Weekly/Monthly

Buvidal®

BUPRENORPHINE

PROLONGED-RELEASE
SOLUTION FOR INJECTION

HEALTHCARE PROFESSIONAL INFORMATION BOOKLET

Contents

Introduction

This material is intended for healthcare professionals prescribing Buvidal (buprenorphine) prolonged-release solution for injection for treatment of patients with opioid dependence.

IMPORTANT: This material is not intended as a standalone document but should be read together with the Summary of Product Characteristics (SmPC) and the product Package Leaflet.

Detailed information on this medicinal product is available on the website of the European Medicines Agency, https://www.ema.europa.eu/en/medicines/human/EPAR/buvidal.

- Buvidal is indicated for the treatment of opioid dependence within a framework of medical, social and psychological support.
- Treatment is intended for use in adults and adolescents aged 16 years or over.
- Weekly and monthly Buvidal are buprenorphine prolonged-release solutions for injection in single-dose pre-filled syringes.
- The prolonged-release properties of Buvidal are based on FluidCrystal® injection depot technology.
- **Administration of Buvidal is restricted to healthcare professionals.**
- Weekly and monthly Buvidal are administered by subcutaneous injection.
- Other routes of administration, such as intravascular, intramuscular and intravenous injection of Buvidal, must be avoided.

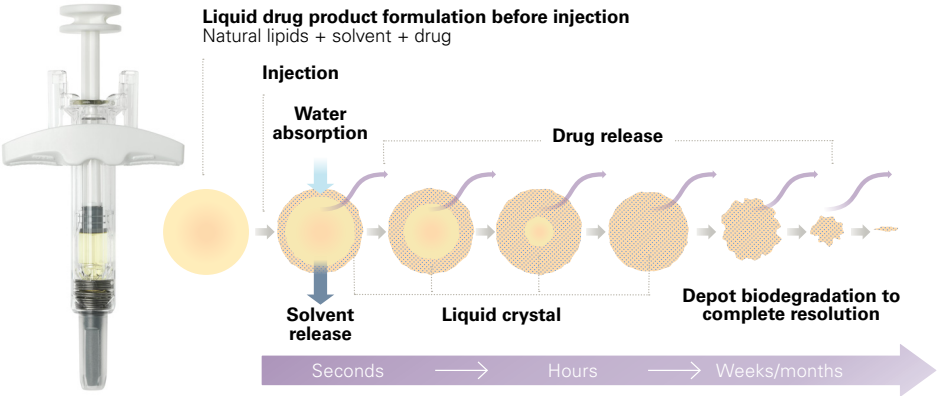
Product overview

Weekly and monthly Buvidal are buprenorphine prolonged-release solutions for injection provided in single-dose prefilled syringes. The syringe is assembled in a safety device to prevent post-injection needlestick injury.

Buvidal syringe

The prolonged-release property of Buvidal is based on FluidCrystal® injection depot technology. Once injected, special combinations of natural polar lipids spontaneously form liquid crystal gel nanostructures in aqueous environments, resulting in long-acting drug release (figure below).[1,2]

FluidCrystal® injection depot technology releasing buprenorphine over a period of a week or a month[1,2]



References: 1. Tiberg F, Johnsson M, Nistor C, Joabsson F. Self-assembling lipid formulations. In: *Long Acting Injections and Implants*. Springer; 2012:315–333. **2.** EPAR, EMEA/H/C/004651/0000 https://www.ema.europa.eu/en/medicines/human/EPAR/buvidal

