

Use of long-acting injectable buprenorphine for opioid substitution therapy

A national position statement
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Executive summary

Drug-related deaths in Scotland continue to rise, with Scotland reporting the highest levels in Europe. The 1,339 drug-related deaths registered in Scotland in 2020 is the largest annual total ever recorded and represents an increase of almost 100% since 2015. Accidental poisoning, including drug-related death was the fourth most frequently occurring cause of premature death in people aged under 75 in Scotland in 2020, after ischaemic heart disease, lung cancers and coronavirus.

Opioid substitution therapy (OST) is effective in reducing opioid misuse, with methadone hydrochloride currently the most commonly prescribed medication for opioid dependency in Scotland. Buprenorphine, which causes significantly less sedation than methadone, is also licenced and approved for use as OST in Scotland. A long-acting injectable formulation of buprenorphine (Buvidal®) is currently available for subcutaneous administration in a range of doses (8–160 mg), allowing dosage intervals of up to several weeks. Based on the results of a pilot study on the use of Buvidal® in Scottish prisons, the Scottish Government commissioned the rapid development of a document to address the variations in practice regarding the initiation of Buvidal® for OST in all settings within NHS Scotland.

This position statement was not developed using the standard process employed by SIGN for evidence-based guidance. The evidence base is relatively new and emerging but, in recognition of the significant harm from illicit drugs in Scotland, there was a desire to support health and social care professionals further by establishing key principles of care which relate to use of long-acting injectable buprenorphine. The statements in this document are based on statutory advice and formal consensus developed from previously published guidelines using a modified Delphi technique. Assurance was provided in the form of rapid peer review by a panel of experts in the management of opioid dependence. This position statement should be read in conjunction with the Summary of Product Characteristics (SmPC) and Scottish Medicines Consortium (SMC) advice for Buvidal®.

Key points

Patient Selection

Buvidal® is indicated for use in patients aged 16 years or over, to treat opioid dependence within a framework of medical, social and psychological support. Advice from SMC restricts the use of Buvidal® to patients for whom methadone is not suitable and for whom the use of buprenorphine is considered appropriate. The national standards for Medication Assisted Treatment (MAT) support individuals to make informed decisions about choice of medication and appropriate dosage of OST.

Changes to service delivery

Administration of OST treatment and key working are two separate but complementary elements of recovery. Treatment with long-acting injectable buprenorphine potentially confers the opportunity to change the way in which opioid substitution services are structured and delivered.

Consent

Service users should be assessed as having capacity to provide informed consent to their usual dose and to understand warnings regarding risks of sedation and overdose from polysubstance use. If there are concerns that the service user is very intoxicated and unable to understand or follow instructions, the administration of the dose may be deferred and rescheduled.

Training

NHS organisations and contracted services must ensure that appropriate members of staff are trained and competent to administer medicines. Additional training is required to administer Buvidal®, which is currently only available in dosed prefilled syringe formulations. Standard operating procedures should be developed with members of staff.

1. Introduction

The illicit use of drugs, particularly opiates, causes significant social issues within Scotland as it does in other parts of the UK and Europe. Some of these issues include, for example, acquisitive crime, inadequate income, family breakdown and homelessness. Other issues are more clearly associated with health problems, for example, the transmission of communicable diseases (eg human immunodeficiency virus (HIV), hepatitis), injecting-related injuries and a wide range of mental health issues. Increasing illicit drug use has led to increased demands upon healthcare services.

Collecting accurate information on illicit drug use is difficult because of its hidden and illegal nature, therefore prevalence figures can only ever be estimates. Information on the extent of illicit drug use is derived from surveys of samples of the general population.

1.1 Use of illicit drugs

In 2018–20, 9.7% of respondents to the Scottish Crime and Justice Survey (aged 16 years and over) had used illicit drugs compared with 7.4% in 2017–18. Higher levels of problem drug use were reported among males than females and the age group most likely to report using drugs in 2018–20 was aged 16–24.

The most recent national data available on drug use in Scotland was published in 2019 and describes estimated national and local prevalence of problem drug use in Scotland for 2015–16.¹ The estimated number of individuals with problem drug use (routine/prolonged use of illicit opiates and/or benzodiazepines) in Scotland during 2015/16, aged 15–64 years old, was 57,300 (95% confidence interval (CI) 55,800 to 58,900). Expressed as a percentage of the population, this represents 1.62% (95% CI 1.58% to 1.67%).

1.2 Drug-related healthcare harms

In 2020–21 there were 14,310 drug-related hospital stays (270 stays per 100,000 population).² The highest stay rate (127 per 100,000 population) was associated with use of opioids (drugs similar to heroin). Approximately half of the patients with a drug-related hospital stay lived in the most deprived areas in Scotland. The illicit drug overdose rate was 42 stays per 100,000 population and has effectively doubled since 2012/13.

The National Records for Scotland (NRS) reported that 1,339 drug-related deaths were registered in Scotland in 2020; 59 (5%) more than in 2019.³ This was the largest number ever recorded, and nearly twice the number recorded in 2015. Males accounted for 73% of drug-related deaths in 2020. Most drug-related deaths were of people who used more than one substance.

Of the 1,339 drug-related deaths in 2020, one or more opiates or opioids (including heroin/morphine and methadone) were implicated in, or potentially contributed to, 1,192 deaths (89% of the total).

In 2019, NRS published a report comparing Scotland's drug-related deaths with those of other countries.⁴ Based on the UK Drugs Strategy definition Scotland's 2018 drug-related death rate (218 per million population) was 3.4 times that of the UK (63 per million population). The European Monitoring Centre for Drugs and Drug Addiction uses a "drug-induced death" definition that covers only deaths directly caused by illegal drugs in those aged 15 to 64. For Scotland in 2019 the drug-induced death rate was 318 per million population aged 15–64.³ This was higher than any other European country, the next highest being 77 deaths per million population in both Sweden and Norway. The corresponding rate for the UK is not available but the figure for Scotland, England and Wales combined was 76 deaths per million population.

1.3 Treatment for problem drug use

The Scottish Drug Misuse Database, which is managed by Public Health Scotland (PHS), was set up in 1990 to collect information about people in Scotland with problem drug use. Data are collected when individuals make contact with services providing tier 3 and 4 interventions (ie structured community and residential treatment). In 2019–20, initial assessments for specialist drug treatment relating to 10,900 people resident in Scotland were recorded on the Scottish Drug Misuse Database.

Just over half of people assessed for specialist drug treatment were from older age groups; in 2019–20 the percentage of people who were aged 35 years or over was 54%, a large increase from 29% in 2006–07.

More people reported requiring support with heroin than any other substance. In 2019–20, among those who indicated recent drug use, the percentage of people reporting heroin as their main drug was 36%.⁵

1.4 Prescribing for opioid dependency

Methadone hydrochloride is the most commonly used pharmacological treatment for people with opioid dependency in Scotland.⁶ In 2020–21, the number of dispensed items for OST drugs (including methadone) was 438,147. This was lower than the equivalent figure for 2019–20 (501,037). While a decreasing trend in the dispensing of OST drugs has been evident since 2011–12, Public Health Scotland notes that the decrease observed in 2020–21 is likely to reflect changes in OST dispensing due to the coronavirus 2019 (COVID-19) pandemic rather than underlying changes in prescribing activity.⁷

Defined Daily Doses (DDD) were developed by the World Health Organization and are defined as “the assumed average maintenance dose per day used on its main indication in adults.” Given these contextual changes, the number of DDDs per 1,000 population per day is now regarded as the most robust measure of OST dispensing over time. In 2020–21, the dispensing of OST drugs (including methadone) was equivalent to 13.5 DDDs per 1,000 population per day. This was an increase compared with the 2018–19 figure (12.8 DDDs per 1,000 population per day), which was the lowest in the recent time series.⁷

Buprenorphine dispensing (including Buvidal® long-acting injectable formulations) continued to increase in 2020–21, rising to 1.3 DDDs per 1,000 population per day. The use of buprenorphine to treat opioid dependence has increased markedly since 2016–17 (0.2 DDDs per 1,000 population per day) and in 2020–21 was 27% higher than the figure for the previous year. Unlike for methadone, the number of buprenorphine items dispensed increased in 2020–21 in spite of the changes associated with COVID-19. The 2020–21 total of 80,908 buprenorphine items dispensed was 6% higher than the 2019–20 total (76,359).⁷

1.5 Aims

The purpose of this national position statement is to provide NHSScotland with advice on using long-acting injectable buprenorphine for opioid substitution therapy. Dependency on prescribed opioids is not included in the remit of this document and long-acting injectable buprenorphine is not licensed for use in detoxification.

This document is for:

- health and social care professionals, key workers and other staff prescribing long-acting injectable buprenorphine for OST
- health and social care professionals who provide support for the treatment of people with problem drug use and dependence

- Police Scotland and Scottish Prison Service staff who work in partnership with health and social care professionals.

The position statement provides:

- statutory advice from the summary of product characteristics (SmPC) and the Scottish Medicines Consortium (SMC)
- consensus statements developed by a multidisciplinary working group of clinical and non-clinical stakeholders using a formal Delphi process
- links to published guidance on long-acting injectable buprenorphine.

These statements have been developed in response to a request by Scottish Government for rapid advice and so have not followed the standard process used by SIGN to develop evidence-based guidance. The statements are based on statutory advice and consensus developed from published guidelines based on expert opinion, with fast expert peer review as assurance. This position statement is not intended as a standalone document but should be read together with the SmPC and advice from SMC for Buvidal®.

1.6 Terminology

In the UK, long-acting injectable buprenorphine has marketing authorisation for the treatment of opioid dependence within a framework of medical, social and psychological treatment. At time of writing the only available product is Buvidal®. Literature describing this product has used a range of terms to describe the formulation including “long-acting”, “prolonged-release” and “depot”. Buvidal® comprises a lipid-based liquid containing a dissolved active pharmaceutical ingredient (buprenorphine) which is injected subcutaneously. Aqueous fluids in the tissue immediately transform the liquid into a highly viscous liquid, gel-like depot which encapsulates the active pharmaceutical ingredient. Naturally occurring enzymes in the tissue slowly degrade the depot. As it degrades the active pharmaceutical ingredient is released. The formulation’s lipid composition controls the rate of degradation from one week to one month therefore releasing a therapeutic dose of the active pharmaceutical ingredient over a prolonged period.

For consistency, the working group has chosen the term “long-acting injectable buprenorphine” for use throughout this position statement to differentiate Buvidal® from other prolonged-release formulations, for example transdermal patches or subcutaneous implants. Readers should be aware that some information in this position statement is reproduced verbatim from SmPC and SMC, which may use alternative terms to describe the same formulation.

2. Product description

Buvidal® is a prolonged-release subcutaneous injection containing buprenorphine. It is available in two different formulations which are administered at either weekly (8 mg, 16 mg, 24 mg, 32 mg) or monthly (64 mg, 96 mg, 128 mg, 160 mg) intervals.

The weekly and monthly Buvidal® products are differentiated by the colour of the cardboard boxes, and the text “once weekly” or “once monthly” printed on the respective boxes. The individual doses are also differentiated by different colours on the boxes (see *Figure 1*).



It should be noted that the 8 mg, 16 mg, 24 mg and 32 mg strengths contain small amounts of ethanol (alcohol), at less than 100 mg per dose (see *section 4.2*).

3. Patient selection

Most adults who experience harm from problem drug use and are in treatment in the UK report opioids (primarily heroin) as their main problem drugs.^{5,8} Opioid dependence is often associated with other harmful substance use (eg amphetamines, benzodiazepines, cannabis, cocaine, gabapentinoids or tobacco), and other medical, psychiatric and social problems. Addressing these issues involves co-ordinated treatment with other health and social service providers over an extended period.

For most people with opioid dependence, the use of medications (combined with psychosocial treatment) is superior to psychosocial treatment on its own; this is true for agonist, partial agonist, and antagonist medications. Evidence suggests that both methadone and buprenorphine maintenance treatments are superior to withdrawal management alone and both significantly reduce illicit opioid use. Mortality is lower in people treated with methadone or buprenorphine, compared with those not undergoing treatment.⁹

Guidelines from the UK and Australia note that OST has been demonstrated to be a safe and effective treatment approach for addressing opioid dependence and provides the opportunity to engage people with other health and psychosocial interventions. The key elements of OST are:

- safe and effective use of medicine
- regular clinical reviews and monitoring
- participation in psychosocial interventions
- addressing medical, psychiatric and social comorbidities.^{8,10}

Buvidal® is indicated for the treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over.

