

# Interim Brief Clinical guidelines for use of depot buprenorphine (Buvidal<sup>®</sup> and Sublocade<sup>®</sup>) in the treatment of opioid dependence

## For South Australian Community MATOD prescribers

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# Contents

## Table of Contents

<b>Introduction</b> .....	2
<b>Regulatory requirements</b> .....	3
<b>Depot buprenorphine products: Buvidal® and Sublocade®</b> .....	4
Framework for treatment with depot BPN products .....	4
Delivering treatment with depot BPN.....	4
Dosing recommendation for Buvidal®.....	5
Dosing recommendations with Sublocade®.....	7
<b>Safety issues regarding use of depot products</b> .....	8
<b>Other issues</b> .....	11
Accessing depot BPN supplies and storage considerations.....	11
Transferring from one depot to the other product.....	11
Record Keeping .....	11
Monitoring Treatment.....	12
COVID-19 pandemic planning .....	12
<b>Getting support &amp; more information</b> .....	13
South Australian Health .....	13
Consumer and Product information .....	13
Administration videos .....	14
Clinical guidelines .....	14

## Acronyms

AE	Adverse Event
BPN	Buprenorphine
DDI	Drug drug interaction
DDU	Drugs of Dependence Unit
MATOD	Medication Assisted Treatment for Opioid Dependence
SL	Sublingual

# Introduction

The NSW brief clinical guidelines for the use of long-acting injected depot buprenorphine (depot BPN) <sup>1</sup> form the basis of this document. With permission, this has been adapted for use in South Australia. This document contains some additional information specific to South Australian.

BPN is one option available for MATOD and the [National Guidelines for Medication-Assisted Treatment of Opioid Dependence 2014](#) outlines the general principles of this treatment.

Prescribers of depot BPN should be aware of both the National MATOD guidelines and the [SA Health treatment guidelines](#) that guide the provision of MATOD in South Australia.

It is recommended that this interim brief clinical guideline be used in conjunction with the full Product Information, Consumer Information materials and demonstration videos provided by each of the depot BPN manufacturers. These guidelines are likely to require updating following further clinical experience with depot in South Australia.

This brief clinical guideline has been developed to assist decision-making by clinicians and clients in the use of the depot BPN preparations. It is important to understand that clinical guidelines are intended to guide clinical decision-making and practise and they cannot address every conceivable situation or exceptional circumstance.

As part of exercising good clinical judgement, it may be prudent to obtain additional assistance with decision-making and practise support via discussion with peers, referral for specialist advice and/or seeking a second opinion.

If practise outside of recommendations is considered necessary, the reasoning, together with required additional risk management measures, should be noted in the patient's treatment plan, and the patient's informed consent should also be documented.

*Patients appropriate to be prescribed depot BPN.* It is recommended that treatment initiation with depot buprenorphine is most appropriate for patients already under treatment with buprenorphine (e.g. stable on a Suboxone or Subutex program). This allows a patient's tolerance to buprenorphine to be established, before exposing them to long acting depot BPN products.

## *Recommended Indications:*

- Opioid Dependence (currently on buprenorphine)
- Stability on MATOD e.g. on multiple take-away doses.
- Facilitates drug rehabilitation goals e.g. maintain employment.

## *Special Precautions:*

- CYP3A4 Inhibitors and Inducers, Serotonergic Drugs, QTc, OSAS etc.
- Pregnancy.

## *Contraindications:*

- Allergy/sensitivity to buprenorphine (or depot excipients).
- Severe hepatic disease e.g. Child Pugh C
- Unstable ongoing drug use.
- Alcohol Dependence.

### **Special warnings and precautions for use**

#### **Sublocade®**

**Risk of serious harm or death with intravenous administration.** Intravenous injection presents significant risk of serious harm or death as SUBLOCADE forms a solid mass upon contact with body fluids. Occlusion, local tissue damage, and thrombo-embolic events, including life threatening pulmonary emboli, could result if administered intravenously. Do not administer intravenously or intramuscularly.

#### **Buvidal®**

**Risk of Serious Harm or Death with Intravenous Administration** Serious harm or death could result if administered intravenously. Buvidal® Weekly and Buvidal® Monthly forms a gel depot upon contact with body fluids and may cause occlusion, local tissue damage and thromboembolic events, including life threatening pulmonary emboli, if administered intravenously.

<sup>1</sup> Lintzeris N, Dunlop A, Masters D (2019) Brief Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence. NSW Ministry of Health, Sydney Australia.

# Regulatory requirements

Depot BPN is a Schedule 8 drug, regulated in South Australia by the [Controlled Substances Act 1984](#) and monitored by SA Health's Drugs of Dependence Unit (DDU).

There will be a phased approach to the consideration by DDU of the granting of authorities for MATOD using depot BPN to specific prescribers/sites in South Australia.

**Phase 1:** Accredited DASSA prescribers for DASSA clients (6 months from September 2019).

**Phase 2:** Medical practitioners and nurse practitioners who are accredited prescribers of methadone and buprenorphine ([see below](#)) who have undertaken specific depo BPN training approved by DDU ([see below](#)).

In special circumstances a medical practitioner who is not accredited, that has undertaken the specific depo BPN training may be approved by DDU.