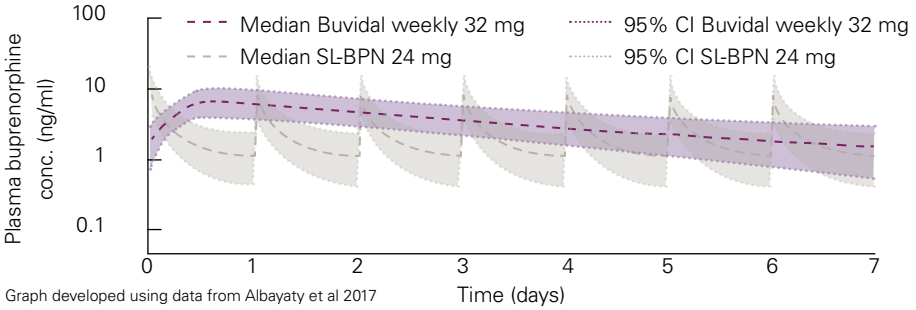
Properties of Buvidal

Buprenorphine, the active substance in Buvidal, is an opioid partial agonist/antagonist that binds to the μ (mu) and K (kappa) opioid receptors with high affinity. Its activity in opioid dependence treatment is attributed to its slowly reversible properties with the μ-opioid receptors which, over a prolonged period, may reduce craving and withdrawal symptoms and block the effects of other opioids, such as drug liking. Its activity in opioid maintenance treatment is attributed to its slowly reversible properties with the mu-opioid receptors which, over a prolonged period, might minimise the need of illicit opioids for patients with opioid dependence.

Pharmacokinetic properties

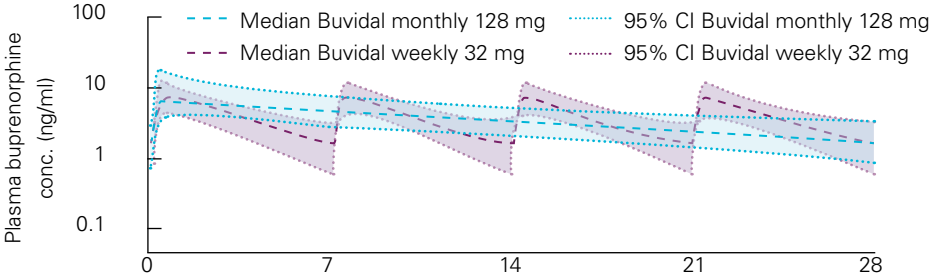
Population pharmacokinetic profiles at steady state after dosing of weekly and monthly Buvidal and daily sublingual buprenorphine[1]

Weekly Buvidal vs. daily sublingual buprenorphine



Graph developed using data from Albayaty et al 2017

Weekly Buvidal vs. monthly Buvidal



Graph developed using data from Albayaty et al 2017

Reference: 1. Albayaty M, et al. Adv Ther. 2017;34(2):560–575.

Precautions to consider before prescribing Buvidal

Please refer to the SmPC for full details.

Administration of Buvidal is restricted to healthcare professionals.
Take-home use or self-administration of Buvidal by patients is not allowed.
Before commencing buprenorphine treatment, it is recommended to obtain baseline liver function tests and to document viral hepatitis status. Patients who are positive for viral hepatitis, taking other medicines and/or with existing liver dysfunction are at greater risk of liver injury. Regular monitoring of liver function is recommended.
The prolonged-release properties of weekly and monthly Buvidal should be considered during treatment, including initiation and termination.
Appropriate precautions, such as conducting patient follow-up visits with clinical monitoring according to the patient's needs, should be taken when prescribing and dispensing buprenorphine.

Cautions for use
- Elderly populations
- Moderate hepatic impairment
- Severe renal impairment

Contraindications
- Hypersensitivity to buprenorphine or to any of the excipients in Buvidal:
  - Weekly Buvidal – soybean phosphatidylcholine, glycerol dioleate, ethanol anhydrous
  - Monthly Buvidal – soybean phosphatidylcholine, glycerol dioleate, N-Methylpyrrolidone
- Severe respiratory insufficiency
- Severe hepatic impairment
- Acute alcoholism or *delirium tremens*

Interactions with other medicines
No interaction studies have been conducted with Buvidal.
Buprenorphine should be used with caution if co-administered with:
- Serotonergic medicinal products, e.g. MAO inhibitors, selective serotonin re-uptake inhibitors (SSRIs), serotonin-noradrenaline re-uptake inhibitors (SNRIs) or tricyclic antidepressants
- Benzodiazepines