SUMMARY
OF PRODUCT
CHARACTERISTICS

Advice from the Scottish Medicines Consortium restricts use of Buvidal® to patients for whom methadone is not suitable and for whom the use of buprenorphine is considered appropriate.

SCOTTISH
MEDICINES
CONSORTIUM

The national standards for Medication Assisted Treatment (MAT) support individuals to make an informed choice on what medication to use for OST and the appropriate dose. The standards highlight methadone and buprenorphine as appropriate treatment options for OST and note that each NHS board should have documented guidelines to ensure that methadone and buprenorphine in long- and short-acting formulations are equally available in local formularies and dispensing locations. See *section 8.3* and *Annex 1* for further information on the MAT standards.

3.1 Choosing an appropriate opioid substitute for people with opioid dependence

The Drug Misuse and Dependence: UK Guidelines on Clinical Management (hereafter 'UK Drug Misuse Guideline') provides guidance on the treatment of people with problem drug use and dependence in the UK.⁸ It is based on current evidence and informal professional consensus on how to provide drug treatment for the majority of people, in most instances. This guideline was published in 2017, before the marketing authorisation of long-acting injectable buprenorphine, and therefore any information relating to buprenorphine refers to other formulations available at that time (sublingual or oral lyophilisate). The guideline provides important information about a wide range of elements of treatment provision, including psychosocial and pharmacological interventions, and treatment considerations for specific populations, including those in the criminal justice system.

The UK Drug Misuse Guideline states that oral methadone and oral buprenorphine are both effective at achieving positive outcomes in opioid-dependent individuals. Both are cost effective

and recommended by the National Institute for Clinical Health and Care Excellence (NICE) for the treatment and prevention of withdrawals from heroin and for maintenance programmes.

In Scotland, long-acting injectable buprenorphine is indicated for use in people for whom methadone is not suitable and buprenorphine is considered appropriate.

In terms of selection of people for whom methadone is not suitable and buprenorphine is considered appropriate, the UK Drug Misuse Guideline notes that some people hold strong views against starting buprenorphine and others against starting methadone. There is no simple formula that can be recommended to determine the clinical suitability of either methadone or buprenorphine. This is because there is minimal evidence for greater effectiveness or superior patient safety characteristics of either drug. Other factors, such as concerns about sedation, may also influence the selection of a particular treatment regimen. However, for both of these medications, the guideline suggests that there is a substantial evidence base for effectiveness and it is appropriate for clinicians to discuss these complex issues with patients when obtaining informed consent for their treatment. It is essential that clinicians do not exaggerate what is currently known to support one drug over another, so that patients are empowered to make their own decision, taking account of the reasonable informed advice of the prescriber, which also helps the patient to take account of their own personal circumstances.⁸

A number of clinical factors should be taken into account when selecting the most appropriate medication for a patient. These include:

- a patient's pre-existing preference for either drug
- the benefits and risks of rapid induction onto effective maintenance
- previous substantial benefit from maintenance on either medication
- specific safety concerns (eg with methadone, potential diversion or previous overdose on it; and, with buprenorphine, previous early disengagement from treatment)
- a likely need for strong opioids other than buprenorphine for acute pain management (eg, for pending surgery) or for chronic pain management (eg if on the advice of a pain clinic)
- any relevant interactions that should be taken into account when prescribing for patients taking other drugs or medication
- local pragmatic factors, such as lack of geographical availability of supervised administration (which may favour buprenorphine in some cases).

3.2 Choosing an appropriate formulation of buprenorphine

No research evidence has been identified supporting decision making between the long-acting injectable and sublingual formulations of buprenorphine. In this context it is important to consider individual patient factors and clinical circumstances.

A guideline developed by the Regional Medicines Optimisation Committee describes considerations for OST with long-acting injectable buprenorphine in community settings and secure environments in England.¹³ It notes insufficient clinical experience in the UK to identify specific cohorts who may benefit from this formulation. This guideline and a NICE evidence review¹⁴ recognise that long-acting injectable buprenorphine may offer a range of benefits and reduction in harms, for example:

- offering greater convenience for service users who would no longer be required to attend treatment sites for frequent supervised administration of treatment. Weekly or monthly appointments would be more convenient for service users who:
 - travel abroad
 - have work or study commitments
 - have mobility issues

- live in rural areas where access to community pharmacies will be difficult
- have regular release from custody on license for short periods
- supporting service users who have highly complex lifestyles
- preventing diversion of opioid substitution medicines
- reducing the need for safe storage of medications at home
- optimising OST treatment regimens with potential reduction in the requirement for additional opioid medication.

Long-acting injectable buprenorphine is not recommended under the following circumstances in community settings:

- contraindications stated in the SmPC (see *section 4.2*)
- service users who refuse treatment
- service users who lack capacity to consent to treatment (see *section 8.1*).

Advantages and disadvantages of different delivery models for administering Buvidal® are summarised in *Annex 2*.

4. Initiation and administration

Administration of Buvidal® is restricted to healthcare professionals. Appropriate precautions, such as to conduct patient follow-up visits with clinical monitoring according to the patient's needs, should be taken when prescribing and dispensing buprenorphine. Take-home use or self administration of the product by patients is not allowed.

SUMMARY
OF PRODUCT
CHARACTERISTICS

4.1 Precautions to be taken before initiation of treatment

To avoid precipitating symptoms of withdrawal, treatment with Buvidal® should be started when objective and clear signs of mild to moderate withdrawal are evident (see *section 4.4* of the full *SmPC*). Consideration should be given to the types of opioid used (that is long- or short-acting opioid), time since last opioid use and the degree of opioid dependence.

- For patients using heroin or short-acting opioids, the initial dose of Buvidal® must not be administered until at least 6 hours after the patient last used opioids.
- For patients receiving methadone, the methadone dose should be reduced to a maximum of 30 mg/day before starting treatment with Buvidal® which should not be administered until at least 24 hours after the patient last received a methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients.

SUMMARY
OF PRODUCT
CHARACTERISTICS

4.2 Contraindications

Buvidal® is contraindicated for individuals with hypersensitivity to the active substance or to any of the following excipients:

- soybean phosphatidylcholine
- glycerol dioleate
- ethanol anhydrous (weekly dose formulations only)
- N-Methylpyrrolidone (monthly dose formulations only).

It is contraindicated for individuals with:

- severe respiratory insufficiency
- severe hepatic impairment
- acute alcoholism or delirium tremens.

SUMMARY
OF PRODUCT
CHARACTERISTICS

4.3 Method of administration

Buvidal® is intended for subcutaneous administration only. It should be injected slowly and completely into the subcutaneous tissue of different areas (buttock, thigh, abdomen, or upper arm), provided there is enough subcutaneous tissue. Each area can have multiple injection sites. Injection sites should be rotated for both weekly and monthly injections. A minimum of eight weeks should be left before re-injecting a previously used injection site with the weekly dose. There is no clinical data supporting re-injection of the monthly dose into the same site. This is unlikely to be a safety concern. The decision to re-inject at the same site should also be guided by the attending physician's clinical judgement. Administered dose should be as a single injection and not divided. See *Annex 3* for detailed administration instructions.

Care must be taken to avoid inadvertent injection of Buvidal®. The dose must not be administered intravascularly (intravenously), intramuscularly or intradermally. Intravascular, such as intravenous, injection would present a risk of serious harm as Buvidal® forms a solid mass upon contact with body fluids, which potentially could cause blood vessel injury, occlusion, or thromboembolic events.

SUMMARY
OF PRODUCT
CHARACTERISTICS

To minimise the risk of misuse, abuse and diversion, appropriate precautions should be taken when prescribing and dispensing buprenorphine. Healthcare professionals should administer Buvidal® directly to the patient. Take-home use or self administration of the product by patients is not allowed. Any attempts to remove the depot should be monitored throughout treatment.

SUMMARY
OF PRODUCT
CHARACTERISTICS

4.4 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 one 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 1* and once patients have been stabilised on weekly treatment (four weeks or more, where practical).

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

Dose of daily oromucosal buprenorphine (Espranor®)	Dose of daily sublingual buprenorphine (Subutex®)	Weekly Buvidal® dose	Monthly Buvidal® dose
2-4 mg	2-6 mg	8 mg	-
6-8 mg	8-10 mg	16 mg	64 mg
10-12 mg	12-16 mg	24 mg	96 mg
14-18 mg	18-24 mg	32 mg	128 mg
	26-32 mg		160 mg

SUMMARY
OF PRODUCT
CHARACTERISTICS

*Espranor® has a 25-30 % higher bioavailability compared with other sublingual buprenorphine products such as Subutex®.*¹⁵

Table adapted from <https://buvidal.co.uk/buvidal/treatment-with-buvidal/switching-from-transmucosal-buprenorphine-bpn/>

4.5 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.

Patients may be switched from sublingual buprenorphine 26-32 mg directly to monthly Buvidal® 160 mg with close monitoring during the dosing period after the switch.

The dose of buprenorphine in milligrams can differ between sublingual products, which needs to be taken into consideration on a product-by-product basis.

Closer monitoring of patients is recommended by the manufacturer of Buvidal® during the dosing period after the switch from Espranor®. Refer to the full SmPC for further details on the pharmacokinetic properties of Buvidal®.

SUMMARY
OF PRODUCT
CHARACTERISTICS

5. Maintenance treatments and dose adjustments

5.1 Maintenance treatments 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 1*. Following switching, patients may need closer monitoring.

SUMMARY
OF PRODUCT
CHARACTERISTICS

Doses should generally be reduced under the following conditions:

- the service user reports buprenorphine dose-related adverse events (eg sedation or lethargy, persistent headaches, nausea) or has elevated liver function tests
- the service user wishes to be supported to work towards withdrawal of opioid substitution therapy
- the service user is reporting the dose is 'too high' and/or is seeking a dose reduction and there are no significant concerns regarding deterioration in clinical condition (eg substance use, physical or mental health symptoms) that may arise with a dose reduction.

CONSENSUS
STATEMENT

Individuals who develop abnormal liver function test results while on long-acting injectable buprenorphine should have these appropriately investigated and other causes excluded. Consideration should be given to the balance of risks and benefits of continuing treatment. Additional monitoring should be considered if continuing.

Doses should generally be increased under the following conditions:

- the current dose is not meeting the needs of the service user (eg they are experiencing withdrawal symptoms or cravings)
- the service user reports their dose is 'too low' and they would like a dose increase, there are no significant clinical safety concerns AND the service user is not experiencing adverse events related to buprenorphine (eg sedation or lethargy, persistent headaches, constipation, nausea) or elevated liver function tests.

CONSENSUS
STATEMENT

In general, doses should be maintained if the service user:

- is comfortable and not experiencing opioid withdrawals or cravings; and
- is achieving their own treatment goals and wishes; and
- is not experiencing clinically significant dose-related adverse events related to buprenorphine (eg sedation or lethargy, persistent headaches, nausea); and
- is satisfied with their current dose and requesting the dose be maintained.

CONSENSUS
STATEMENT

5.2 Supplemental and missed 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 160 mg.

To avoid missed doses, the weekly dose may be administered up to two days before or after the weekly time point, and the monthly dose may be administered up to one week before or after the monthly time point. If a dose is missed, the next dose should be administered as soon as practically possible.

SUMMARY
OF PRODUCT
CHARACTERISTICS

5.3 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* of the full *SmPC*). 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. Special warnings and precautions for use

6.1 Prolonged-release properties

The prolonged-release properties of the product should be considered during treatment including initiation and termination. In particular, patients with concomitant medicinal products and/or comorbidities, should be monitored for signs and symptoms of toxicity, overdose or withdrawal caused by increased or decreased levels of buprenorphine. See *section 5.3* for further information on treatment termination.

Refer to the full SmPC for pharmacokinetic properties and further information on the following risks of harm associated with Buvidal®:

- respiratory depression
- central nervous system (CNS) depression
- dependence
- serotonin syndrome
- hepatitis and hepatic events
- drug withdrawal syndrome
- precipitation of opioid withdrawal syndrome
- hepatic impairment
- renal impairment
- QT prolongation
- class effects of opioids.

SUMMARY
OF PRODUCT
CHARACTERISTICS

6.2 Interaction with other medicinal products

Buprenorphine should be used cautiously when coadministered with:

- benzodiazepines
- gabapentinoids
- alcoholic drinks or medicinal products containing alcohol
- other CNS depressants
- opioid analgesics
- naltrexone and nalmeferne
- CYP3A4 inhibitors or CYP3A4 inducers
- UGT1A1 inhibitors
- monoamine oxidase inhibitors
- serotonergic medicinal products.