**Phase 3:** Based on the evaluation and experience of phase 1 and 2, widening of the availability of consideration for granting of authorities will be considered to other medical practitioners.

**Accredited prescriber.** To be considered for recognition by DDU as an accredited prescriber of methadone and buprenorphine for MATOD, medical practitioners must undergo additional training approved by the DDU. Details of the [South Australian MATOD training course](#) can be found on the SA Health website [here](#) and the online theory component of this training can be accessed [here](#).

**DDU approved Depo BPN training.** From April 2020 a module on depo BPN has been incorporated into the online theory component of the South Australian MATOD training course.

MATOD accredited prescribers need to have completed the depo BPN Module. If a prescriber has recently become accredited, their training included the depo-BPN module. All accredited prescribers who completed the theory component after 1/4/20 are recognised by DDU as eligible to prescribe depo BPN.

If training was prior to April 2020, they will need to complete the module. This module is hosted on the AOGP website, available [here](#).

To be granted eligibility to prescribe depot BPN, forward a copy of the completion certificate provided for this module to DDU when first applying for an authority to prescribe depot BPN.

[Note: DDU can also be contacted to grant eligibility to prescribe depot BPN when an accredited prescriber can demonstrate:

1. familiarity with the manufacturers' product information and these guidelines, [and](#)
2. has seen depot BPN administration performed in person or viewed the video of depot BPN provided by the manufacturer.]

**Authorities.** The granting of each authority will continue to be considered on a case by case basis by DDU. All patients commencing treatment with depot BPN injections must be eligible for MATOD treatment under currently existing [SA Health treatment guidelines](#).

- After 28/08/2020, authorities issued to eligible accredited MATOD prescribers include depot BPN.
- For new authorities or authorities issued before 28/08/2020, applications for depo BPN are made using the currently available [MATOD Application Form](#), specifying the request is for BPN depot.

**Prescriptions and supply.** All depot BPN scripts must comply with the same requirements as other MATOD scripts as per [Controlled Substances Act 1984](#).

Depot BPN is indicated under the PBS S100 scheme for treatment of opiate dependence and the Australian Government funds the cost of this medication supplied as pharmaceutical benefits through clinics and pharmacies approved by State and Territory governments.

**Buvidal® and Sublocade® medications should not be handled by, be accessible to, or dispensed DIRECTLY to patients or carers. All steps should be taken to avoid any possibility of diversion of depot injection/s to unauthorised persons. Buvidal® and Sublocade® must be administered by registered health practitioners. Serious harm or death could result if administered intravenously.**

Arrangements will be needed to obtain the depot BPN product from pharmacists or wholesalers to be available to be administered to the patient by the health practitioner. The transport and storage of schedule 8 drugs is controlled by the Code of Practice for the [Storage and Transport of Drugs of Dependence](#).

It is likely that in 2021, RTPM (real-time prescription monitoring) will be operational in SA and all S8 drugs (also some other drugs of dependence like benzodiazepines) will be monitored by this system; this system may also involve (as currently operating in Victoria) a mandatory requirement for prescribers to view the RTPM before prescribing S8 drugs.

# Depot buprenorphine products: Buvidal® and Sublocade®

The Clinical Guideline has been developed to inform decision-making by clinicians and clients in the use of the following long-acting injected depot buprenorphine (depot BPN) preparations, Buvidal® and Sublocade®.

**Buvidal®** (manufactured by Camurus) is a modified release formulation of BPN, registered in Australia for 'maintenance treatment of opioid dependence within a framework of medical, social and psychological support'. Buvidal® is designed to be administered by subcutaneous injection once a week (Buvidal® Weekly) or once a month (Buvidal® Monthly).

- **Buvidal® Weekly** is available in **four dose strengths** in prefilled syringes with a 23-gauge needle:  
8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL or 32 mg/0.64 mL BPN as the active ingredient.
- **Buvidal® Monthly** is available in **three dose strengths** in prefilled syringes with a 23-gauge needle:  
64 mg/0.18 mL, 96 mg/0.27 mL or 128 mg/0.36 mL BPN as the active ingredient.

**Sublocade®** (manufactured by Indivior) is an extended-release formulation of BPN, administered **monthly** by subcutaneous (SC) injection and provides sustained plasma levels of BPN over the monthly dosing interval.

- **Sublocade®** is available in **two dose strengths**:  
100 mg/0.5 mL and 300 mg/1.5 mL provided in a prefilled syringe with a 19 Gauge 5/8-inch needle.

## Framework for treatment with depot BPN products

The key elements of safe and effective BPN treatment for opioid dependence are (a) safe and effective use of medicine; (b) regular clinical reviews and monitoring; (c) participation in psychosocial interventions; and (d) addressing medical, mental health and social comorbidities.

It is essential that patients are provided accurate information and options regarding their medication and treatment, as part of informed decision making and consent. Once-a-week and once-a-month depot injections reduce the need for daily supervised and/or 'take-away' doses of Sublingual (SL) BPN formulations. Potential benefits of depot BPN treatment include:

- Greater convenience for patients in that they will not have to attend dosing sites (pharmacies, clinics) on a frequent basis for supervised dosing.
- Reduced treatment costs.
- Greater medication adherence and enhanced treatment outcomes for some patients who struggle to attend regularly for dosing with SL BPN.
- Less risk of diversion and non-medical use of the medication, enhancing community safety.