- Gabapentinoids
- Alcohol
- CNS depressants
- Opioid analgesics
- Opioid antagonists: naltrexone and nalmefene
- CYP3A4 inhibitors and inducers:
  - CYP3A4 inhibitors may inhibit the metabolism of buprenorphine, resulting in increased Cmax and AUC of buprenorphine and norbuprenorphine. Buvidal avoids first-pass effects, and CYP3A4 inhibitors (e.g. protease inhibitors such as ritonavir, nelfinavir and indinavir, or azole antifungals such as ketoconazole and itraconazole, or macrolide antibiotics) are expected to have less effects on buprenorphine metabolism when co-administered with Buvidal than when co-administered with sublingual buprenorphine. When switching from sublingual buprenorphine to Buvidal, patients may need to be monitored to ensure plasma buprenorphine levels are adequate.
  - Patients already on Buvidal who start treatment with CYP3A4 inhibitors should be treated with weekly Buvidal and be monitored for signs and symptoms of overtreatment. Conversely, if a patient who is concomitantly treated with Buvidal and a CYP3A4 inhibitor stops treatment with the CYP3A4 inhibitor, the patient should be monitored for symptoms of withdrawal.
  - CYP3A4 inducers may induce the metabolism of buprenorphine, resulting in decreased buprenorphine levels. Buvidal avoids first-pass effects, and CYP3A4 inducers (e.g. phenobarbital, carbamazepine, phenytoin or rifampicin) are expected to have less effects on buprenorphine metabolism when co-administered with Buvidal than when co-administered with sublingual buprenorphine. When switching from sublingual buprenorphine to Buvidal, patients may need to be monitored to ensure plasma buprenorphine levels are adequate. Patients already on Buvidal who start treatment with CYP3A4 inducers should be treated with weekly Buvidal and be monitored for signs and symptoms of withdrawal. Conversely, if a patient who is concomitantly treated with Buvidal and a CYP3A4 inducer stops treatment with the CYP3A4 inducer, the patient should be monitored for symptoms of overtreatment.
  - UGT1A1 inhibitors may affect the systemic exposure of buprenorphine.

Correct use of Buvidal

Correct use of the product is very important. Remember to always adhere to administration instructions.

IMPORTANT: Care must be taken to avoid incorrect administration of Buvidal. The dose must not be administered intravascularly (intravenously), intramuscularly or intradermally.

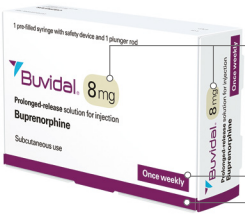
Intravascular administration, such as intravenous injection, would present a risk of serious harm, as Buvidal forms a solid mass upon contact with body fluids, which could potentially cause blood vessel injury, occlusion or thromboembolic events.

The products
Due to the depot formulation and the prolonged release characteristics of Buvidal, it is important to be aware that there are two different products. Buvidal is available either as a **weekly** or **monthly** treatment, and there are several doses for each product:

- Weekly Buvidal is available in four doses: 8, 16, 24 and 32 mg
- Monthly Buvidal is available in four doses: 64, 96, 128 and 160 mg

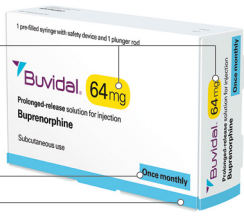
How to distinguish between the products
The weekly and monthly Buvidal products are differentiated by the colour of the cardboard boxes, and the text “once weekly” or “once monthly” printed on the respective boxes. The individual doses are also differentiated by different colours on the boxes.

Buvidal product overview for weekly and monthly doses.

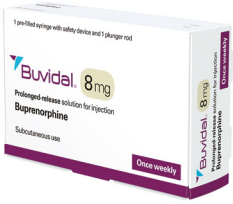


The dose is printed in different colours on the respective cartons

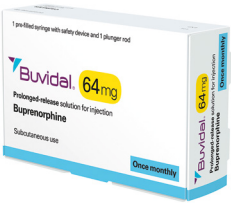
Different colour cartons and the text “once weekly” or “once monthly”



Weekly Buvidal
(8, 16, 24 and 32 mg)



Monthly Buvidal
(64, 96, 128 and 160mg)



Treatment with Buvidal

Buvidal can be administered weekly or monthly. Dosing with Buvidal should be individualised to patients' needs.

Initiation of treatment in patients not already receiving buprenorphine
Patients who have not previously been 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.

Prior to induction, consideration should be given to:
- Type of opioid dependence (i.e. long- or short-acting opioids)
- The time since last opioid use
- The degree or level of opioid dependence

To avoid precipitating an opioid withdrawal syndrome, the first dose of buprenorphine should be started only when objective signs of mild to moderate withdrawal are evident.

Treatment with monthly Buvidal can be started after treatment initiation with weekly Buvidal, once patients have been stabilised on weekly treatment (four weeks or more, where practical).

Starting dose recommendations

Day 1	During week 1	Week 2
16 mg injection	One or two additional 8 mg doses at least one day apart. **The target dose during the first week of treatment is 24 mg or 32 mg.**	The recommended dose for the second treatment week is the total dose administered during the week of initiation.

