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

For Western Australian CPOP prescribers and pharmacists

July 2023

GOVERNMENT OF WESTERN AUSTRALIA
Department of Health
Mental Health Commission

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Lintzeris N, Dunlop A, Masters D (2019). Clinical guidelines for use of depot Buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence. NSW Ministry of Health, Sydney Australia.

McDonough, M, Holmwood C, Scarborough, J (2020). Interim Brief Clinical guidelines for use of depot Buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence For South Australian Community MATOD prescribers. Drug and Alcohol Services South Australia (DASSA), SA Ministry of Health.

Policy for maintenance pharmacotherapy for opioid dependence (addendum). Long-acting injectable buprenorphine. Department of Health Victoria, March 2021. Available at Pharmacotherapy policy in Victoria.
https://www2@health.vic.gov.au/public-health/drugs-and-poisons/pharmacotherapy/pharmacotherapy-policy-in-victoria

Long-acting injection buprenorphine in the treatment of opioid dependence – Queensland Clinical Guidelines 2019. Published by the State of Queensland (Queensland Health), December 2019.

Depot buprenorphine long-acting subcutaneous injections (Buvidal® and Sublocade®) Guidance note for pharmacists and medical practices. October 2020. Government of Western Australia. Department of Health.

Prepared by the Community Pharmacotherapy Program (Mental Health Commission) in consultation with the Community Program for Opioid Pharmacotherapy Management Committee.

For further information, or to obtain copies of these Guidelines, please contact
Community Pharmacotherapy Program (Next Step)
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On-line training and associated resources can be found at:
https://aodlearning.mhc.wa.gov.au or email CPOPtraining@mhc.wa.gov.au

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ACRONYMS

AE	Adverse Event
BPN	Buprenorphine
CAS	CPOP Advice and Support
CPOP	Community Program for Opioid Pharmacotherapy
CPOP CRC	CPOP Clinical Review Committee
CPP	Community Pharmacotherapy Program
DACAS	Drug and Alcohol Clinical Advisory Service
DDI	Drug-Drug Interaction
HDWA	Western Australian Department of Health (the Department)
MATOD	Medication Assisted Treatment of Opioid Dependence
MPRB	Medicines and Poisons Regulation Branch
NDE	National Data Exchange
OST	Opioid Substitution Treatment
PSA	Pharmaceutical Society of Australia
SASA	Structured Administration and Supply Arrangement
SC	Subcutaneous
SL	Sublingual

Introduction

These revised Western Australian Clinical Guidelines have been adapted with permission from The New South Wales clinical guidelines for the use of long-acting injected depot Buprenorphine (depot BPN)[1], the South Australian brief clinical guidelines[2] and the Queensland Clinical Guidelines 2019[3]

This document contains information that is specific to the Western Australian CPOP and reflects current policy and procedures. The *Western Australian Clinical Policies and Procedures for the Use of Methadone and Buprenorphine in the Treatment of Opioid dependence* (the Manual) outlines the general principles of this and other substitution treatments available in WA. This guideline has been developed to assist decision-making by clinicians and clients in the use of the depot BPN preparations and should be used in conjunction with the full Product Information, Consumer Information materials and demonstration videos provided by each depot BPN manufacturer. These resources are available at https://aodelearning.mhc.wa.gov.au/cpop

It is important to understand that clinical guidelines are intended to guide clinical decision-making and practice and do not address every conceivable situation or exceptional circumstance. These guidelines may be updated with further clinical experience with use of depot in Western Australia and with changes in product information. Where clinical issues are not addressed within these Guidelines, an Addiction Medicine specialist and/or the CPOP CRC should be consulted.

Regulatory requirements

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

Depot BPN is a Schedule 8 drug regulated by the *Medicines and Poisons Act 2014* and the *Medicines and Poisons Regulations 2016*. The *Schedule 8 Medicines Prescribing Code*, a legislative instrument of the Act, governs the prescribing of Schedule 8 medicines and outlines the responsibilities of prescribers and requirements of the Department of Health. It is a legal requirement to adhere to the Code at all times when prescribing.

Under Part 6 of the Medicines and Poisons Regulations 2016 (external site), the Chief Executive Officer of Health (Department of Health) has issued a Structured Administration and Supply Arrangement (SASA) that authorise registered pharmacists to provide depot buprenorphine products. A SASA is a written direction that authorises a health practitioner to administer or supply a medicine to any patient meeting the specified circumstances, and the conditions under which a health practitioner is authorised to administer or supply the medicine.

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[1] Lintzeris N, Dunlop A, Masters D (2019) Clinical guidelines for use of depot Buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence. NSW Ministry of Health, Sydney Australia.

[2] McDonough, M, Holmwood C, Scarborough, J (2020). Interim Brief Clinical guidelines for use of depot Buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence For South Australian Community MATOD prescribers. Drug and Alcohol Services South Australia (DASSA), SA Ministry of Health.