However, BPN formulations may not suit all patients, and some will prefer SL BPN or methadone treatment, and these options should remain available.

**Buvidal® and Sublocade® must be administered by registered health practitioners. Buvidal® and Sublocade® medications must not be handled by or dispensed DIRECTLY to patients or carers. Serious harm or death could result if administered intravenously.**

## Delivering treatment with depot BPN

The key characteristics of Buvidal® and Sublocade® and recommended dosing regimens are summarised in Table 2. Specific recommendations regarding medication regimens for each product are described below. See the full guidelines and product information for an overview of the clinical pharmacology, evidence of safety and efficacy of these products, and issues regarding special populations. There is no evidence directly comparing the safety or efficacy of Buvidal® and Sublocade® products. It is not recommended to temporarily substitute one product with another.

## Dosing recommendation for Bupival®

**Transferring from SL BPN.** Patient should usually be treated with  $\geq 7$  days of SL BPN prior to transferring to Bupival®, with either Bupival® Weekly or Bupival® Monthly starting on the day after the last daily SL dose. Bupival® doses are 'matched' to SL BPN doses as shown in Table 1.

Table 1: Dose conversions between SL BPN, depot Bupival® Weekly and Bupival® Monthly doses

Daily SL BPN dose	Bupival® Weekly depot dose	Bupival® Monthly depot dose
$\leq 6$ mg	8 mg	No monthly equivalent
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-32 mg	32 mg	128 mg

Patients should be reviewed prior to the next scheduled dose and assess for adverse events, withdrawal, cravings, substance use and patient's rating of dose adequacy. Titrate doses upwards or downwards accordingly. Steady-state equilibrium is usually achieved after three to four doses.

### Commencing BPN treatment with Bupival®.

Whilst not recommended as routine practice, Bupival® Weekly can be initiated directly from short acting opioids (e.g. heroin) or after less than 7 days of SL BPN treatment (e.g. a patient unable to access dosing sites for daily SL dosing). For patients reporting current dependent opioid use, initiate Bupival® Weekly 24mg doses and review for subsequent dose titration.

**Flexible dosing schedule.** Patients may switch between Bupival® Weekly and Bupival® Monthly (see Table 1). Individual dose adjustment may be required.

- Bupival® Weekly doses may be given up to 2 days before or after the weekly time point (days 5-9),
- Bupival® Monthly may be given up to 1 week before or after the monthly time point (weeks 3-5).

If a dose is missed, the next dose should be administered as soon as possible. Re-induction may be required if  $> 14$  days has elapsed between Bupival® Weekly doses, or  $> 8$  weeks between Monthly doses.

**Supplemental or 'top up' BPN doses.** Supplemental Bupival® injections may be used if clinically indicated (patient experiencing opioid withdrawal, cravings or persistent unsanctioned opioid use). Patients may receive additional 8 mg Bupival® Weekly injections at least 24 hours apart, to a maximum total weekly dose of 32 mg, and maximum total monthly dose of 160mg. If supplemental Bupival® Weekly doses cannot be administered, supplemental doses of SL BPN (8mg daily) may be used for a limited period of time until the next depot injection can be organised.

### Dosing where patient transferred onto Bupival® Monthly when receiving 32mg SL BPN daily doses.

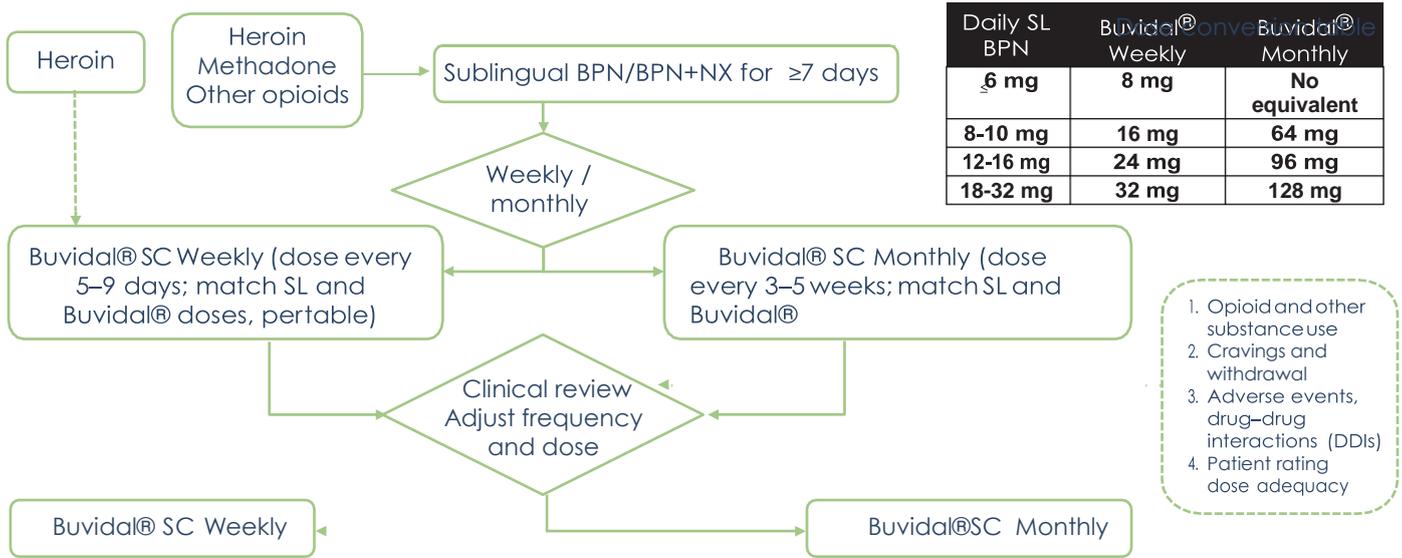
In Australia, the 128mg Bupival® depot is the highest monthly dose available for this product and the recommended maximum monthly dose. The current dosing guide suggests this dose formulation is for SL dose ranges 18 – 24mg daily. However, in clinical practice to date, when steady state is achieved after 3 – 4 injections of 128mg Bupival® monthly formulation, this dose has typically been found effective to hold patients previously receiving up to 32mg SL BPN daily doses.