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. Close monitoring of patients is recommended during the dosing period after the transition.

Conventional SL-BPN or LYO-BPN daily treatment dose and recommended corresponding doses of weekly and monthly Buvidal®[1]

Dose of daily SL-BPN	Dose of weekly Buvidal®	Dose of monthly Buvidal®
2–6 mg	8 mg	–
8–10 mg	16 mg	64 mg
12–16 mg	24 mg	96 mg
18–24 mg	32 mg	128 mg
26-32 mg	-	160 mg

Dose of daily LYO-BPN*	Dose of weekly Buvidal®	Dose of monthly Buvidal®
2–4 mg	8 mg	–
6–8 mg	16 mg	64 mg
10–12 mg	24 mg	96 mg
14–18 mg	32 mg	128 mg
-	-	160 mg

*25–30% higher bioavailability for Espranor than for SL Subutex tablet (MHRA Public Assessment Report Decentralised Procedure Espranor 2 mg and 8 mg lyophilisate)

The maximum single daily dose of Espranor is 18mg (Espranor 2 mg oral lyophilisate Summary of Product Characteristics (SmPC) and Espranor 8 mg oral lyophilisate Summary of Product Characteristics (SmPC).

SL-BPN: sublingual buprenorphine; LYO-BPN: oral lyophilisate buprenorphine.

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

Reference: 1. MHRA. Public Assessment Report Espranor 2mg & 8mg oral lyophilisate (buprenorphine hydrochloride).

Maintenance treatment and dose adjustments
Doses may be adjusted up or down, and patients can be switched between weekly and monthly products. Flexible dosing allows use across the different treatment phases, from initiation and stabilisation to maintenance treatment.

Buvidal should be administered weekly or monthly according to:
- Individual patients' needs
- Clinical judgement
- Doses established during treatment initiation or before switching between treatments

A maximum of one supplemental Buvidal 8 mg dose may be administered at an unscheduled visit between regular weekly or monthly doses, based on individual patients' 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.

Missed doses
To avoid missed doses:
- Weekly Buvidal doses may be administered up to two days before or after the weekly scheduled appointment.
- Monthly Buvidal doses may be administered up to one week before or after the monthly scheduled appointment.

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

Termination of treatment
If Buvidal treatment is discontinued, its prolonged-release characteristics and any withdrawal symptoms experienced by the patient must be considered.

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 the table on page 11.

Acute pain management – For management of acute pain during continued use of Buvidal, a combination of use of opioids with high mu-opioid receptor affinity (e.g. fentanyl), non-opioid analgesics and regional anaesthesia might be necessary.

Titration of oral or intravenous short-acting opioid pain medicinal products (immediate-release morphine, oxycodone or fentanyl) to the desired analgesic effect in patients treated with Buvidal might require higher doses. Patients should be monitored during treatment.

Use with other medications – 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.

Adverse reactions – The adverse reactions most frequently reported for buprenorphine, including Buvidal, are headache, nausea, hyperhidrosis, insomnia, drug withdrawal syndrome and pain. The most common injection site reactions reported in the double-blind, phase 3 efficacy trial for Buvidal were injection site pain, injection site pruritus and injection site erythema - all of mild or moderate severity, with most events being transient. Injection site-related adverse reactions of abscess, ulceration and necrosis have been reported during post-marketing use with Buvidal.
Injection site reactions could potentially be minimised by using the correct administration technique, as described in the SmPC for Buvidal and ensuring that the product is not injected intradermally.

Adverse reactions may include:

