/assess patients when initiating Buvidal®. For example, initiating on a Friday removes the ability to check how the patient is doing or administer a top up dose over the weekend.
- Ensure that prescriptions and PSD are written to allow flexibility in administration. 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 two working days in advance of intended collection date to allow time for stock to be ordered.

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 daily dose. Weekly administration may be the preferred first step for patients to allow them time to adapt to the new formulation and changes in plasma levels of buprenorphine that may be experienced moving from oral to depot formulations.

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

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

Due to hepatic contraindications and cautions, assessment of hepatic function and documentation of viral hepatitis status prior to initiation is recommended (see [Section 8.1](#)).

Initiation of any buprenorphine product has potential to precipitate symptoms of withdrawal due to its high affinity for opioid receptors. These can be significant.

To avoid this, clinicians should time the first administration of Buvidal® 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. **This does not apply to transfers from oral buprenorphine** (see [Section 6.2](#)).

As a minimum, patients who have never been prescribed buprenorphine should receive **an oral dose of buprenorphine 4 mg** 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 allows 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.

<i>Type of opioid</i>	<i>Current dose</i>	<i>When to initiate</i>
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. Will depend on formulation of opioid, i.e. short or long acting.

A [clinical opioid withdrawal scale](#) 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.

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.
- Patients can be transferred to monthly Buvidal® (see [Table 1, Section 6.2](#)) on reaching a stable dose of weekly treatment (usually week four week onwards).

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.
- From week 3 onwards a **maximum of one** supplemental Buvidal® 8mg dose may be administered between regular weekly and monthly doses, based on patient response and prescriber judgement. Future weekly or monthly doses should be reviewed where additional doses have been needed.
- The maximum dose per week for patients on weekly Buvidal® is 32mg with an additional supplementary 8mg dose (i.e. 40mg).
- The maximum dose per month for patients on monthly Buvidal® is 128mg with an additional supplementary 8 mg dose (i.e. 136mg).

In general, doses should be maintained if (adapted from SMMGP guidance):

- 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.

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 next dose should be administered as soon as practically possible. If sufficient time has passed that tolerance to the current dose is uncertain, the patient should be re-titrated following clinical assessment. Consideration of half-lives will assist the decision making process:

- The weekly formulation has a half-life in the range of 3-5 days
- The monthly formulation has a half-life in the range of 19-25 days.

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 sadly drug related death. Collaboration of 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 health care 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 they could take a few weeks to appear if they do occur. Clinicians should assess each patient individually and collaboratively decide on the most suitable intervention.

- It is recommended that the patient is transferred to the lowest dose of **monthly** Buvidal® 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 3 months before reducing allows 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.

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.

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® is restricted to authorised and appropriately trained health care professionals who have been approved by their professional manager as competent.

Health Care 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 health care professional to administer medication a [Patient Specific Direction](#) (PSD) is required⁶. 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 also 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/
- The most common injection site reactions are pain (8.9%), pruritus (6.1%) and erythema (4.7%). All were mild or moderately severe and most were short lived.

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. www.medicines.org.uk

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 8.1](#))

- 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.

8.1. Hepatitis, Hepatic Events and Liver Disease

Substance Misuse Management in General Practice (SMMGP) guidance provides detailed advice on caution for patients with hepatitis and hepatic events as follows.

“Moderate or severe hepatic impairment (Child Pugh B or C) slows down hepatic metabolism of BPN [buprenorphine] resulting in higher plasma levels (estimated at 1.6 greater in Child B and, 2.8 times greater in Child C) and longer half-lives. Furthermore, cases of cytolytic hepatitis and hepatitis with jaundice have been (rarely) observed in individuals using BPN. The spectrum of abnormalities ranges from transient asymptomatic elevations in hepatic transaminases to case reports of hepatic failure, hepatic necrosis, hepatorenal syndrome, hepatic encephalopathy and death. In many cases, other causes of pre-existing liver disease (e.g. viral hepatitis, use of other potentially hepatotoxic drugs such as alcohol) may have played a causative or contributory role. Acute hepatitis has been reversed on BPN cessation in some cases, but not others.

The effect of hepatic impairment on the pharmacokinetics of depot BPN has not been studied. Due to the long-acting nature of the product, adjustments to depot BPN dosages are not rapidly reflected in plasma BPN levels. Because BPN levels cannot be decreased rapidly, patients with moderate hepatic impairment should be prescribed Buvidal® with caution. Buvidal® should not be used in patients with severe hepatic impairment.

An assessment of hepatic function (including liver function tests) and documentation of viral hepatitis status prior to treatment initiation with depot BPN is recommended. 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 SL BPN (e.g. one-to-three months) may be an option. This allows for monitoring of liver function to ensure that BPN does not worsen hepatic function, and for titration of BPN dose, prior to initiating depot BPN treatment. If Buvidal® is administered in preference to SL BPN 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 depot BPN (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 depot BPN should be monitored for signs and symptoms of

precipitated opioid withdrawal, toxicity or overdose caused by increased levels of buprenorphine. Sedation following the initial dose may occur with high doses, and the patient should be warned accordingly. Termination of depot BPN treatment may be warranted if a patient's hepatic function significantly deteriorates; depot BPN should be stopped and specialist consultation is recommended. For patients who develop severe hepatic impairment, Buvidal® should be stopped and the patient switched to an alternative OST. As in moderate hepatic impairment the patient should continue to be monitored regularly following cessation of Buvidal®.

8.2. Driving

At time of writing the DVLA guidance for [Assessment of Fitness to Drive](#) states that only those patients prescribed oral buprenorphine will be eligible for consideration. A request to add injectable formats has been approved and documented in agenda point 5 of recent [DVLA minutes](#), included in advance of the guidance document being updated.

9. Consultation List

Dr Seonaid Anderson	Consultant Psychiatrist, Aberdeen Integrated Alcohol Service
Dr Steve Beason	Associate Specialist in Addiction Psychiatry, Aberdeen
Dr Bruce Davidson	Consultant Psychiatrist, Moray Mental Health Directorate
Dr Richard Legg	Consultant Psychiatrist, Aberdeenshire Drug and Alcohol Services
Lynsey Murray	Lead Nurse, Moray Integrated Drug and Alcohol Service
Elaine Neil	Lead Pharmacist, Aberdeenshire HSCP (inc HMP Grampian)
Laura Rothney	Lead Nurse, Aberdeen City Drug and Alcohol Services
Dr Bruce Strachan	Lead GP, HMP Grampian
Anne Taylor	Lead Pharmacist, NHS Grampian Controlled Drug Team
David Taylor	Lead Nurse, Aberdeenshire Drug and Alcohol Services
Dr Mike Turner	Consultant Psychiatrist, Aberdeenshire Drug and Alcohol Services

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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