**Bupival® and pregnancy.** Although BPN (sublingual formulations, Subutex & Suboxone) is approved for use in pregnancy and lactation, because Bupival® is a new formulation, it is recommended to advise about other options, provide special precaution and obtain an informed consent before prescribing to women planning pregnancy or who are already pregnant. As with any medication use in pregnancy, use of Bupival® depot BPN could be considered for continued use if the potential benefit justifies the potential risks to the mother and baby. A neonatal opioid withdrawal syndrome is considered likely to occur as it has been reported with the sublingual formulations.

**Discontinuing Bupival®.** At this point in time, no studies have been performed to examine discontinuation of Bupival®. It may have a duration of effect lasting longer than the anticipated effect of the Weekly or Monthly depot injection, especially after prolonged use and with steady-state blood levels. Therefore withdrawal symptoms and signs may be delayed for days – weeks. Withdrawal is likely to emerge within 1 – 4 weeks following regular dosing with the Weekly depot or 4 – 12 weeks following the Monthly depot injection.

There are multiple dose formulations of Bupival® so a slow reducing titration can be provided by using successively lower depot injections. At the end of such a discontinuation procedure, some patients may still require continued buprenorphine weaning using sublingual Suboxone/Subutex. It is good practise to document why a patient (or you) has decided to discontinue treatment and to always provide relapse prevention education together with access to Naloxone.

Figure 1: Overview dosing with Buvidal®



## Dosing recommendations with Sublocade®

### Commencing Sublocade® treatment.

Sublocade® treatment requires preceding treatment with SL BPN for at least 7 days, preferably achieving SL doses  $\geq 8\text{mg}$  daily. Sublocade® is generally not recommended for patients on daily SL BPN doses  $< 8\text{mg}$ .

The first Sublocade® dose should usually be administered approximately 24 hours after the last SL BPN dose but may be administered on the same day. For most patients, commence 300mg doses for the first 2 months (2 x monthly doses), reflecting 'loading' doses that elevate plasma BPN levels more rapidly during the initial treatment period.

Sublocade® may be initiated with 100mg doses where there may be safety concerns of high BPN plasma levels (e.g. severe hepatic disease, DDIs).

After the initial two doses Sublocade® (each monthly) select between 100mg or 300mg 4-weekly doses. For most patients, 100mg 4-weekly Sublocade® doses will be adequate, maintaining plasma levels (at steady state equilibrium) achieved with the first two 300mg 'loading' doses. Maintenance 300mg doses should be considered for those patients who had previously stabilised on high dose SL BPN (e.g. 24 to 32mg daily), or continue to experience cravings, withdrawal or unsanctioned opioid use during the first 2 month period of Sublocade® dosing or with 100mg Sublocade® doses.

### Sublocade® flexible dosing schedules.

Sublocade® doses can be administered up to 2 days ahead of a scheduled dose (i.e. 26 days since the last injection), or up to 14 days after the 28 day interval (i.e. to 42 days since the last injection) without dose adjustments.