- Very common side effects (≥ 1/10 people):
  - Insomnia
  - Headache

  - Nausea
  - Hyperhidrosis, drug withdrawal syndrome, pain
- Common side effects (≥ 1/100 to < 1/10):
  - Infection, influenza, pharyngitis, rhinitis
  - Lymphadenopathy
  - Hypersensitivity
  - Decreased appetite
  - Anxiety, agitation, depression, hostility, nervousness, abnormal thinking, paranoia, medical dependence
  - Somnolence, dizziness, migraine, paraesthesia, syncope, tremor, hypertonia, speech disorders
  - Lacrimal disorder, mydriasis, miosis
  - Palpitations
  - Vasodilation, hypotension
  - Cough, dyspnoea, yawning, asthma, bronchitis
  - Constipation, vomiting, abdominal pain, flatulence, dyspepsia, dry mouth, diarrhoea, gastrointestinal disorder
  - Rash, pruritus, urticaria
  - Arthralgia, back pain, myalgia, muscle spasms, neck pain, bone pain
  - Dysmenorrhoea
  - Injection site pain, injection site pruritus, injection site erythema, injection site swelling, injection site reaction, injection site induration, injection site mass
  - Oedema peripheral, asthenia, malaise, pyrexia, chills, neonatal withdrawal syndrome, chest pain
  - Abnormal liver function tests
- Uncommon side effects (≥ 1/1,000 to < 1/100):
  - Injection site cellulitis
  - Vertigo
  - Alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzymes increased
  - Rash macular
  - Injection site inflammation, injection site bruising, injection site urticaria
  - Procedural dizziness
- Not known (frequency cannot be estimated from the available data):
  - Hallucinations, euphoric mood

- Erythema
- Urinary retention
- Injection site abscess; ulceration; necrosis

Serotonin syndrome
Concomitant administration of Buvidal and other serotonergic agents, such as MAO inhibitors, selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs) or tricyclic antidepressants may result in serotonin syndrome, a potentially life-threatening condition. If concomitant treatment with other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

Symptoms of serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms.

CNS depression – Buprenorphine may cause drowsiness, dizziness or impaired thinking, especially during treatment induction and dose adjustment. These effects may be increased if taken with alcohol or other CNS depressants such as benzodiazepines, tranquilisers, sedatives, gabapentinoids or hypnotics.

Effects on ability to drive and use machinery
For GB - 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.

For ROI and NI - 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 central nervous system depressants, the effect is likely to be more pronounced.

The patient should be cautioned not to drive or operate hazardous machinery whilst 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.

For full information please refer to the Summary of Product Characteristics for weekly and monthly Buvidal.

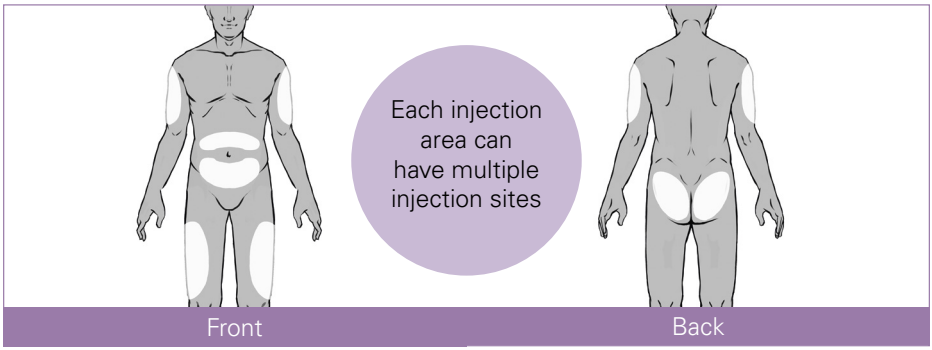
How to administer weekly and monthly Buvidal

An administration video can be found on the Buvidal.co.uk website

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 injection area can have multiple injection sites. Injection sites should be rotated for both weekly and monthly injections. A minimum of eight weeks should be allowed before re-injecting a previously used injection site.

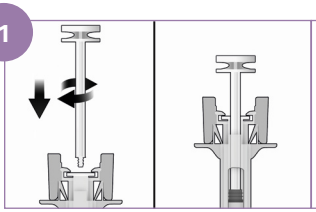
Injection areas for Buvidal



The dose should be administered as a single injection and not divided.

- The dose must not be administered intravascularly (intravenously), intramuscularly or intradermally
- Injection site reactions could potentially be minimised by using the correct administration technique, as described in the SmPC for Buvidal and ensuring that the product is not injected intradermally
- The product 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 injury. 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

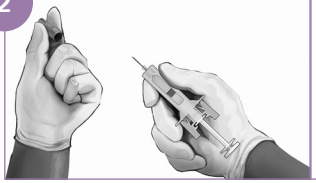
1



Take the syringe out of the cardboard box; pick up the syringe by the syringe guard body.

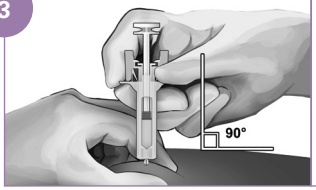
While holding the syringe by the needle shield, insert the plunger rod into the plunger stopper by gently rotating the plunger rod clockwise until secured.