Refer to the full SmPC for details of the specific pharmacological effects of coadministration with these products.

SUMMARY
OF PRODUCT
CHARACTERISTICS

6.3 Driving and operating machinery

Buprenorphine has minor to moderate influence on the ability to drive and use machines when administered to opioid-dependent patients. Buprenorphine may cause drowsiness, dizziness or impaired thinking, especially during treatment induction and dose adjustment. If used together with alcohol or CNS depressants, the effect is likely to be more pronounced (see *sections 4.4* and *4.5* of the full SmPC).

SUMMARY
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CHARACTERISTICS

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- the medicine is likely to affect your ability to drive
- do not drive until you know how the medicine affects you
- it is an offence to drive while under the influence of this medicine.

However, you would not be committing an offence (called 'statutory defence') if:

- the medicine has been prescribed to treat a medical or dental problem; and
- you have taken it according to the instructions given by the prescriber and in the information provided with the medicine; and
- it was not affecting your ability to drive safely.

The Substance Misuse Management in General Practice (SMMGP) clinical guideline for use of depot buprenorphine (Buvidal®) in the treatment of people with opioid dependence includes the following information for healthcare professionals on the implications of long-acting injectable buprenorphine use on their patient's driving.

Doctors and other healthcare professionals should:

- advise the patient on the impact of their medical condition for safe driving ability
- advise the patient on their legal requirement to notify the Driver and Vehicle Licensing Agency (DVLA) of any relevant condition
- treat, manage and monitor the patient's condition with ongoing consideration of their fitness to drive
- notify the DVLA when fitness to drive requires notification but an individual cannot or will not notify the DVLA themselves.

The DVLA guidance makes specific reference to long-acting injectable buprenorphine aligning its guidance alongside that for individuals on healthcare-provider-approved oral methadone or buprenorphine programmes. Chapter 5 of the DVLA guidance should be adhered to under usual situations.

Prescribers of long-acting injectable buprenorphine may advise patients that applicants or drivers may be licensed subject to favourable assessment and normally annual medical review when all of the following conditions can be met:

- patients must comply fully with a consultant- or appropriate healthcare practitioner-supervised long-acting injectable buprenorphine maintenance programme for opioid dependence (adherence to prescription and appointments, and toxicology testing with sustained stability)
- patients are stable on the treatment programme for a minimum of one year
- patients have no non-prescribed psychoactive drug use during the programme or extra use of prescribed drugs such as methadone, buprenorphine or benzodiazepines
- there is no toxicological evidence of problem drug use
- there is no adverse effect from treatment likely to affect safe driving
- there is no problem alcohol use or dependence
- there are no other relevant medical conditions, eg mental health issues
- there are no other disqualifying conditions (these include seizures and cardiac problems).

The patient should be cautioned not to drive or operate hazardous machinery while taking this medicine until it is known how the patient is affected by the medicine. An individual recommendation should be given by the treating healthcare professional.

See *the UK Drug Misuse Guideline, Appendix 7* for further information on drugs and driving.⁸

6.4 Fertility, pregnancy and lactation

There are no or limited data on effects of buprenorphine on human fertility. An effect of buprenorphine on fertility in animals has not been seen.

There are no or limited data from the use of buprenorphine in pregnant women. Animal studies do not indicate reproductive toxicity. Buprenorphine should be used during pregnancy only if the potential benefit outweighs the potential risk to the foetus.

Towards the end of pregnancy, buprenorphine may induce respiratory depression in the newborn infant even after a short period of administration. Long-term administration during the last three months of pregnancy may cause a withdrawal syndrome in the neonate (eg hypertonia, neonatal tremor, neonatal agitation, myoclonus or convulsions). The syndrome is generally delayed from several hours to several days after birth.

Due to the long half-life of buprenorphine, neonatal monitoring for several days after birth should be considered to prevent the risk of respiratory depression or withdrawal syndrome in neonates.

Buprenorphine and its metabolites are excreted in human breast milk and Buvidal® should be used with caution during breastfeeding.

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6.5 Overdose and polydrug use

Symptoms

Respiratory depression, as a result of CNS 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.

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 (ie 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, (see *section 6.1* and refer to the full *SmPC*). Naloxone can be cleared more rapidly than buprenorphine, allowing for a return of previously controlled buprenorphine overdose symptoms.

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7. Changes to service delivery associated with use of long-acting injectable buprenorphine

Administration of OST treatment drugs and key working are two separate but complementary elements of recovery. While the process of administering a treatment drug does not offer all of the options for formal review, it provides an opportunity to make regular observations on the service user's wellbeing and general state. When treatment administration changes from daily to weekly or monthly, although this does not influence the frequency of key working, it reduces the scheduled contact between service user and a healthcare professional and this should be discussed with the individual in the context of choosing the most appropriate treatment options for their needs.

Treatment with long-acting injectable buprenorphine potentially confers the opportunity to change the way in which opioid substitution services are structured and delivered. The less frequent dosing with long-acting injectable buprenorphine formulations may reduce the opportunity for daily contact between service user and a care provider. This may offer advantages for some individuals as it gives them the opportunity to have time to attend recovery activities and other priorities. For all service users, careful scheduling of clinical reviews, for example, in the setting where the depot can be delivered, and flexible approaches to care planning should be considered and be based on the individual's needs.

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8. Barriers to the delivery of long-acting injectable buprenorphine

8.1 Consent

Prescribing is the responsibility of the healthcare professional signing the prescription.

The General Medical Council (GMC) ethical guidance on good practice in prescribing and managing medicines and devices includes information on deciding if it is safe to prescribe.¹⁸ It reminds prescribers that “you should only prescribe medicines if you have adequate knowledge of the patient’s health and you are satisfied that the medicines serve the patient’s needs.” Among the elements required in establishing a dialogue and obtaining consent from the patient, is the assessment of capacity.

The GMC guidance notes:

- “You must begin with the presumption that every adult patient has capacity to make decisions about their care. Assessing capacity is a core clinical skill and doesn’t necessarily require specialist input. You should be able to draw reasonable conclusions about your patient’s capacity during your dialogue with them.”
- “If you are unsure if a patient has capacity to make a decision, you should assess their capacity using the test under the relevant legislation. Our guidance on ‘[Decision making and consent](#)’ gives detailed advice on assessing capacity and making decisions where a patient is known not to have capacity, (see *paragraphs 76 to 91*).”
- “Medicines may be prescribed without consent if it is likely to be of overall benefit to adults who lack capacity, or in accordance with mental health legislation.”
- “For patients under 18 this guidance should be read alongside ‘[0–18: guidance for all doctors](#)’”.

Opioid substitution therapy has a range of goals that aim to reduce dependence and improve health, wellbeing and recovery. The key worker will explore these with the service user over time. The treatment and recovery care plan can be an important mechanism for reflecting on, and recording, informed consent to treatment and the goals agreed with the service user.⁸

As part of the process of gathering consent patients should understand the implications of different treatment options, including potential risks and benefits, side effects, financial and other commitments.

A decision to prescribe, what and how much to prescribe will depend upon:

- the overall treatment plan for the individual patient
- clinical guidelines
- locally agreed protocols
- the clinician’s experience and competencies
- any discussion with other members of a multidisciplinary team
- advice, where necessary, from a specialist in problem drug use.⁸

Obtaining informed consent requires that relevant issues, including the evidence-based potential benefits and harms of treatments, are discussed with the patient.

Service users should be assessed as having capacity to provide informed consent to their usual dose, and to understand warnings regarding risks of sedation and overdose from polydrug use. If there are concerns that the service user is very intoxicated and unable to understand or follow instructions, the administration of the dose may be deferred and rescheduled.

8.2 Individuals who do not attend or are unsuitable for administration of long-acting injectable buprenorphine

In community settings, it is recommended to have 'did not attend' and 'unsuitable for administration' procedures in place for situations where service users do not attend their scheduled appointments or the dose is not administered for a clinical reason (eg the service user is too intoxicated to provide consent). The procedures should contain the following:

- communication system (ie who to inform - key worker, clinician),
- documentation of actions to be taken to contact and recall the service user if applicable. It should detail who is responsible for carrying out these actions.

Key workers should prepare an individualised 'did not attend' plan for each person prescribed long-acting injectable buprenorphine. This will inform staff unfamiliar with the service user of the actions to be taken if they do not attend appointments.

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8.3 Individuals at risk of poor engagement

National MAT standards were published in 2021 to help reduce deaths, and other harms, and to promote recovery for people who experience problems with drug use.¹² The ten standards provide a framework to ensure that MAT is sufficiently safe, effective, acceptable, accessible and person centred to enable people to benefit from treatment for as long as they need (see *Annex 1*). The purpose of the standards is to improve access and retention in MAT and enable people to make an informed choice about care. A number of standards specifically support engagement between services and people experiencing problems with drug use.

The standards report that evidence shows elevated mortality risks during the first four weeks of starting treatment and the first four weeks after leaving treatment. This suggests that these are critical intervention points to support people in MAT and to prevent drug-related deaths. Standard 3 requires all people at high risk of drug-related harm to be proactively identified and offered support to commence or continue MAT. The objective of this standard is to prevent harms by rapidly providing that individual with support for engagement or re-engagement with holistic care including MAT. Standard 5 states that all people will receive support to remain in treatment for as long as requested.

The biggest structural drivers of problematic drug use are poverty and deprivation. Problematic drug use is more prevalent among people from more deprived areas and from less advantaged backgrounds. Studies have consistently shown a high prevalence of comorbidity of mental health disorders in people experiencing problem drug use and a clear association with experiences of homelessness and the criminal justice system.¹⁹ People who experience poverty and deprivation are more likely to engage in problem drug use. They are also more likely to experience stigma and further barriers to service use, as well as self stigma.

Standard 8 requires all people experiencing problems with drug use to have access to independent advocacy and support for housing, welfare and income needs. The criteria that support this standard require service providers to develop flexible pathways that allow access to services at a range of intensities to suit individuals with varying needs and across various settings. The criteria also describe the agreement of a plan setting out actions for services, the individual and family members or a nominated person in the event of the service user disengaging from treatment. The plan should be focused on the value of care and may include the option of anticipatory care planning.

In people at risk of poor engagement with opioid substitution therapy due to:

- comorbid health conditions (eg cognitive impairment, severe psychiatric conditions or poor mobility)
- socioeconomic marginalisation (eg inadequate income, criminal justice system involvement, incarceration, homelessness, social stigma or isolation, poor literacy or poverty)
- safeguarding issues (eg domestic violence or child protection concerns)
- protected characteristics (eg people from a variety of ethnic groups, people with a minority sexual orientation, women, or older people)

particular attention to informed consent to treatment with long-acting injectable formulations is required, and advocacy services should be available. Service providers and service users should collaboratively implement strategies that aim to enhance attendance for dosing and clinical reviews. Service providers should consider active follow-up strategies for service users who do not attend for scheduled appointments.

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9. Clinical handover

A service user's care may be transferred (temporarily or permanently) to another provider (eg acute, community, mental health, health and justice) and vice versa. There should be clear documentation and communication between professionals at both settings to minimise disruption to the service user's treatment and ensure continuity of care.

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As a minimum, the following needs to be communicated to the receiving provider upon transfer:

- the formulation of long-acting injectable buprenorphine that was administered (weekly or monthly)
- the date and dose of last dose administered
- the date and dose of the next dose due
- the preferred site of administration, including last site of administration
- the dose titration regimen if the service user is not on a stable regimen
- if applicable, where the service user normally receives treatment (eg directly from substance misuse service provider, community pharmacy)
- any monitoring required
- any adverse events, risks or concerns regarding long-acting injectable buprenorphine treatment that is relevant to other healthcare providers
- contact details of the transferring team, if further information is required.

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10. Pain management

10.1 Management of acute pain

For management of acute pain during continued use of Buvidal®, a combination of use of opioids with high mu-opioid receptor affinity (eg fentanyl), non-opioid analgesics and regional anaesthesia might be necessary. Titration of oral or intravenous short-acting opioid pain medicinal products (immediate-release morphine, oxycodone or fentanyl) to the desired analgesic effect in patients treated with Buvidal® might require higher doses. Patients should be monitored during treatment and caution should be exercised due to the potential risk of overdose and/or death.

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The working group suggests caution in the use of fentanyl lozenges for acute pain management which are highly addictive due to their potency. Transdermal fentanyl patches are licensed only for use in chronic pain management.