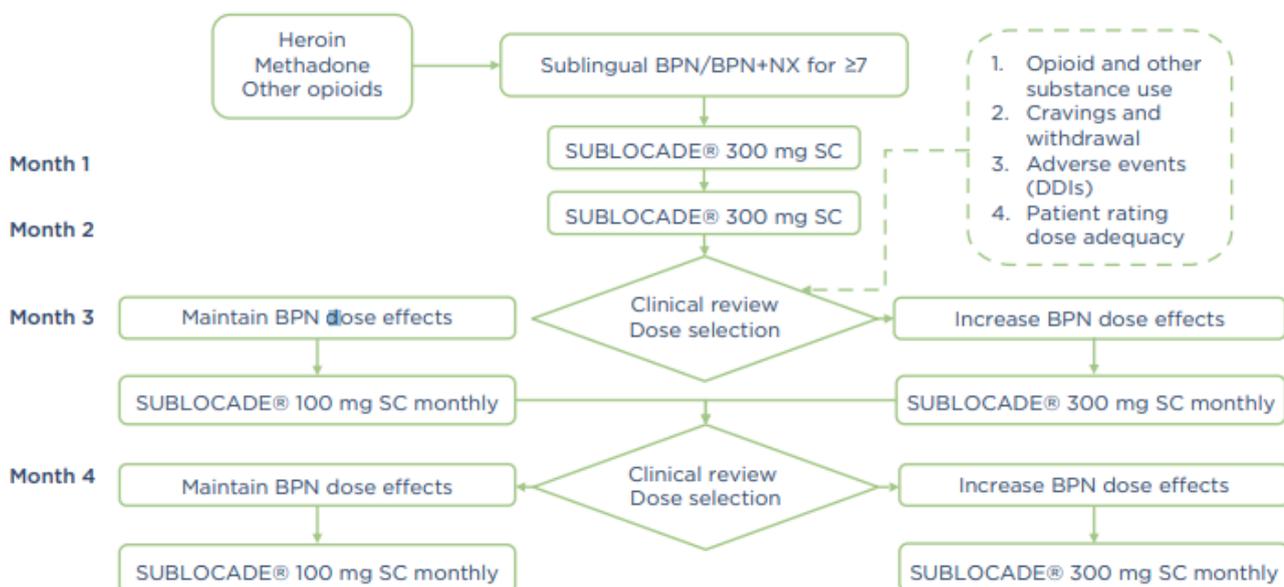
If a dose is missed, the next Sublocade® dose should be administered as soon as practically possible. Re-induction may be required if more than eight weeks between Sublocade® doses has elapsed.

### Supplemental or 'top up' BPN doses.

Supplemental SL BPN doses may be given if clinically indicated (patient experiencing opioid withdrawal, cravings or persistent unsanctioned opioid use). Additional SL BPN ( $\leq 8\text{mg}$  daily) may be used for a limited period of time until the next depot injection can be organised.

**Ceasing Sublocade.** Sublocade® may last significantly longer than the month for which the different formulations are designed. Peak withdrawal features may emerge 4-24 weeks after last 300mg dose or 4-12 weeks after last 100mg dose. If a slow dose taper is desired, then titrate down the Sublocade® dose as tolerated. Monitor for withdrawal. SL preparations might need to be considered in addition to, or as a substitute for, the Sublocade®. It is good practise to document why a patient (or you) has decided to discontinue treatment and to always provide relapse prevention education together with access to Naloxone.

Figure 2: Overview dosing with Sublocade



Sublocade® is for abdominal subcutaneous injection only; do not administer Sublocade® intravenously or intramuscularly. Serious harm or death could result if administered intravenously

# Safety issues regarding use of depot products

**Precautions and contraindications.** Depot products should not be administered to anyone hypersensitive to BPN or any of the excipients of Buvidal® or Sublocade® (see Product Information for details). Precautions regarding the use of Buvidal® and Sublocade® are similar to treatment with SL BPN and include patients with high-risk sedative use (e.g. alcohol, benzodiazepines), severe hepatic disease, cardiac arrhythmias, and respiratory depression. (see Product Information for details).

**Adverse events (AEs).** Both depot products can be associated with local injection site AEs – redness, pain, tenderness and swelling in 5-10% patients. These are usually mild, transient and resolve spontaneously. Sublocade® doses appear to be more commonly associated with a palpable lump at the injection site, which dissolves with time. Systemic AEs as per SL BPN (e.g. nausea, headache, constipation).

**Drug-drug Interactions (DDI).** DDIs are expected to be the same as for SL BPN, however the long duration of depot BPN effects may result in prolonged DDI. If concerns, stabilise on SL BPN and monitor DDI before transferring to depot BPN products.

**Pregnancy and breastfeeding.** SL BPN has an acceptable safety profile and is effective in pregnancy. There is a lack of research data on the safety and effectiveness of depot BPN formulations in pregnancy and breastfeeding. A neonatal opioid withdrawal syndrome is likely to occur. Pregnant women on depot BPN should be transferred to SL BPN, although may be continued on depot products if the potential benefit justifies the potential risks to the mother and baby.

**Driving, operating machinery.** BPN may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Patients should be cautioned about driving or operating hazardous machinery.

## **Withdrawal from depot BPN products.**

The prolonged duration of action of the depot products means that withdrawal symptoms are likely to emerge long after the last depot dose. Withdrawal features may emerge 4-12 weeks after last Buvidal® Monthly dose, or 1-4 weeks after last Buvidal® Weekly dose. For Sublocade® peak withdrawal features may emerge 4-24 weeks after last 300mg dose or 4-12 weeks after last 100mg dose. Withdrawal symptoms may persist for weeks (or months) and are expected to be less severe than withdrawal from shorter-acting opioids. Although there is little documented experience of withdrawal from depot BPN products. It is generally recommended to taper the depot dose to the lowest possible before discontinuing treatment, and to review the patient at regular intervals.

## **Administration of depot products**

**by other routes.** Both depot products are intended for subcutaneous administration and *should never be injected intramuscularly, intra-dermally, intravenously or intra-arterially*. For this reason, depot formulations must be administered by a suitable health care professional, and never be dispensed or supplied directly to the patient or carer.

**Transfer from methadone:** there is limited experience and no documented evidence regarding transferring patients from methadone directly to depot BPN products. Transfer to SL BPN is recommended for at least 7 days prior to commencing depot treatment.