2



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



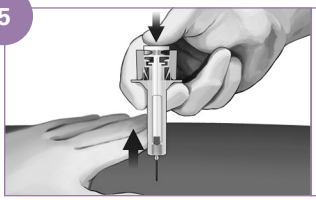
Pinch the skin at the injection site between the thumb and finger as shown.

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

4

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



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 of the injection site.

6

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 wool ball or gauze.

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

After administration of Buvidal

1. **Give the patient a copy of the patient information booklet and/or the patient information leaflet**

2. **Schedule the next appointment for the patient**

3. **Advise the patient what to do if they experience any suspected adverse reactions**

Camurus medical information email medicalinfo@camurus.com

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/** (or search for MHRA Yellow Card in the Google Play or Apple App Store) for the UK and **http://www.hpra.ie/homepage/about-us/report-an-issue** for Ireland. Adverse events can also be reported to Camurus AB via email: **safety@camurus.com**

Prescribing Information for Buvidal® (buprenorphine prolonged-release solution for injection)

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Active ingredient: Buprenorphine. Prolonged-release solution for injection in pre-filled syringes. Weekly injection (8 mg, 16 mg, 24 mg, 32 mg) or monthly injection (64 mg, 96 mg, 128 mg, 160 mg).

Indication: 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.

Dosage: To avoid precipitated withdrawal, initiate when objective and clear signs of mild to moderate withdrawal are evident, considering the duration of action of the opioid, time since last dose and degree of opioid dependence. Do not start until ≥6 hours after last heroin or short-acting opioid. Reduce methadone to ≤30 mg/day and start Buvidal® ≥24 hours after the last methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients. *Initiation in patients not already receiving buprenorphine:* Patients not previously exposed to buprenorphine, administer 4 mg sublingual buprenorphine and observe for an hour to confirm tolerability. Recommended starting dose of Buvidal® is 16 mg, with one or two additional 8 mg doses at least 1 day apart (target dose of 24 mg or 32 mg during the first week). The dose for the second week is the total dose administered during the first week. May transfer to monthly Buvidal® after four weeks and once stabilised. *Switching from sublingual buprenorphine:* Switch directly to weekly or monthly Buvidal®, starting on the day after the last sublingual buprenorphine dose. See SmPC for dose recommendations. *Maintenance:* Weekly or monthly as needed. One supplemental Buvidal® 8 mg dose may be administered between regular weekly or monthly doses (except 160 mg). The maximum dose is 32 mg weekly, with an additional 8 mg dose, or 160 mg monthly. Weekly doses may be administered up to 2 days before or after the weekly time point, and monthly doses may be administered up to 1 week before or after the monthly time point. If a dose is missed, administer the next dose as soon as practical. *Termination:* Consider prolonged-release characteristics and any withdrawal symptoms. If switching to sublingual buprenorphine, do so one week after the last weekly dose or one month after the last monthly dose of Buvidal®. *Elderly:* No dosing recommendations over 65 years. Consider renal and hepatic function.

Administration: Administration of Buvidal® is restricted to healthcare professionals only. For subcutaneous administration only. Inject slowly and completely into sufficient subcutaneous tissue of the buttock, thigh, abdomen, or upper arm area. Do not re-inject the same injection site for at least 8 weeks (each area can have multiple injection sites).

Contraindications: Hypersensitivity to buprenorphine or excipients. Severe respiratory insufficiency. Severe hepatic impairment. Acute alcoholism or *delirium tremens*.