10.2 Management of chronic pain

Chronic pain is common in patients receiving OST, estimated to affect 23–68% of patients worldwide compared with an estimated prevalence in the general population of 8.7–64.4%.²⁰

The Faculty of Pain Medicine of the Royal College of Anaesthetists notes the following general considerations for managing chronic pain in patients receiving OST:²¹

- medications should be part of a wider plan to support self management
- mental health diagnoses and emotional difficulties need to be identified and managed
- physical rehabilitation, exercise and psychological treatments are essential to support chronic pain management
- close collaboration with drug services and the service user's general practitioner (GP) is mandatory (including confirmation of substance misuse)
- regimens should avoid prescription of multiple opioids.

The College provides high-level [information on pain management in palliative care for individuals with recognised drug problems](#). It notes that “the principles of analgesic practice in [people with problem drug use] are fundamentally no different from those for other adult patients needing palliative care.”

[SIGN 136, Management of chronic pain](#) provides recommendations based on current evidence for best practice in the assessment and management, in non-specialist settings, of adults with chronic non-malignant pain, defined as pain that has been present for more than 12 weeks. Self management, pharmacological, psychological, physical, complementary and dietary therapies are covered.²²

General principles of chronic pain management should be followed and include patient education and engagement in the treatment process, physical interventions (eg exercise or physiotherapy), psychosocial interventions (eg cognitive-behavioural therapy) and the appropriate use of other medications.

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Long-acting injectable buprenorphine is used for opioid substitution therapy, and not pain management.

The manufacturer of Buvidal® has submitted a licence extension to the European Medicines Agency to extend the licence to include the treatment of chronic pain. At time of writing this has not been considered.

11. Training

The UK Drug Misuse Guideline states that clinicians need to have appropriate competencies for their clinical roles and receive training to achieve those competencies. They need to have appropriate certification, such as specialist registration, and take account of any requirements for professional revalidation. Non-clinical skills such as leadership and management are also important. Clinicians benefit from individual or peer supervision, personal development plans, mentoring or other forms of professional support. Volunteers and peer mentors may also have relevant qualifications for their roles.⁸

Clinicians have an obligation to update their knowledge and skills base according to emerging evidence and developments in professional practice. Appraisal is mandatory for all clinicians working in the NHS and is good practice in other settings.

It is particularly important for non-professional staff who may not have recourse to professional bodies to be supported and supervised to carry out their roles effectively.

The professional regulatory bodies (such as the Health and Care Professions Council, the GMC, the General Pharmaceutical Council and the Nursing and Midwifery Council) are responsible for setting the standards of behaviour, competence and education of regulated healthcare professionals. They also have responsibility for registering professionals who meet those standards, and taking action where the standards are not met. For other clinical and care staff, national occupational standards (including the Drugs and Alcohol National Occupational Standards) set out the competencies and qualifications required.

Scottish Government's alcohol and drug treatment strategy, "Rights, Respect And Recovery"¹⁹ notes an intention to "ensure that people have the right values, knowledge and experience as well as access to training and ongoing support to put these into practice. Our approach needs to reach beyond those working in treatment and other public services - to volunteers, those leading recovery communities, family members as well as the public. We are committed to developing a workforce development framework which will set out our shared expectations for this workforce."

NHS organisations and contracted services must ensure appropriate staff are trained and competent to administer medicines, including as subcutaneous injections. There are no established formal prescribing or administration training standards for long-acting injectable buprenorphine. Additional training is required to deliver long-acting injectable buprenorphine as it is currently available only in dosed prefilled safety syringe formulations. Standard operating procedures should be developed with staff.

Substance misuse service providers are advised to have sufficient staff (including locums) trained to ensure service resilience. If the administration is delivered by a third party (eg community pharmacy or residential rehabilitation service), service providers are advised to have evidence of training to ensure competence and that training and training records are up to date.

- Further advice on administration of long-acting injectable buprenorphine is available from the manufacturer.
- The development and delivery of training at national level on the pharmacodynamics and administration technique of long-acting injectable buprenorphine will promote consistency, skills maintenance and quality assurance in the appropriate use of this product. A combination of training delivery mechanisms, such as LearnPro, TURAS|Learn and key trainers may offer focus on the range of different skills and knowledge required.

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12. Patient information

This section covers the issues likely to be of most concern to service users and their families and carers. The following points are provided for use by health professionals when discussing long-acting injectable buprenorphine with individuals and carers and in guiding the development of local information materials.

What is Buvidal®?

Buvidal® is a long-acting buprenorphine injection that is provided on a weekly or monthly basis. You may have been offered buprenorphine in tablet form previously (Subutex®, Espranor® or Suboxone®), and this version works in the same way, but over a longer period of time.

Is it right for me?

Buvidal® has had a positive impact on the recovery of many service users, however it will not suit everyone. It is important that you make a well-informed choice when it comes to the right treatment for you, and your clinical teams and independent advocate are available to offer support and guidance. Experience in Scotland has shown that Buvidal® has been very effective for:

- people who are stable and doing well, but still feel their daily life is restricted by their treatment, for example, by having to visit clinics or collect medication from pharmacies and store them securely
- people with a more complex lifestyle who find it challenging to make routine appointments, and have struggled to achieve treatment stability.

What support can I expect?

You may wish to consider if it would help having others present to support you in meetings and reviews. This could include staff who can provide independent advocacy or mental health support, or a key worker or other members of your care team or a friend or family member.

Things to consider:

- The treatment can allow you more freedom, as you will no longer need to make frequent visits to the pharmacy to collect medication.
- The treatment offers you some protection from the risk of accidental opiate overdose, however this benefit is reduced if you are taking other depressant drugs such as benzodiazepines or gabapentinoids. It is unclear whether Buvidal® offers a different level of protection to oral buprenorphine or methadone.
- There is a chance you could feel unwell at first as your body adjusts to the new treatment.
- If your initial dose feels too low for you, you could experience mild withdrawal symptoms. If this happens you will be able to discuss this with your care team who can arrange a top-up dose.
- You will not experience euphoria when taking heroin if you use on top of Buvidal®.

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CONSIDER

Do I need to be in withdrawal before starting Buvidal®?

If you are not currently receiving OST, you need to be in mild withdrawal to begin treatment. You do not need to become terribly unwell, but should be at the point of early opiate withdrawal, where you begin to feel aches, yawn and have some goosebumps. This usually occurs after no heroin has been used for 12–16 hours. Unfortunately, you won't feel great for the remainder of the day, but by the next day people usually report feeling well. If you've never had buprenorphine before but wish to try Buvidal®, your team will give you a buprenorphine tablet first, to make sure you can tolerate it.

What happens if I still feel like I'm in withdrawal after my first injection?

Your care team will consider a top-up dose, by trying to work out what you need, what you normally use and what prescriptions you take. If you are feeling unwell, the team will ask you to return as soon as possible.

Remember that if you are feeling ill, trying to top up with heroin will not have the desired effect.

What happens if I use drugs on top of Buvidal®? For example opiates or cocaine?

If you decided to take opiates on top of Buvidal®, you are not likely to feel the effect of the opiates you are taking. Feedback from patients has been that buying heroin was a waste of money – you won't experience the sensation you are looking for. If you take cocaine, the Buvidal® will not interfere with this and you will feel the cocaine hit, however you will not be able to use opiates to come down from the effect of the cocaine. Any side effects you may experience will be similar to those felt when using other drugs on top of buprenorphine tablets.

What would I need to do if I wanted to switch from methadone treatment to Buvidal®?

If you are on methadone and want to change to Buvidal®, you will be helped to get your methadone dose down to 30 mg/day. There must be a gap of at least 24 hours between your last 30 mg dose of methadone and your first Buvidal® injection.

Can I drink alcohol while having Buvidal®?

A small amount of alcohol (3 units or less) is unlikely to affect the actions of Buvidal®, however Buvidal® is not recommended for people drinking large amounts of alcohol. Similarly to oral buprenorphine, it is not usually prescribed to people who have problems with alcohol because you need to have reasonable liver function to for this treatment to be effective.

If your team suspects you have liver problems, you have been diagnosed with jaundice, or had been admitted to hospital with liver problems, they may discuss other treatment options with you.

Is there a risk of overdose if opiates or alcohol are used on top of Buvidal®?

Like buprenorphine tablets, Buvidal® is very protective from opiate overdose.

Buvidal® won't protect you from overdose no matter what. It helps people who may have an accidental overdose with opiates, but it is not clear what would happen if someone was determined to see how much they could take before they overdose.

When it comes to alcohol, unfortunately Buvidal® will have no effect on an alcohol overdose. This means that if you did drink too much, you are still at risk of respiratory depression and possibly choking.

If I overdose, what would be the effect of being given a shot of naloxone?

The effect of the naloxone would be the same as if you were on buprenorphine tablets.

The naloxone would try to reverse the effects of the overdose opiate drug, and then the Buvidal® would start acting again. So after a few hours, you should start to feel better. In some cases, because of the longer action of Buvidal® than other treatments, you may need to be monitored closely for some time and if required, given naloxone through a drip in hospital.

If you had overdosed on other substances (for example benzodiazepines or gabapentanoids) the naloxone would have no effect but do no harm.

What happens if I miss my injection?

There is a two-day grace period with weekly Buvidal® injections, so if you were unable to make

your scheduled appointment, receiving your injection two days either side of that appointment will not impact on your treatment. There is a seven day grace period either side of the monthly injection.

It is important to remember that getting the best results with this treatment depends on you following up with your scheduled injections.

If I had an accident and needed an opioid for pain relief, what would happen?

Buvidal® is not used for pain relief but may have some effect on your experience of pain. Depending on the level and type of pain caused by your accident, you may be given non-opioid pain relief (eg paracetamol or ibuprofen) or local or regional anaesthesia which involves an injection near to a nerve or group of nerves, and which makes part of your body go numb. If the clinical team decides to use an opioid they may give this to you at a higher dose than usual to achieve the required pain relief. This is because of the way Buvidal® works to block some of the opioid receptors in your brain.

Can the injection be reversed if I was allergic to it?

No, it cannot be reversed. For this reason, you will receive a buprenorphine tablet before your first Buvidal® injection. If you show no side effects, you can have your first injection as soon as 30 minutes after the tablet.

What if I am pregnant, or get pregnant when I am on it?

Buvidal® has been approved for use in pregnancy by the medical regulators when the benefit to you outweighs any risks to your baby. The decision to use weekly or monthly formulations will be made with you based upon your personal situation. If you are already on Buvidal® and became pregnant, your treatment will continue and your team will discuss with you whether you should switch to buprenorphine tablets at some stage in your pregnancy.

Would my treatment be continued in prison if I was sentenced?

The use of Buvidal® was tried in Scottish prisons during the COVID-19 pandemic. It is expected that it will be available to those who would benefit from it in future. If Buvidal® was not available for any reason, your treatment would be switched to the equivalent dose of buprenorphine tablets.

Will Buvidal® prevent natural endorphin highs from sex, exercise and so on?

No, the Buvidal® will have no impact on naturally occurring endorphins. They will not be enhanced or reduced by Buvidal®.

If I have been on Buvidal® and want to come off, what's the process?

The length of time it takes for withdrawal is different for each individual. As Buvidal® is a long-acting treatment, if you experience withdrawal symptoms, these may appear weeks or months after your last dose, but are likely to be less severe than symptoms after withdrawing from long-term buprenorphine tablets. Your care team could start reducing the monthly injection dose, aiming to bring you down to 64 mg monthly for a few months and then stop the injection. Some people have found that they are able to comfortably come off of Buvidal® this way, as it will slowly come out of your body.

If you find it hard then your team will discuss with you what might work for you. This might be to extend the periods between your monthly injections, or to change to weekly doses. They may suggest switching you to buprenorphine tablets for a short period, and then reduce your doses of these. When the time comes, there are several ways of stopping treatment, and your team will discuss this with you to help you to find a way that best suits your needs.

12.1 Sources of further information

Scottish Drugs Forum

Scottish Drugs Forum is Scotland's national resource of expertise on drugs and related issues. It seeks to lead and represent the drugs field in Scotland in order to improve Scotland's response to problem drug use by working with policy makers, service planners and commissioners, service managers and staff as well as people who use or have used services to ensure service quality and evidence-based policy and practice. Scottish Drugs Forum has a range of programmes to improve services, reduce harms associated with problem drug use and research and training resources.