**Special populations, treatment settings and clinical scenarios.** The use of depot BPN products in certain patient populations and treatment settings (correctional facilities, hospitals, residential rehabilitation), and in the management of particular clinical scenarios (acute and chronic pain management, overdose, intoxicated presentations) is described in the full Guidelines document.

Table 2: Overview of BPN products available for treatment of opioid dependence in Australia

	SL Suboxone® and Subutex®	Buvidal® Weekly and Monthly	Sublocade®
Formulations	<p>Suboxone® contains buprenorphine (BPN) and naloxone in 4:1 ratio 2/0.5mg and 8/2mg sublingual film</p> <p>Subutex® contains buprenorphine in 0.4mg, 2mg and 8mg sublingual tablets</p>	<p>Buvidal® Weekly and Monthly contain BPN in FluidCrystal® injection depot technology Subcutaneous (SC) injections in prefilled syringes with 23 gauge needle. Administration via upper arm, thigh, abdomen or buttocks</p> <p>Buvidal® Weekly: 8mg/0.16mL, 16mg/0.32mL, 24mg/0.48mL; 32mg/0.64mL</p> <p>Buvidal® Monthly: 64mg/0.18 mL, 96mg/0.27 mL; 128/0.36 mL</p>	<p>Sublocade® contains BPN in the ATRIGEL® Delivery System</p> <p>SC injections in prefilled syringes with 19 gauge needle administered in abdomen</p> <p>Monthly doses: 100mg/0.5mL or 300mg/1.5mL</p>
Storage requirements	Store at room temperature (below 30°C)	Store at room temperature (below 25°C) Do not refrigerate or freeze.	Cold storage requirements (2-8°C). May be stored at room temperature (below 25°C) for up to 7 days before use. Remove from cold storage for at least 15 minutes prior to SC injection
Clinical pharmacology	<p>Bioavailability 10-30%</p> <p>Onset effects within 1 hour, with peak effects 2-4 hours after dose</p> <p>Duration effects usually 24 hours but dose dependent and can vary from 8 to 72 hours</p>	<p>Bioavailability = 100%</p> <p>Time to peak plasma level (t<sub>max</sub>)</p> <ul style="list-style-type: none"> <li>Buvidal® Weekly = 24hrs</li> <li>Buvidal® Monthly = 6-10 hrs</li> </ul> <p>Half life</p> <ul style="list-style-type: none"> <li>Buvidal® Weekly = 3-5 days</li> <li>Buvidal® Monthly = 19-25 days</li> </ul> <p>Steady-state equilibrium by 4<sup>th</sup> dose</p>	<p>Bioavailability = 100%</p> <p>Time to peak plasma levels (t<sub>max</sub>) = 24hrs</p> <p>Half life = 43 to 60 days</p> <p>Steady-state equilibrium by 2<sup>nd</sup> (300/100mg) to 6<sup>th</sup> dose (300/300mg)</p>
Frequency of dosing	Daily, two or three day doses Take-aways and unsupervised dosing available for low risk	<p>Buvidal® Weekly dose can be administered every 7±2 days (5-9 day schedule)</p> <p>Buvidal® Monthly dose can be administered every 4±1 weeks (3-5 week schedule)</p>	Sublocade® dosed every 4 weeks (26-42 day schedule)
Key Drug – Drug Interactions (DDIs)	<p>Systemic BPN DDI include:</p> <ul style="list-style-type: none"> <li>Opioids agonists: can reduce effects other opioids (blockade); BPN may precipitate withdrawal on induction</li> <li>Sedatives (e.g. benzodiazepines, alcohol, TCAs, antipsychotics, gabapentinoids): sedation, respiratory depression, overdose</li> </ul> <p>A number of potential DDI can occur but are rarely of clinical significance (e.g. interactions with medications that induce or inhibit CYP450 and can lower or increase BPN plasma levels); or are rare (e.g. serotonergic syndrome in combination with medication such as SSRIs, MAOIs, tramadol; or medications that can cause QT prolongation and increase risk of cardiac arrhythmias).</p> <p>Long duration of effects of depot BPN products precludes timely dose adjustment for DDI. If concerned re: potential DDI – initiate treatment with 'short acting' SL BPN for 1-4 weeks, monitor DDI and adjust medications accordingly, prior to transfer to depot injection.</p>		