[3] Long-acting injection buprenorphine in the treatment of opioid dependence – Queensland Clinical Guidelines 2019 Published by the State of Queensland (Queensland Health), December 2019.

Prescribers and medical practices

Prescriber approval/accreditation:

In Western Australia, a prescriber of BPN must be appropriately trained to be authorised by the Department of Health CEO to prescribe methadone and buprenorphine for the treatment of opioid dependence.

Medical practitioners prescribing depot BPN must have undertaken approved training with successful completion of a face-to-face or online training and assessment package delivered by the Community Pharmacotherapy Program (CPP). Prescribers are encouraged to contact the Coordinator, Provider Support at CPP on 9219 1896 to discuss current available training options.

Prescribers must also agree to comply with the conditions of the WA Clinical Policies and Procedures for the use of Methadone and Buprenorphine in the Treatment of Opioid Dependence and receive endorsement from the Director of Clinical Services at Next Step.

Pharmacists

Pharmacist accreditation:

All pharmacists dispensing and/or administering depot BPN for treating patients under the Community Program for Opioid Pharmacotherapy (CPOP) must have undertaken additional training provided by the Community Pharmacotherapy Program (CPP). Pharmacists are encouraged to contact the Coordinator, Provider Support at CPP on 9219 1896 to discuss current available training options.

For pharmacists to administer depot buprenorphine on the order of a prescriber it is expected that they are familiar with and understand the requirements of the WA CPOP, that they understand requirements for injection administration by completing an injection/ immunisation course approved by the Department of Health and that they understand the requirements specific to depot buprenorphine treatment and administration by completing the required training provided by CPP.

It is the responsibility of the pharmacist to complete the expected training and product familiarisation to ensure that they are practising within their field of competency.

Pharmacy authorisation:

Pharmacies supplying depot BPN must have received additional written authorisation from the Department prior to ordering from the relevant wholesaler. Pharmacist with Overall Responsibility (PWOR) must have completed the Pharmacist Accreditation and is responsible to ensure that all pharmacists participating in the Program have also completed the Pharmacist Accreditation. Application forms are available on the MPRB website: https://ww2.health.wa.gov.au/Articles/N_R/Opioid-substitution-treatment

Other health professionals

Other health professionals involved in the prescribing, dispensing or administration of depot BPN products must complete additional training modules via the CPP. This includes health practitioners working in hospital inpatient and corrective service environments.

Buvidal® and Sublocade® medications should not be handled by, be accessible to, or be 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.

Access to Depot Buprenorphine

Ordering

Ordering depot BPN is by a pharmacy approved by the Department of Health. Prior to administration by a health professional the depot must be dispensed by the pharmacy or dosing point on the prescription from an authorised CPOP prescriber.

Delivery

Arrangements will be needed to obtain the depot BPN product from an approved pharmacy if pharmacist administration is not available or utilised. The patient or a carer is never to be utilised to deliver the depot to a medical practice for administration.
A fee structure and method of payment by the patient for any cost for the supply of the medication will need to be negotiated with the pharmacy/prescriber and communicated to the patient as part of the treatment plan. Most patients will be charged a service and delivery fee with payment made prior to dosing.
Deliveries of depot BPN must be handed directly to an authorised health professional (pharmacist, medical practitioner or registered nurse) with appropriate recording of date, name and signature of receiver on the delivery receipt.

Original CPOP prescriptions including paper and electronic prescriptions must be provided to the pharmacist or their agent upon delivery to a medical centre where a copy of the prescription has been provided to enable urgent supply. Pharmacists must receive the original prescription from the prescriber where pharmacist administration is utilised.

Pharmacist Administration

Pharmacists who are appropriately endorsed must comply with the conditions of the SASA in order to participate in the administration of prescribed depot buprenorphine and will act within the scope of their practice. Pharmacists may be approached by an authorised CPOP prescriber or by CPP to provide in-pharmacy administration of prescribed depot buprenorphine within an approved pharmacy.

Pharmacists will administer a medicine that has been dispensed in accordance with the WA Medicines and Poisons legislation and the relevant SASA.

The Treatment Plan will reflect the agreement between the prescriber, the pharmacy and the patient prior to pharmacist administration of a depot buprenorphine formulation. This will include documentation of consent by the patient, agreement on record keeping and communication of dosing issues between parties.

Record Keeping

Prescribing

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

- HDWA Authorisation number
- Name of patient, DOB and current address
- Pharmacy supplying/administering the depot formulation and name of the practice for

delivery/administration
- Name of the medication (if Buvidal specify Monthly or Weekly)
- Dose (no date range required)
- Prescriber's name, signature and prescriber number
- injection
- Planned date of administration and interval in which the injections are to be administered
- Number of repeats
  *Where pharmacist administration is agreed, there will be no repeats

Dispensing

The dispensing, delivery, administration and any other movement of depot BPN must be recorded in an approved S8 Register available from the preferred wholesaler (HA14 for medical practices, HA176 for pharmacies). Entries in the register must be completed and countersigned when required by an authorised health professional (pharmacist, medical practitioner or registered nurse). All other record keeping requirements apply in full, including retention of the signed delivery receipt.