91 Mitchell Street
Glasgow G1 3LN

Tel: 0141 221 1175
www.sdf.org.uk

Scottish Families Affected by Alcohol and Drugs

Scottish Families Affected by Alcohol and Drugs is a national charity that supports anyone concerned about someone else's alcohol or drug use in Scotland. It offers a number of local and national family support services and delivers workforce development through training courses, communications and campaigning work. It is one of the Scottish Government's Nationally Commissioned Organisations for alcohol and drugs and is recognised as Scotland's leading charity for families affected by alcohol and drugs.

Edward House, 2nd Floor,
199 Sauchiehall Street
Glasgow G2 3EX

Tel: 0141 465 7523
Email: info@sfad.org.uk
www.sfad.org.uk

Scottish Recovery Consortium

Scottish Recovery Consortium supports, represents and connects recovery across Scotland. The team works nationally across Scotland to develop and provide events, training, representation and community development. It uses a rights-based approach with lived experience central to the work to develop, design and deliver recovery services and interventions. The Consortium works with Scottish Government and Public Health Scotland to make sure that the MAT standards are implemented across Scotland.

2/1, 30 Bell Street
Glasgow G1 1LG

Tel: 0141 552 1355
scottishrecoveryconsortium.org

Turning Point Scotland

Turning Point Scotland specialises in supporting people facing the most complex and challenging situations. It offers confidential and effective support to those wishing to address their drug and alcohol use. Turning Point Scotland's services include:

- provision of sterile equipment and safe rooms for injecting and safe disposal of used needles
- blood borne virus testing
- advice on dealing with risk of overdose and provision of naloxone
- short-term residential support.

54 Govan Road
Glasgow G51 1JL

Tel: 0141 427 8200

Email: info@turningpointscotland.com

www.turningpointscotland.com

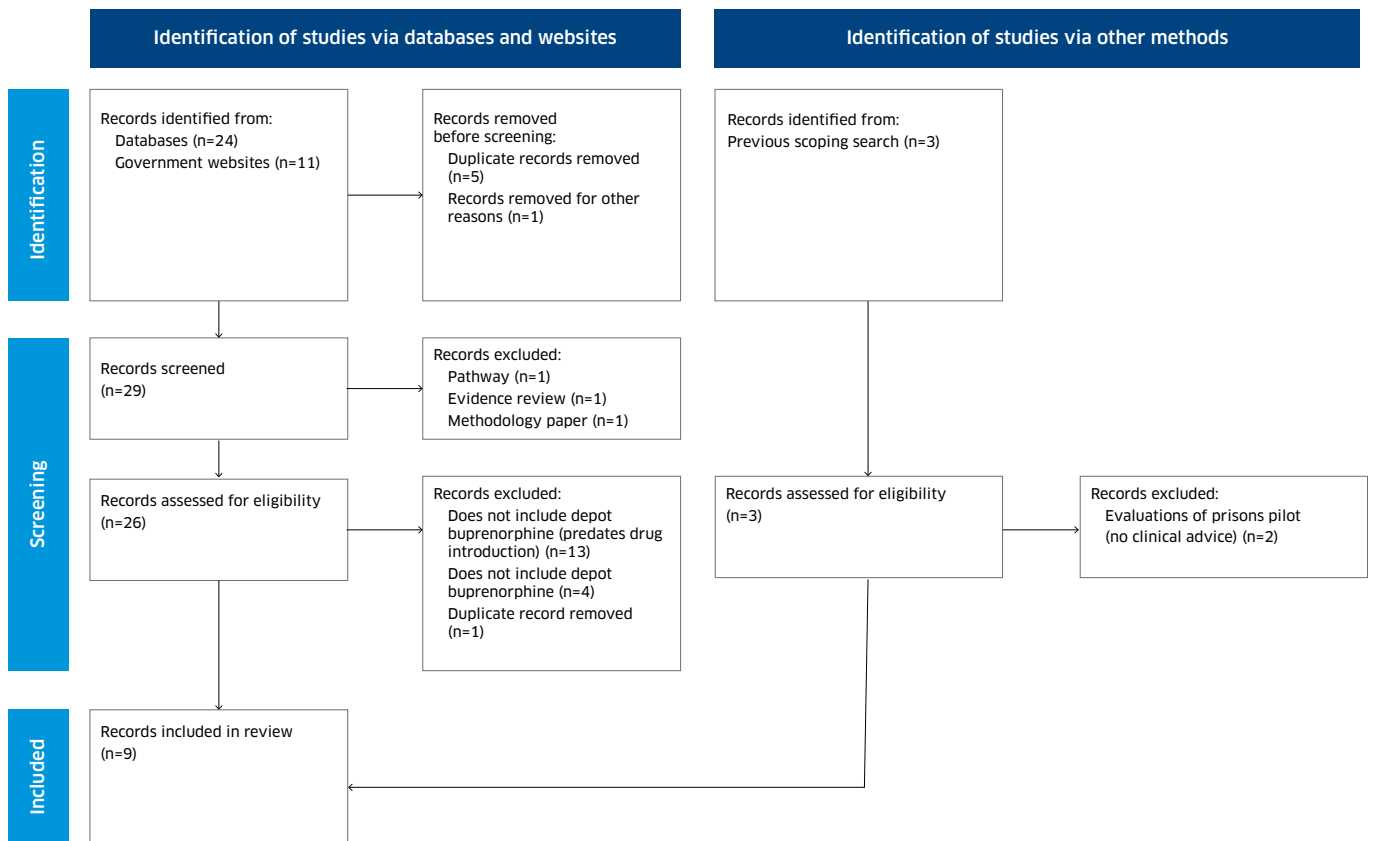
13. Methodology

13.1 Systematic literature review

A focused literature search was conducted using an in-house checklist developed to search for guidelines and guidance (a search narrative is available in the supporting material section for this position statement at www.sign.ac.uk). While the scope was international, the focus was on countries similar to Scotland in terms of population characteristics and healthcare settings. Guidelines were restricted to those including information on the use of long-acting injectable buprenorphine for opioid substitution treatment in those aged over 16 years.

The focused search identified 35 items. Three additional items were added from earlier scoping searches. Search results included evidence-based guidelines based on a systematic development methodology, guidelines based on expert opinion, best practice statements, evidence reviews, service evaluations and general reports. The results were reviewed for relevance by a Programme Manager from SIGN and checked by the working group Chair. Items were retained if they were guidelines (of any quality) which contained directly relevant information on the use of the product, or robust evidence-based guidelines containing information on management of opioid dependence which could be extrapolated to the population of interest (see *Figure 2*).

Figure: 2 Literature search flow diagram



13.2 Quality of evidence

After sifting, nine guidelines^{9,10,13,16,23,24,25,26,27} were retained and independently appraised by two researchers from Healthcare Improvement Scotland using the Appraisal of Guidelines for Research & Evaluation (AGREE) II Instrument.²⁸ The AGREE II Instrument consists of 23 key items organised within six domains. Each domain assesses a different dimension of guideline quality. The global rating items were not used in this assessment. Domain scores were calculated for each guideline and are presented in *Figures 3-8*.