	SL Suboxone® and Subutex®	Buvidal® Weekly and Monthly	Sublocade®
Recommended dosing regimen Commencing treatment	<p>From heroin, morphine:</p> <ul style="list-style-type: none"> <li>– Commence 8mg Day 1 when patient in early / mild opioid withdrawal (usually &gt;8-12hrs after last dose or use).</li> <li>– Titrate upwards on daily basis as required.</li> </ul> <p>From methadone:</p> <ul style="list-style-type: none"> <li>– Initiate BPN when patient in moderately severe withdrawal (e.g. COWS≥12) (e.g. 1-2 days after last methadone dose)</li> <li>– Day 1: 2mg + 6mg after 1-2 hrs, with additional 2-8mg doses every 2-4 hrs as required to alleviate opioid withdrawal.</li> <li>– Day 2 onwards: titrate BPN dose daily as required.</li> </ul>	<ul style="list-style-type: none"> <li>– Buvidal® dose should be determined according to patient's SL BPN dose (see Table 1).</li> <li>– Titrate subsequent doses after clinical review.</li> <li>– Note increasing effects during first few doses (accumulation to steady state after about 4 doses)</li> </ul> <p>Buvidal® may be initiated directly (without transition via SL BPN) if required. Initiate 24mg Buvidal® Weekly dose, and titrate dose until stable.</p>	<p>Initiate treatment with SL BPN (at least 8mg) for ≥7 days, then transfer to Sublocade®.</p> <p>Recommended induction:</p> <ul style="list-style-type: none"> <li>– 300mg monthly injections x 2 doses (8 weeks)</li> <li>– then 100mg monthly doses (if patient 'stable' on initial 2 x 300mg doses) or 300mg monthly doses if require additional BPN effects (e.g. cravings, withdrawal, continued opioid use)</li> </ul> <p>Patients may be initiated with 100mg Sublocade® (after at least 7 days SL BPN treatment) doses if</p> <ul style="list-style-type: none"> <li>– safety concerns (e.g. severe hepatic disease)</li> <li>– DDI concerns: e.g. overdose risk from polysubstance use</li> </ul> <p>There is no published safety data for initiating Sublocade® in patients on low dose SL BPN (&lt;8mg), and Buvidal® should be preferred for such patients.</p>
Maintenance phase	Adjust dose to achieve treatment goals (reduced use of other opioids, reduced withdrawal and cravings; blockade effects). Range 2-32mg daily; most patients require 12-24mg daily	Titrate dose to achieve treatment goals. Adjust doses when transferring between weekly and monthly doses	Titrate dose to achieve treatment goals. 100mg or 300mg monthly injections.
Withdrawal phase	Gradually taper dose over several weeks-months (e.g. 2-4mg weekly reductions)	Gradually taper doses (reducing dose strengths every 1-2 injections). Peak withdrawal features may emerge 4-12 weeks after last Buvidal® Monthly dose, or 1-4 weeks after last Buvidal® Weekly dose (CS).	Reduce dose to 100mg monthly injections prior to stopping. Peak withdrawal features may emerge 4-24 weeks after last 300mg dose or 4-12 weeks after last 100mg dose (CS).
Key adverse events	Systemic BPN adverse events	<p>Systemic BPN adverse events</p> <p>Local injection site</p> <ul style="list-style-type: none"> <li>– Redness, pain, tenderness, swelling in approximately 5-10% patients.</li> <li>– Usually mild and transient and resolves spontaneously</li> </ul>	

# Other issues

## Accessing depot BPN supplies and storage considerations

**Buvidal® and Sublocade® medications should not be handled by, be accessible to, or dispensed DIRECTLY to patients or carers. All steps should be taken to avoid any possibility of diversion of depot injection/s to unauthorised persons. Buvidal® and Sublocade® must be administered by registered health practitioners. Serious harm or death could result if administered intravenously.**

Each prescriber of depot BPN will need to make arrangements for the supply of this product to be available for administration to the patient. Supply from a pharmacist and transport to the administration location is one possibility. Individual pharmacists will need to be contacted in this regard. If courier arrangements are required these must meet [Code of Practice for the Storage and Transport of Drugs of Dependence](#). If a pharmacist is co-located there may be no need for courier arrangements.

Alternatively, the products can be sourced directly from the manufacturer with the medical practitioner responsible for complying with the [Code of Practice for the Storage and Transport of Drugs of Dependence](#).

A fee structure and method of payment by the patient for any cost for the supply of the medication will need to be determined and communicated with the patient as part of the treatment planning. Currently most patients are charged a dispensing fee and payment is made prior to dosing.

There are particular storage considerations for depot BPN products. Buvidal® is stable at room temperature and can be stored for up to two years, Sublocade® requires refrigeration in an S8 compliant fridge wherein it can be stored for up to two years. Sublocade® can only be stored for a maximum of one week at room temperature after which it must be discarded or returned to the manufacturer. The size of the packaging should be considered to ensure that there is capacity to store the medication in a compliant manner.

## Transferring from one depot to the other product.

Currently, there are no studies to provide evidence about transferring between BPN depot products. There are very limited anecdotal reports of transferring between depot BPN products and while suggesting this can be done if necessary, it should proceed with caution.

The prolonged duration of effect with both depot products and especially Sublocade® 300mg, would generally require delaying such a transfer until the withdrawal process can be reasonably established, following which induction onto the other depot could commence. In some circumstances, if the new depot BPN injection is not able to be provided at a time when withdrawal has commenced, it may be necessary for the patient to be temporarily provided SL BPN to manage withdrawal until the new depot BPN can be initiated. It is recommended that referral to an Addiction Medicine Specialist be undertaken for a patient seeking a transfer of depot BPN treatment, or at least, conferring with such a specialist about management.

## Record Keeping

The prescriber must indicate in the patient's file a record of prescription, including:

- the patient's name and address,
- date of prescribing, date of administration,
- site of injection,
- the drug name (including the brand name),
- strength and
- the interval in which the injections are to be administered.

Along with the usual Informed Consent process required for medical treatment, the prescribing medical practitioner should provide an alert card for patients (provided with the product or from the manufacturer) and specific printed depot BPN information, available online and from the manufacturer.