Special warnings and precautions for use: Must not be administered intravenously, intramuscularly or intradermally. Monitor for any attempts to remove the depot. Some precautions associated with buprenorphine class. *Prolonged-release properties* of the product should be considered during treatment. Patients with concomitant medicines and/or co-morbidities should be monitored for signs and symptoms of toxicity, overdose or withdrawal. *Respiratory depression:* Deaths reported with buprenorphine. Care in respiratory insufficiency. *CNS depression:* Buprenorphine may cause drowsiness. *Dependence:* Chronic administration of buprenorphine can produce opioid dependence. *Serotonin syndrome:* Concomitant serotonergic agents (e.g. monoamine oxidase inhibitors, selective serotonin re-uptake inhibitors, serotonin and noradrenaline re-uptake inhibitors or tricyclic antidepressants) may result in serotonin syndrome, a potentially life-threatening condition - if clinically warranted, observe carefully, particularly during initiation and dose increases and consider reducing or discontinuing therapy if serotonin syndrome is suspected. *Hepatitis, hepatic events and hepatic impairment:* Recording of baseline liver function tests and viral hepatitis status recommended. Hepatic injury reported with buprenorphine. Caution with buprenorphine in moderate hepatic impairment – monitor for signs and symptoms of opioid withdrawal, toxicity and overdose. Monitor hepatic function regularly. *Drug withdrawal syndrome (GB):* Before starting any opioids, discuss withdrawal strategy with the patient. Dose tapering over weeks or months may be required. Risk of neonatal withdrawal syndrome following use in pregnancy. *Precipitation of opioid withdrawal syndrome:* Buprenorphine products have precipitated withdrawal symptoms in opioid-dependent patients when administered before the agonist effects from recent opioid use or misuse have subsided. *Renal impairment:* Caution in severe renal impairment. *QT-prolongation:* Caution with other medicines that prolong the QT interval and in patients with a history of long QT syndrome or other risk factors for QT prolongation. *Acute pain management:* A combination of opioids with high mu-opioid receptor affinity, non-opioid analgesics and regional anaesthesia might be necessary. Monitor and titrate, considering potential risk of overdose and/or death. *Sleep-related breathing disorders:* Opioids can cause sleep-related breathing disorders. *Opioid class effects:* See SmPC for details. *Interactions:* See SmPC for buprenorphine interactions. *Pregnancy and lactation:* Caution – see SmPC for details. *Driving and operating machines:* Minor to moderate influence, including drowsiness, dizziness or impaired thinking – likely to be pronounced by alcohol or CNS depressants. See SmPC for details of what individual patients should be told by the prescriber.

Undesirable effects: *Very common:*

insomnia, headache, nausea, hyperhidrosis, drug withdrawal syndrome, pain. *Common:* infection, influenza, pharyngitis, rhinitis, lymphadenopathy, hypersensitivity, decreased appetite, anxiety, agitation, depression, hostility, nervousness, abnormal thinking, paranoia, medical dependence, somnolence, dizziness, migraine, paraesthesia, syncope, tremor, hypertonia, speech disorders, lacrimal disorder, mydriasis, miosis, palpitations, vasodilation, hypotension, cough, dyspnoea, yawning, asthma, bronchitis, constipation, vomiting, abdominal pain, flatulence, dyspepsia, dry mouth, diarrhoea, gastrointestinal disorder, rash, pruritus, urticaria, arthralgia, back pain, myalgia, muscle spasms, neck pain, bone pain, dysmenorrhea, injection site reactions (pain, pruritus, erythema, swelling, reaction, induration, mass), peripheral oedema, asthenia, malaise, pyrexia, chills, neonatal withdrawal syndrome, chest pain, abnormal liver function tests. *Other:* urinary retention, injection site reactions (abscess, ulceration and necrosis). See SmPC for further details.

Overdose: Apply general supportive measures, closely monitoring and treating respiratory and cardiac status. Consider long duration of action of buprenorphine and prolonged release from the depot.

Package quantities and UK net price: 1 pre-filled syringe per pack. Weekly injection (8 mg (0.16 ml), 16 mg (0.32 ml), 24 mg (0.48 ml), 32 mg (0.64 ml)): £55.93. Monthly injection (64 mg (0.18 ml), 96 mg (0.27 ml), 128 mg (0.36 ml), 160 mg (0.45 ml)): £239.70. **Marketing authorisation numbers:** *GB:* PLGB 42800/0001, PLGB 42800/0003-9. **ROI and NI:** EU/1/18/1336/001-7, EU/1/18/1336/009. **Legal category:** POM. **Marketing authorisation holder:** Camurus AB, Ideon Science Park, SE-223 70 Lund, Sweden. Email: Camurus.uk@camurus.com Additional information available on request.

Date of revision: May 2024 FPI-0008

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard (or search for MHRA Yellow Card in the Google Play or Apple App Store) for the UK and http://www.hpra.ie/homepage/about-us/report-an-issue for Ireland. Adverse events should also be reported to Camurus AB via email: safety@camurus.com

UK-BUV-240076, June 2024

camurus®

Camurus Ltd | The Officers' Mess Business Centre, Royston Road, Duxford, Cambridge. CB22 4QH
T +44 (0)1223 919700 | Camurus.UK@camurus.com | **www.buvidal.co.uk**