Figure 3: Domain 1 – Scope and purpose

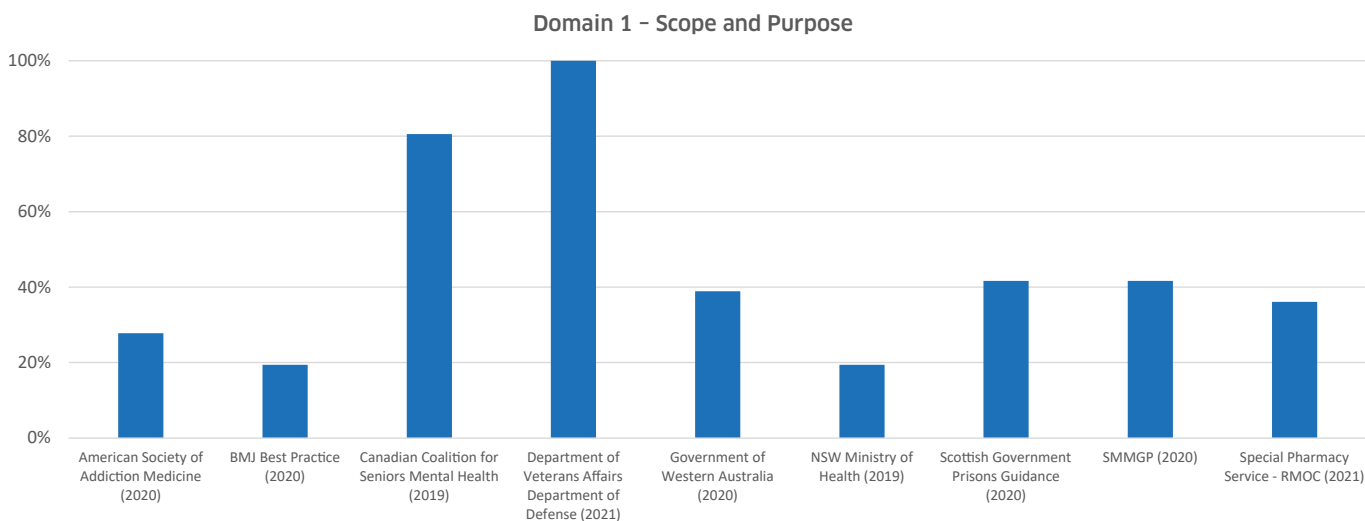


Figure 4: Domain 2 – Stakeholder involvement



Figure 5: Domain 3 – Rigour of development

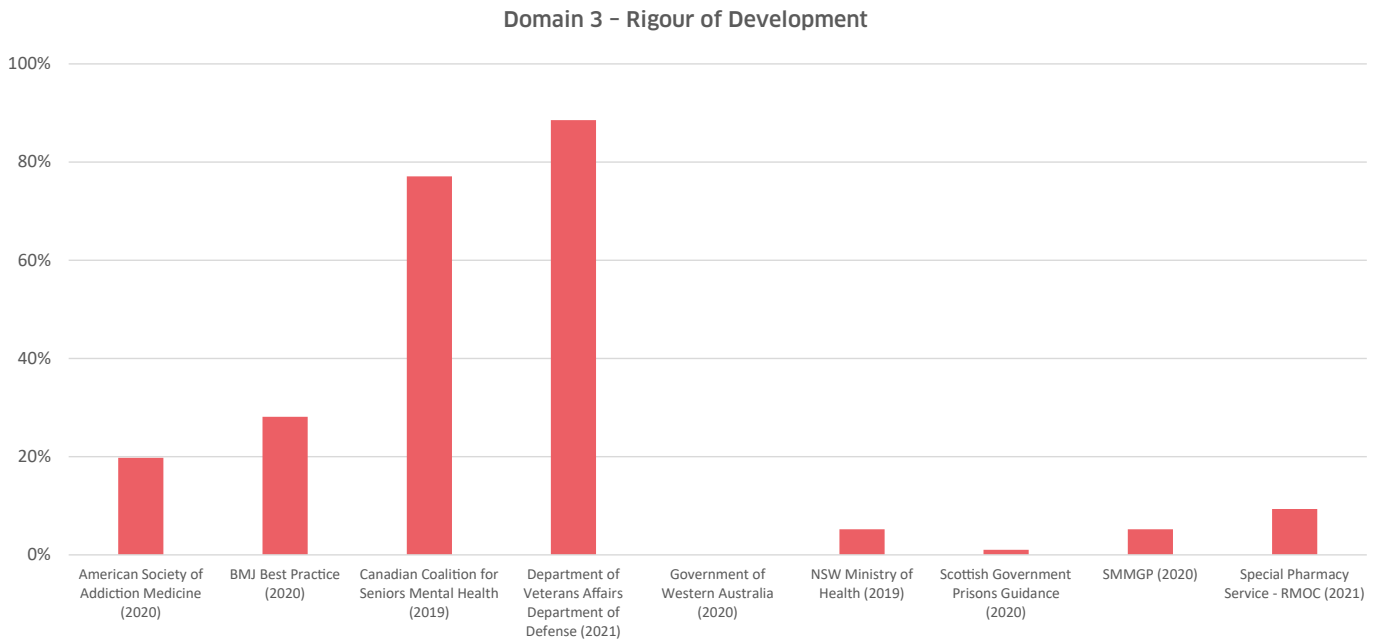


Figure 6: Domain 4 – Clarity of presentation

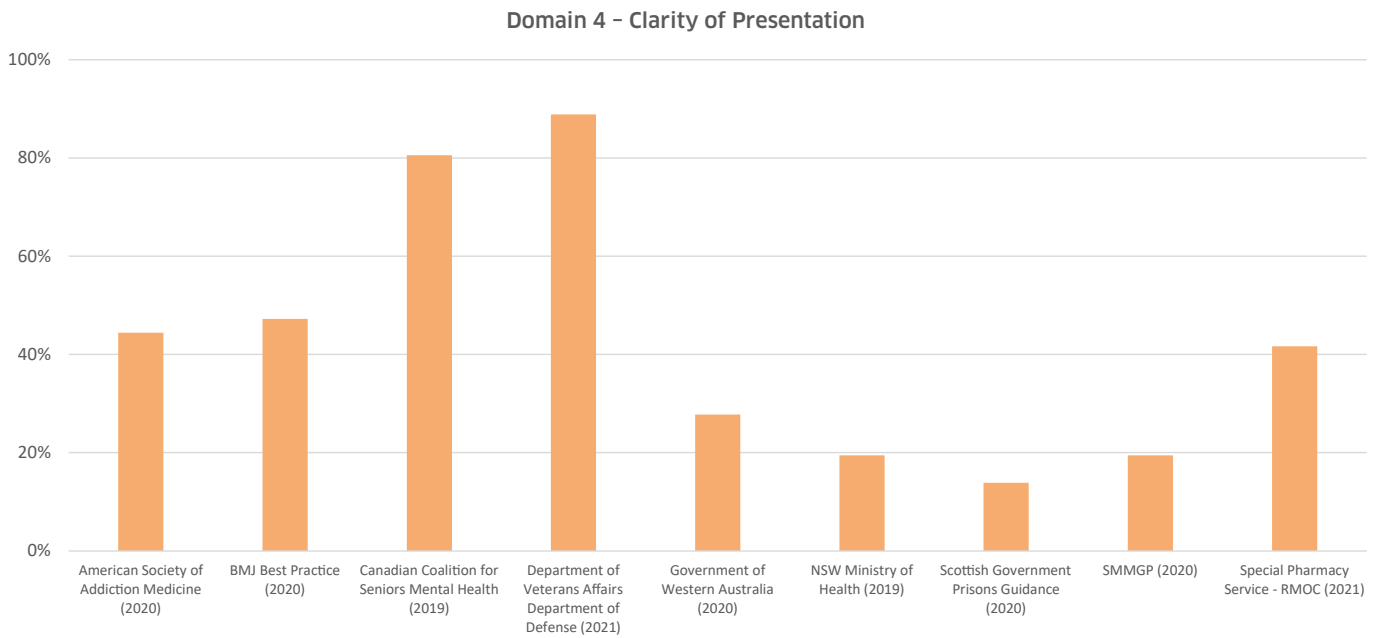


Figure 7: Domain 5 - Applicability

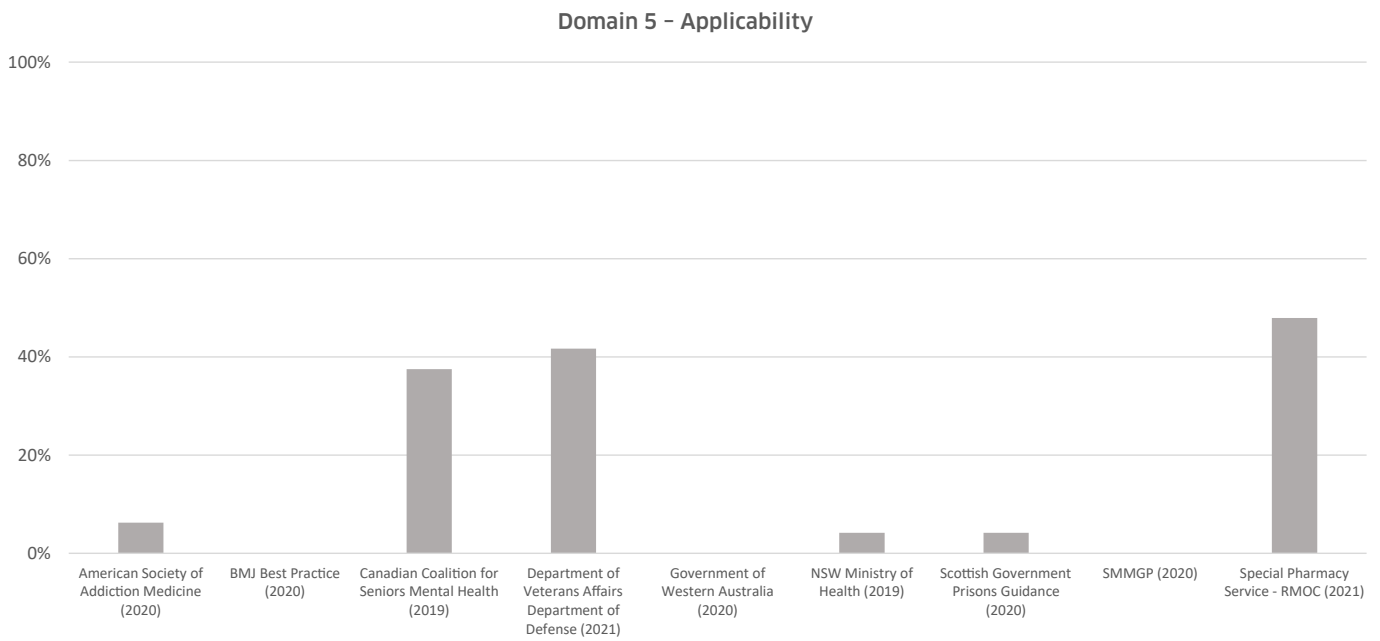
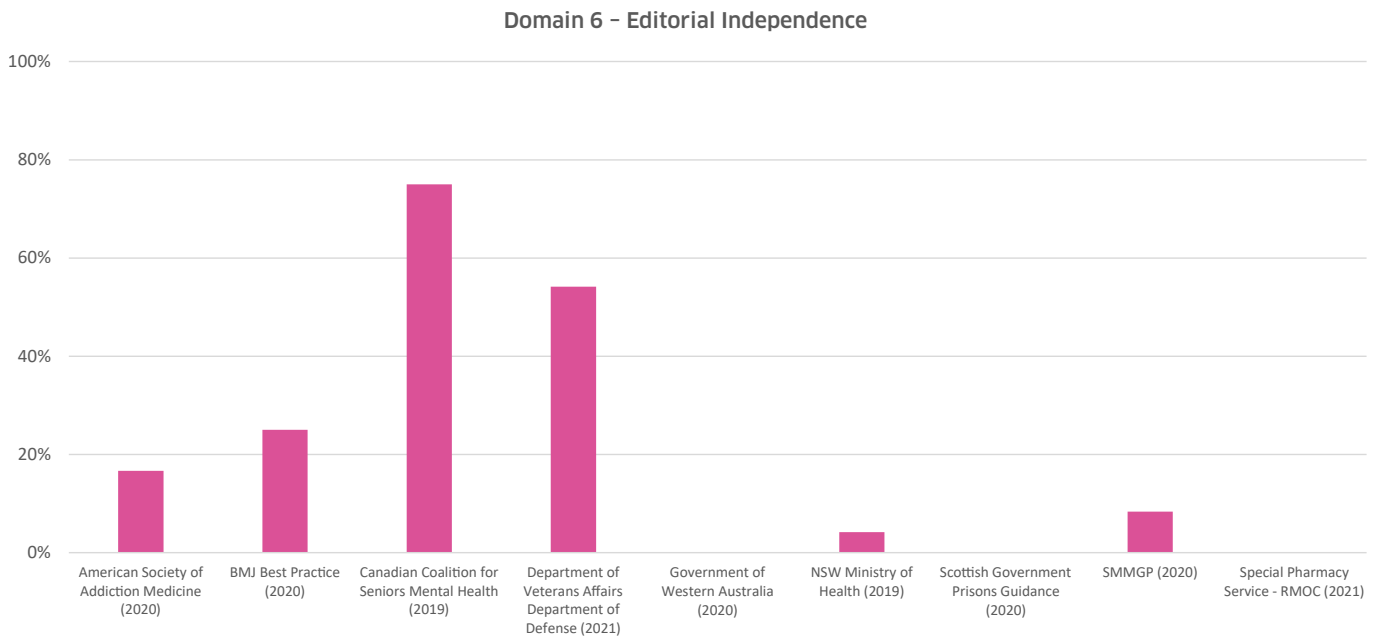


Figure 8: Domain 6 - Editorial independence



13.3 Development of consensus statements

Scoping searches carried out in the planning stages of this project identified insufficient randomised controlled trials of long-acting injectable buprenorphine use that could provide evidence to support recommendations for interventions in an evidence-based guideline. The existing evidence base reflected the regulatory trials and included safety and pharmacokinetic data, but lacked pragmatic information about use scenarios.

In order to provide advice within a short timescale, a position statement supported by formal consensus methodology was selected as the optimal approach.

A systematic search identified no high-quality guidelines on the use of long-acting injectable buprenorphine which had used a robust evidence-based methodology. In the absence of existing evidence-based recommendations which could be adapted for the Scottish context a pool of mixed quality evidence was selected. This consisted of six lower quality guidelines directly relevant to long-acting injectable buprenorphine,^{10,13,16,23,26,27} two higher-quality guidelines on aspects of opioid substitution (but without including long-acting injectable buprenorphine),^{24,25} and one further national guideline on opioid use disorder, based on existing guidelines and expert opinion⁹ (see *section 13.1*). The quality of these publications was assessed (see *section 13.2*).

Three researchers from SIGN and Healthcare Improvement Scotland independently extracted directive statements which were based on informal expert opinion from these sources on use of long-acting injectable buprenorphine. Topics with no similar statutory advice (ie from SmPC or SMC) were considered eligible for development of consensus statements. For the remaining topics, where there was significant overlap with information in SmPC or SMC publications, the relevant statutory advice was reproduced in the position statement and this topic was not developed further via consensus methods.

Directive statements on eligible topics extracted from the source documents were combined by the research team into draft consensus statements. Using an iterative modified Delphi technique approach (with three rounds), working group members rated their level of agreement with statements using a five-point Likert scale (strongly agree, agree, neither agree or disagree, disagree, strongly disagree). For each statement, members were asked to justify their answer or provide comments to support their level of agreement. After each round, the level of agreement based on votes submitted was calculated. The threshold of 70% agreement was adopted as the definition of formal consensus. Table 2 summarises the development of consensus across three rounds of voting.

The research team removed statements from the voting process if they failed to reach the threshold for formal consensus and when:

- comments were extremely polarised suggesting that agreement could not be reached by further revisions to the statement, or
- comments suggested the removal of the statement.

Statements which did not reach consensus are listed in Annex 4. The supporting material for this position statement includes a results document and a report for each consensus round. These include the full voting results, all submitted comments and the actions taken to include, exclude or revise each statement.

Table 2: Summary of consensus voting results and actions

Statement topic	Round 1 (n=25) agreement (%)	Action	Round 2 (n=22) agreement (%)	Action	Round 3 (n=21) agreement (%)	Action
How use of long-acting injectable buprenorphine may change service delivery (see section 7)	76	Revise and reconsider in round 2	81.8	Revise and reconsider in round 3	76.2	Revised statement incorporated into position statement
Training requirements (see section 11)	76	Revise and reconsider in round 2	86.4	Accept and incorporate into position statement		
Consent and intoxication (see section 8.1)	68	Split into two statements and reconsider in round 2	Consent 81.8	Accept and incorporate into position statement		
			Intoxication 40.9	Remove from position statement		
“Did not attend” procedures (see section 8.2)	80	Revise and reconsider in round 2	90.9	Accept and incorporate into position statement		
Populations at risk of poor engagement (see section 8.3)	76	Accept and incorporate into position statement				
Clinical handover (see section 9)	88	Revise and reconsider in round 2	100	Accept and incorporate into position statement		
Clinical handover – minimum dataset (see section 9)	88-96 ^a	Accept and incorporate into position statement				
	60 ^b	Remove from consensus statement				
Dose reduction (see section 5.1)	72	Revise and reconsider in round 2, with suggested addition	90.9	Accept and incorporate into position statement		
				(revision not accepted 45.4% agreement)		

Table 2: Summary of consensus voting results and actions (continued)

Statement topic	Round 1 (n=25) agreement (%)	Action	Round 2 (n=22) agreement (%)	Action	Round 3 (n=21) agreement (%)	Action
Dose increase (see section 5.1)	56	Revise and reconsider in round 2	86.3	Accept and incorporate into position statement		
Dose maintenance (see section 5.1)	80	Revise and reconsider in round 2, with suggested additions	90.9	Accept and incorporate into position statement (revisions not accepted 40.9% and 63.6% agreement)		
Chronic pain management (see section 10.2)	76	Revise and reconsider in round 2, with suggested additions	72.7	Revise and reconsider in round 3	76.2	Revised statement incorporated into position statement
Coadministration with opioid analgesics	52	Revise and reconsider in round 2	40.9	Remove from position statement		

^a 9 of 10 items in minimum dataset reached consensus

^b 1 of 10 items in minimum dataset failed to reach consensus and was recommended for deletion

Green shading	Formal consensus reached and no significant issues of disagreement. Revised statement was incorporated into position statement.
Amber shading	Significant issues of disagreement. Draft consensus statement was revised and recirculated for further consensus voting.
Red shading	Significant issues of disagreement, with polarised views among group. Comments suggest no likely prospect of consensus. Statement was removed from position statement.