## Monitoring Treatment.

The requirements for clinical monitoring of patients maintained on depot BPN are similar to when oral formulations are used for MATOD. The use of depot BPN removes the need to determine take away doses or to monitor pharmacy attendances. Appropriate clinical monitoring is outlined in the [National Guidelines for Medication-Assisted Treatment of Opioid Dependence 2014](#).

Clinical review provides an opportunity to assess:

- The patient's general presentation, the quantity and frequency of any substance use since the last review, general health and wellbeing, social circumstances, living environment and relevant risk factors (child protection, harm to self or others, domestic violence, overdose, blood-borne virus risk);
- The current medication conditions, adequacy of medication dose, side effects, frequency of reviews, monitoring and counselling services; and
- Treatment progress against the treatment plan.

Regarding Urine Drug Screening (UDS) when depot BPN formulations are administered the role of UDS in monitoring for other drug use remains. However, in contrast to the use of UDS where orally administered MATOD formulations are prescribed, the use of depot BPN nullifies the need for UDS to monitor medication adherence or medication diversion.

## COVID-19 pandemic planning

It is strongly advised to be familiar with latest SA Health information relating to COVID-19 preparations and services: <https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/conditions/infectious+diseases/covid-19/about+covid-19/latest+updates/latest+updates+on+covid-19>

The availability of depot BPN may be limited due to the COVID-19 pandemic as international supply limitations may occur, together with increased demand driven by the need for social distancing/isolation. Current stock should be prioritised for people who are confined to their home for 14 days or longer, who are considered at high risk for diversion and will not meet criteria for extended Suboxone take-away dosing. It is advised to check with your supplier i.e. pharmacist or the manufacturer.

# Getting support & more information

## South Australian Health

- *Drugs of Dependence Unit*

Phone: **1300 652 584**

Fax: 1300 658 447

Email: [HealthDrugsofDependenceUnit@sa.gov.au](mailto:HealthDrugsofDependenceUnit@sa.gov.au)

Post: PO Box 6, Rundle Mall, Adelaide South Australia 5000

- [\*Drug and Alcohol Clinical Advisory Service \(DACAS\)\*](#)

Telephone **7087 1742**

DACAS provides a telephone and email service for South Australian health professionals seeking clinical information and clarification around clinical procedures, guidelines and evidence-based practice.

Telephone: (08) 7087 1742 from 8:30am — 10pm 7 days/week including public holidays or e-mail your enquiry to: [HealthDACASenquiries@sa.gov.au](mailto:HealthDACASenquiries@sa.gov.au)

This service does not provide proxy medical cover and cannot assume responsibility for direct patient care.

- [\*Alcohol and Drug Information Service \(ADIS\)\*](#) telephone **1300 13 1340**

Any day between 8.30am and 10pm for information, counselling and referral (South Australian callers - local call fee).

- GP Program Project Officer: (08) 7425 5045 Email: [HealthDASSAGPProgram@sa.gov.au](mailto:HealthDASSAGPProgram@sa.gov.au)

## Consumer and Product information

- AUSTRALIAN PRODUCT INFORMATION Buvidal® Monthly (buprenorphine)

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2018-PI-02611-1&d=202003221016933>

- Buvidal® Monthly Buprenorphine [Consumer Medicine Information](#)

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-CMI-01178-1>

- AUSTRALIAN PRODUCT INFORMATION Buvidal® Weekly (buprenorphine)

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2018-PI-02610-1>

- Buvidal® Weekly Buprenorphine [Consumer Medicine Information](#)

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-CMI-01177-1>

- AUSTRALIAN PRODUCT INFORMATION SUBLOCADE (BUPRENORPHINE)

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2019-PI-01756-1>

- SUBLOCADE® Buprenorphine Consumer Medicine Information

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2020-CMI-01182-1>

## Administration videos

- Sublocade® – Learn how to administer SUBLOCADE® online video

<https://www.sublocade.com/hcp/buprenorphine#>

- Buvidal® – Product demonstration online video

<https://ljsp.lwcdn.com/api/video/embed.jsp?id=caa308ae-07af-4c0a-9a31-0b5b6de154b5&pi=785b7fd1-761b-46d1-9e8c-fe5f8958ac14>

## Clinical guidelines

- National Guidelines for Medication-Assisted Treatment of Opioid Dependence 2014

<https://www.health.gov.au/resources/publications/national-guidelines-for-medication-assisted-treatment-of-opioid-dependence>

- Medication Assisted Treatment for Opioid Dependence (MATOD) Program information

<https://www.sahealth.sa.gov.au/wps/wcm/connect/Public+Content/SA+Health+Internet/Clinical+Resources/Clinical+Programs+and+Practice+Guidelines/Medicines+and+drugs/Programs+for+the+prescribing+and+supply+of+medicines/Medication+Assisted+Treatment+for+Opioid+Dependence+MATOD+Program/Medication+Assisted+Treatment+for+Opioid+Dependence+MATOD+Program+information>

- Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence (NSW)

<https://www.health.nsw.gov.au/aod/Publications/full-depot-bupe-interim-gl.pdf>

- Brief Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence. (NSW)

<https://www.health.nsw.gov.au/aod/Publications/brief-depot-bupe-interim-gl.pdf>