13.4 Updating the position statement

This position statement will be considered for review based on a range of factors, including emergence of new evidence and alignment with Scottish Government initiatives, in consultation with the commissioning body.

13.5 Working group

Professor Angela Timoney	Working group Chair and Chair of SIGN Council
Dr Mithun Barik	Addiction Psychiatrist, South Community Addiction Team, NHS Ayrshire and Arran
Ms Lisa Buchan	Practice Mental Health Nurse, NHS Lothian
Ms Sarah Buchan	Pharmaceutical Services Improvement and Development Manager, NHS Grampian
Mr Tom Byrne	National Prisons Pharmacy Adviser, Healthcare Improvement Scotland
Ms Lesley Campbell	Team Lead, Drug and Alcohol Recovery Service, NHS Highland
Ms Tracey Clusker	Clinical Lead Nurse Consultant, MAT Standards Implementation Support Team, Public Health Scotland
Dr Stephen Conroy	General Practitioner, NHS Lanarkshire
Dr Fiona Cowden	Consultant Psychiatrist, Addiction, NHS Tayside
Ms Jessica Davidson	Clinical Lead Nurse for Justice, MAT Standards Implementation Support Team, Public Health Scotland
Ms Sarah Donaldson	Specialist Pharmacist in Substance Misuse, NHS Tayside
Professor Michael Eddleston	Chair of Clinical Toxicology, University of Edinburgh
Dr Emma Fletcher	Director of Public Health, NHS Tayside
Mr Martin Graham	Development Officer, Living Experience, Scottish Drugs Forum
Ms Cara Halliday	Mental Health Nurse and Team Leader, NHS Forth Valley and Her Majesty's Prison Glenochil
Ms Kelly Hamilton	Prison Healthcare Addictions Team Leader, NHS Forth Valley Prison Estate
Mr Duncan Hill	Specialist Pharmacist in Substance Misuse, NHS Lanarkshire
Mr Andrew Horne	Executive Director, We Are With You Scotland
Ms Lynn Laverty	Clinical Nurse Specialist, Acute Services, NHS Greater Glasgow and Clyde
Ms Heather Macleod	Addiction Community Psychiatric Nurse, NHS Highland
Ms Pauline MacLeod	Advanced Nurse Practitioner, Drug and Alcohol Service, NHS Highland
Mr Paul Maguiness	Lead Pharmacist, Substance Misuse and Prison Services, NHS Lothian
Mr David Morrison	Lead Pharmacist, Adult Mental Health and Learning Disabilities, NHS Tayside
Dr Colin Rae	Consultant in Anaesthesia and Chronic Pain Management, NHS Greater Glasgow and Clyde
Dr Trina Ritchie	Lead Clinician and Senior Medical Officer, Glasgow Alcohol and Drug Recovery Services, NHS Greater Glasgow and Clyde
Ms Linda Smith	Drug Liaison Nurse, Harm Reduction Team, NHS Lothian
Dr James Tidder	Consultant in Addictions Psychiatry and Clinical Lead, NHS Borders Addiction Service
Ms Emily Traynor	Service Manager, Alcohol and Drug Services, Nursing and Midwifery Council
Mr Jason Wallace	Senior Development Officer, Scottish Drugs Forum
Dr Judith Wilson	Lead Clinician in Pain Management, Consultant in Anaesthesia and Pain Management, NHS Forth Valley

The membership of the working group was confirmed following consultation with the member organisations of SIGN and in consultation with Scottish Government. All members of the working group made declarations of interest. A register of interests is available in the supporting material section for this position statement at www.sign.ac.uk

Position statement development and literature review expertise, support and facilitation were provided by staff from the Evidence Directorate (of which SIGN is a part) of Healthcare Improvement Scotland. All members of the Evidence Directorate of Healthcare Improvement Scotland make yearly declarations of interest and further details of these are available on request.

Dr Lola Adewale	Programme Manager, SIGN
Ms Juliet Brown	Health Information Scientist, Healthcare Improvement Scotland
Mrs Joanna Kelly	Health Services Researcher, Healthcare Improvement Scotland
Dr Moray Nairn	Programme Manager, SIGN
Ms Gaynor Rattray	Guideline Co-ordinator, SIGN
Mr Domenico Romano	Publications Designer, Healthcare Improvement Scotland
Miss Zoe Seatter	Project Officer, SIGN
Ms Lorna Thompson	Health Services Researcher, Healthcare Improvement Scotland

13.6 Specialist review

The position statement was reviewed in draft form by the following independent expert referees. The working group addresses every comment made by an external reviewer and must justify any disagreement with the reviewer's comments. A report of the consultation and peer review comments and responses is available in the supporting material section for this position statement on the SIGN website. All expert referees and other contributors made declarations of interest.

Dr Michael Basler	Consultant in Pain Medicine and Anaesthesia, Glasgow Royal Infirmary
Mr Martin Carragher	Senior Charge Nurse Mental Health Hub, commenting on behalf of NHS 24
Dr Tim Elworthy	Consultant Psychiatrist, NHS Tayside
Ms Sarah MacFarlane	Specialist Pharmacist, Substance Use, NHS Fife
Mr Brian Martin	Addictions Advanced Nurse Practitioner, East Ayrshire Addiction Services
Mr Kevin McGinley	Community Mental Health Nurse, The Edinburgh Access Practice, Edinburgh
Ms Pauline McGuire	Principal Pharmacist, commenting on behalf of Scottish Medicines Consortium
Ms Helen McNally	Service Manager, Community Forensic Mental Health Team, Holywell Hospital, Northern Ireland
Mr Ian Morrison	Advanced Nurse Prescriber, South Ayrshire Addiction Services, Ayr
Dr Susan Smith	Consultant Anaesthetist, Glasgow Royal Infirmary
Ms Diane Watson	Advanced Clinical Pharmacist, NHS Greater Glasgow and Clyde
Dr Lars Williams	Consultant in Anaesthesia and Pain Management, NHS Greater Glasgow and Clyde

13.7 Editorial review

As a final quality control check, the position statement is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council and senior managers in Healthcare Improvement Scotland to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the methodology as a whole has been minimised. The editorial group for this position statement was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council Membership page of the SIGN website www.sign.ac.uk

Professor Lesley Colvin	Honorary Consultant in Anaesthesia and Pain Medicine, NHS Tayside and Professor of Pain Medicine, University of Dundee
Dr Roberta James	Programme Lead, SIGN
Dr Safia Qureshi	Director of Evidence, Healthcare Improvement Scotland

Useful resources

[Buvidal® prolonged-release solution for injection: Information for the user](#)

Camurus Ltd. [Buvidal website](#) (for healthcare professionals from the UK and Ireland - registration required)

European Medicines Agency. [Buvidal](#). Overview, authorisation details, product information and assessment history.

Scottish Drug Deaths Taskforce. [Opioid agonist treatment - Guidance for Scotland](#).

Scottish Public Health Observatory. Drug use: [health harm](#)

Scottish Public Health Observatory. Drug use: [social harm](#)

Scottish Public Health Observatory. Drug use: [treatment for drug misuse](#)

Abbreviations

AGREE	Appraisal of Guidelines for Research & Evaluation
CI	confidence interval
CNS	central nervous system
COVID-19	coronavirus 2019
DDD	defined daily dose
DVLA	Driver and Vehicle Licensing Agency
GMC	General Medical Council
GP	general practitioner
HIV	human immunodeficiency virus
MAT	Medication Assisted Treatment
NHS	National Health Service
NICE	National Institute for Clinical Health and Care Excellence
NRS	National Records for Scotland
OST	opioid substitution therapy
PHS	Public Health Scotland
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SMMGP	Substance Misuse Management in General Practice
SmPC	summary of product characteristics
SMSP	substance misuse service provider

Annex 1: Medication Assisted Treatment Standards for Scotland – Access, Choice, Support



Standard 1: All people accessing services have the option to start MAT from the same day of presentation.



Standard 2: All people are supported to make an informed choice on what medication to use for MAT, and the appropriate dose.



Standard 3: All people at high risk of drug-related harm are proactively identified and offered support to commence or continue MAT.



Standard 4: All people are offered evidence based harm reduction at the point of MAT delivery.



Standard 5: All people will receive support to remain in treatment for as long as requested.



Standard 6: The system that provides MAT is psychologically informed (tier 1); routinely delivers evidence-based low intensity psychosocial interventions (tier 2); and supports individuals to grow social networks.



Standard 7: All people have the option of MAT shared with Primary Care.



Standard 8: All people have access to independent advocacy and support for housing, welfare and income needs.



Standard 9: All people with co-occurring drug use and mental health difficulties can receive mental health care at the point of MAT delivery.



Standard 10: All people receive trauma-informed care.

MAT Standards

MAT = Medication Assisted Treatment

what are they?

1. Help on the day you ask

Being in treatment is a matter of life and death - when people ask for help we should be ready to provide it. Services will bring in new guidance to allow this to either be a prescription when clinically appropriate, or to ensure access to other support from day one.

2. Choice

We should all be involved in the decisions that affect our care, after all, it is us that have to live with it. Different medication options that are available will be discussed with people and they will be supported to make the right choice for them.

3. Reaching out

Staff contact and follow up with individuals they are concerned about, especially during times of high risk. Support will also be offered when a person's risk factors might be changing - e.g when a person is leaving hospital.

4. Harm reduction for everyone

While a person is in treatment and prescribed medication, they are still able to access harm reduction services - e.g needles and syringes, testing for blood-borne viruses, injecting risk assessments, wound care and naloxone. They would be able to receive these from a range of providers - including their treatment service - and this would not affect their treatment or prescription.

5. Staying in treatment

People are to be given support to stay in treatment for as long as they like and especially at times when things are difficult for them. All discharges from services should be planned with the person to ensure this is managed safely.

6. Improving mental wellbeing

We know that for many people, substances are used as a way to cope with difficult emotions and issues from the past. Services will focus on supporting people to develop positive relationships and new ways of coping as these are just as important as having the right medication.

7. Involving GPs & primary care

Not everyone needs specialist services throughout their recovery, and people should be able to choose to receive their medication and other support through primary care providers.

8. Meeting everyday needs

To support the whole person not just their drug use, people have the right to ask for support to improve their living circumstances, such as housing and access to their welfare entitlements. Dedicated independent workers will support people to make sure they get what best suits them and that they are treated fairly.

9. Treating mental health

People have the right to ask for support with mental health difficulties and to engage in mental health treatment while being supported as part of their drug treatment and care.

10. Respecting trauma

This ensures we listen to people and offer the kind of relationship that promotes their recovery, does not cause further trauma or harm, and helps build resilience.



Annex 2: Advantages and disadvantages of different delivery models for administering Buvidal®

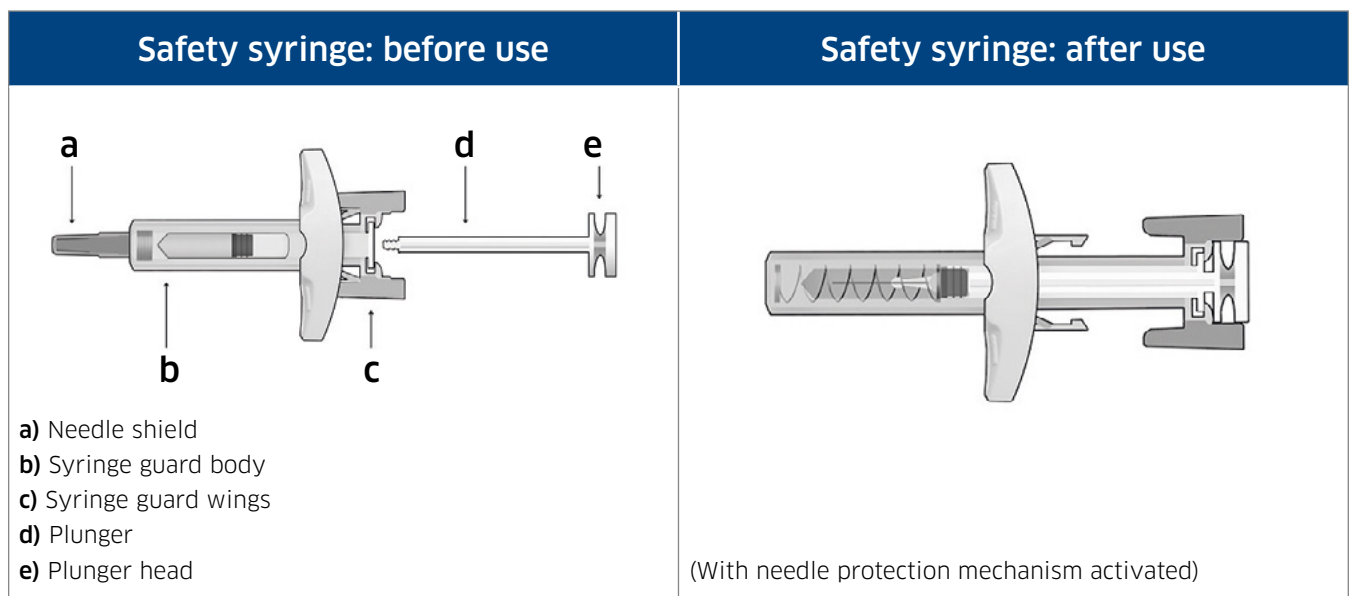
Model	Advantages	Disadvantages
<p>Health and justice</p> <p>Buvidal® administration by suitably trained registered healthcare professional</p>	<ul style="list-style-type: none"> • Reduced supervision time for daily oral OST supervision, which will release personnel time (healthcare and prison security) • Reduce missed doses for people in custody who are unable to pick up their daily OST in the morning due to court hearings/ work • Reduce risk of diversion. 	<ul style="list-style-type: none"> • Depending on the prison's current operational set up and injection appointment availabilities, Buvidal® may not be an operational cost saving. People in custody may require escorting individually if not receiving treatment at the same time. • Overall cost of Buvidal® is still more expensive. • May require people in custody to be escorted to a different part of the prison which is not next to current place of administration. • Additional considerations for secure medicines storage, as normally people in custody are not allowed into rooms where medication is stored. • Potential lack of continuity of care if person in custody moves and the receiving provider does not offer Buvidal® in their service.
<p>Community – model 1</p> <p>Administration on site at substance misuse service provider (SMSP) premises by SMSP with Home Office licence</p>	<ul style="list-style-type: none"> • Reduced administrative burden associated with daily OST supervision • Allows OST administration where service users are banned from community pharmacies due to antisocial behaviour • Ability to detect and address disengagement with service user directly with consistent patient contact • Ability to store and administer drugs on site • Access to locally-agreed drug prices. 	<ul style="list-style-type: none"> • Lack of accessibility to treatment out of clinic hours. • Expensive if require set up of facilities. This includes: <ul style="list-style-type: none"> - Home Office licence or registered pharmacy status - modification to buildings to have appropriate clinic rooms and installation of controlled drugs cabinet. • May need to increase clinic capacity to administer drug. • Need to attend clinic for injection instead of self administration compared with oral OST. • Increased cost if service user does not attend appointments regularly and requires frequent dose titrations.
<p>Community- model 2</p> <p>Administration on site at SMSP premises by SMSP without Home Office licence/ registered pharmacy status</p>	<ul style="list-style-type: none"> • As per model 1 but without the ability to access locally-agreed drug prices • Clinics may be able to store drugs on site if they have controlled drugs cabinets. 	<ul style="list-style-type: none"> • As per model 1 minus the cost of Home Office licensing fee. • Will need an agreement to either have medication delivered directly to site or collected from pharmacy by clinic staff.

Model	Advantages	Disadvantages
Community-model 3 Administration in community pharmacies	<ul style="list-style-type: none"> Better accessibility out of hours Reduce time for daily supervision, which will release community pharmacists' time. 	<ul style="list-style-type: none"> Need to attend pharmacy for injection instead of self administration. Not all pharmacies will sign up for this scheme. May limit service user choice. Relies on good communication between community pharmacy and the substance misuse clinic to identify issues promptly. Reduced contact – reduced potential to identify issues with service users' health promptly. Risk of coercion by service users to give medication not at the scheduled times. Risk of disengagement from psychosocial interventions with substance misuse clinic. Lack of flexibility to give medications as scheduled for service users who genuinely cannot attend their planned administration date. This could be resolved by having a local service level agreement in place.
Community-model 4 Administration at off-site venue at non-SMSP premises by SMSP as part of outreach service with Home Office licence	<ul style="list-style-type: none"> As per model 1, with potentially better access to service users via outreach service. 	<ul style="list-style-type: none"> As models 1 & 2. Difficulty in obtaining permission to modify building which does not belong to SMSP. Additional risk assessments and protocols for safe transportation of controlled drugs. Additional risks assessments to ensure appropriateness of administration venues (ie satellite clinics, service users' homes). Potential safety risk to clinical staff administering if working alone. Additional cost for staffing outreach service.
Community-model 5 Administration at off-site venue at non-SMSP premises by SMSP as part of outreach service without Home Office licence	<ul style="list-style-type: none"> As per model 4, minus the cost of Home Office licensing fee Improves access to treatment for housebound individuals. 	<ul style="list-style-type: none"> As per model 4. Requires access to named patient medication dispensed from an acute SMSP site or pharmacy.

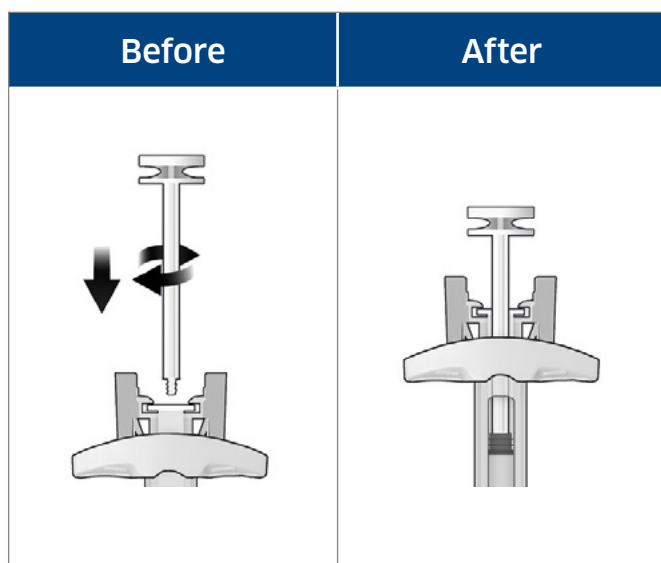
Adapted from the Regional Medicines Optimisation Committee guideline: Buprenorphine – Considerations for opioid substitution treatment use in community settings and secure environments in England. Version 1.0¹³

Annex 3: Buvidal® injection instructions

- Administration should be made into the subcutaneous tissue.
- Intravascular, intramuscular and intradermal administration must be avoided.
- Must not be used if the safety syringe is broken or the packaging is damaged.
- The needle shield of the syringe may contain rubber latex that may cause allergic reactions in latex sensitive individuals.
- Handle the safety syringe carefully to avoid a needle stick. The safety syringe includes a needle protection safety device that will activate at the end of the injection. Do not uncap the safety syringe until you are ready to inject. Once uncapped, never try to recap the needle.
- Dispose of the used safety syringe right away after use. Do not re-use the safety syringe.



Please note that the smallest injection volume is barely visible in the viewing window as the spring of the safety device is “covering” part of the glass cylinder close to the needle.

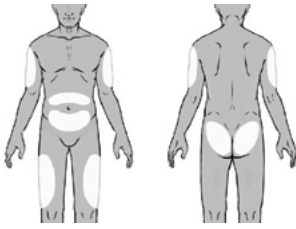


- Take the syringe out of the cardboard box: pick up the syringe by the syringe guard body.
- While holding the syringe by the needle shield, insert the plunger rod into the plunger stopper by gently rotating the plunger rod clockwise until secured.

Inspect the safety syringe closely:

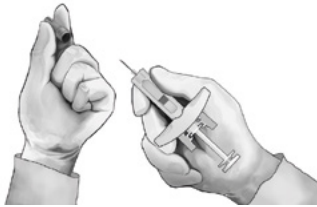
- Do not use the safety syringe after the expiration date shown on the cardboard box or on the syringe label.
- A small air bubble may be seen, which is normal.
- The liquid should be clear. Do not use the safety syringe if the liquid contains visible particles or is cloudy.

1: Choose the injection site



Injections should be rotated between sites in the buttock, thigh, abdomen, or upper arm with a minimum of eight weeks before re-injecting a previously used injection site. Each area can have multiple injection sites. Injections on the waistline or within 5 cm of the navel should be avoided.

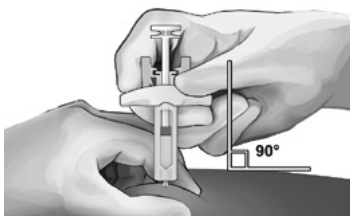
2: Prepare the injection site



Put on gloves and clean the injection site with a circular motion using an alcohol wipe (not provided in the pack). Do not touch the cleaned area again before injecting.

While holding the safety syringe by the syringe guard body as shown, carefully pull the needle shield straight off. Immediately dispose of the needle shield (never try to recap the needle). A drop of liquid may be seen at the end of the needle. This is normal.

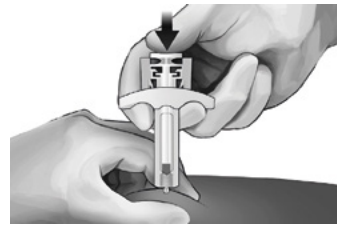
3: Perform injection



Pinch the skin at the injection site between the thumb and finger as shown.

Hold the safety syringe as shown and insert the needle at an angle of approximately 90°. Push the needle all the way in.

4: Administer medication



While holding the syringe as shown, slowly depress the plunger until the plunger head latches between the syringe guard wings and all the solution is injected.

5: Remove needle from skin



Gently pull the needle out of the skin. It is recommended that the plunger is kept fully depressed while the needle is carefully lifted straight out from the injection site.

6: Wipe injection site



As soon as the needle has been completely removed from the skin, slowly take the thumb off the plunger and allow the syringe guard to automatically cover the exposed needle. There may be a small amount of blood at the injection site, if required wipe with a cotton ball or gauze.

Disposing of the syringe

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Annex 4: Statements which did not reach consensus

After each round of voting, the research team removed statements from the voting process if they failed to reach the threshold for formal consensus and:

- comments were extremely polarised suggesting that agreement could not be reached by further revisions to the statement, or
- comments suggested the removal of the statement.

The following statements were removed in rounds 1 and 2 of the voting process.

Round 1

In the statement containing a minimum dataset for clinical handover information (see *section 9*), working group members did not agree with the following item (60% consensus):

As a minimum, the following needs to be communicated to the receiving provider upon transfer:

- *the current dosing regimen (and equivalent dose of sublingual or supralingual buprenorphine should the depot formulation need to be converted back).*

Round 2

Group members did not agree with the following statement (40.9% consensus):

Service users who present intoxicated at the time of dose administration should be assessed to identify any safety concerns regarding dosing. Peak plasma and clinical effects occur approximately 12–24 hours after weekly depot buprenorphine injections and 6–10 hours after monthly depot buprenorphine injection, and hence there is usually little clinical indication to withhold a depot injection due to a service user presenting intoxicated, in contrast to intoxicated presentations for sublingual buprenorphine or methadone dosing, where peak medication effects are likely to occur whilst the service user is still intoxicated.

Group members did not agree with the following addition to the existing statement on dose reduction (see *section 5.1*) (45.4% consensus):

Doses should generally be reduced under the following conditions:

- *the service user is regularly delaying their return appointment longer than the scheduled interval as the medication is still holding them sufficiently.*

Group members did not agree with the following additions to the existing statement on dose maintenance (see *section 5.1*) (40.9% and 63.6% consensus, respectively):

In general, doses should be maintained if the service user:

- *has reached maximum dose.*
- *has not required any additional top-up doses since administration of their last depot.*

Group members did not agree with the following statement (40.9% consensus):

- *Depot buprenorphine should not be used in conjunction with other opioid analgesics (eg morphine, fentanyl, codeine) in chronic pain management, given its 'blockade' effects.*

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