All depot BPN scripts must comply with the requirements above.

Regardless of the location, a clinical record (see Appendix 2) must be maintained on the administration to the patient including:

- Date administered
- Drug administered (including brand)
- Dose administered
- Health Professional administering
- Site of administration on the body
- Next appointment date for administration

If the depot BPN is administered by the pharmacist, then advice to the prescriber (Appendix 3) must be provided following each administration.

Along with the usual informed consent process required for medical treatment, the administering health professional 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.

Storage

All depot BPN products, including doses awaiting administration to patients, must be stored in a compliant safe as defined in the Medicines and Poisons Regulations 2016.

In the interests of public safety, stock levels should always be kept to a minimum.

Buvidal® is stable at room temperature (< 25°C) and can be stored for up to 2 years.

Sublocade® injections are required to be refrigerated at 2 – 8°C. Once outside the refrigerator the product may be stored in its original packaging at room temperature, (< 25°C) , for up to 28 days.

Sublocade® can be stored in a compliant drug safe where an approved S8 refrigerator is not available but the revised expiry date must be recorded on delivery from the wholesaler or on the label when supplied from the pharmacy.

The size of the packaging should be considered to ensure that there is capacity to store the medication in a compliant manner. Sublocade injections are considered expired after 28 days out of refrigeration, should not be administered to patients and should be returned to the pharmacy for destruction.

Storage at medical practices and clinics

Buvidal® and Sublocade® dispensed items awaiting administration to patients or return to pharmacy must be stored in a compliant drug safe at the practice when not in immediate use.

Information about safes for medical practices is available on the Department website https://ww2.health.wa.gov.au/Articles/S_T/Storage-of-Schedule-8-medicines and in the Medicines and Poisons Regulations 2016 Section 94-98.

Where there is no compliant safe within the practice or clinic, referral for pharmacist administration may be considered. Alternatively, processes to deliver to the practice and return the product to the pharmacy on the same day if not administered must be in place to be considered for approval.

Storage at pharmacies

Buvidal® SC injections require storage in a compliant drug safe, as defined in the Medicines and Poisons Regulations 2016.

Pharmacists wishing to apply for approval to supply Sublocade® SC injections must apply to the Department for one of the following:

1. Secure refrigerated storage approval:
    a. Evidence of installation of secure refrigerated storage
    b. Application for alternative S8 storage approval from the Department of Health. An application form is available from the Medicines and Poisons Regulation Branch (Email MPRB@health.wa.gov.au to request an application form, or go to https://ww2.health.wa.gov.au/Articles/A_E/Dispensing-OST
    c. Additional security measures (if any) considered to prevent unauthorised access and theft of S8 medicines.

2. Room temperature storage approval:
    a. Evidence that the existing safe within the pharmacy has adequate storage space (noting large pack size of Sublocade® injections).
    b. Copy of standard operating procedure outlining the management of the revised expiry date once cold chain has been broken.
    c. Confirmation that temperature monitoring of the existing compliant safe has determined that temperatures are maintained below 25° C during normal workflows.
    d. Confirmation that stock levels will always be kept to a minimum.

Dispensing and labelling

Prescriptions for depot BPN require a valid CPOP prescription including a WA Department of Health authorisation number.

The HDWA authorisation number must be sighted prior to dispensing /supply of a depot BPN preparation.

All **dispensed** depot BPN formulations must have a dispensing label attached and be labelled in accordance with the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).
In addition to the standard labelling requirements, labels must also include the warning statement:

"WARNING: FOR SUBCUTANEOUS INJECTION ONLY.
Risk of serious harm or death if given by other routes."

Revised (28 day) expiry date of Sublocade® must also be clearly attached to the product at the time the cold chain is broken.

Dispensed products not used due to patient non-attendance or re-scheduling of appointments must NOT be used for anyone other than the named patient and should be returned to the pharmacy.

Pharmacy monthly CPOP reports

Depot BPN formulations must be included in the pharmacy S8 dispensing report to the Department, via the National Data Exchange (NDE). Supplies of depot BPN from agencies not connected to the NDE must be reported to the Department monthly.

Pharmacists are to include details of any dispensed Sublocade and Buvidal injections returned to the pharmacy (not administered to patient) in the CPOP monthly report to the Department.

Destruction and returns

Dispensed items that are not used must be returned to the pharmacy for destruction.

Destruction must be via an approved method and recorded in an approved Drugs of Addiction Register.
Information regarding destruction and disposal of medicines is available on the Department of Health website:

https://ww2.health.wa.gov.au/Articles/A_E/Disposal-of-medicines

Patient authorisation

All patients commencing treatment with depot BPN must be eligible for OST under the current approved WA Policies and Procedures.

Approved prescribers must obtain an individual patient authority from the Department of Health prior to prescribing methadone or BPN to a drug dependent person.

Patient authorisation:

A combination Suboxone/Buvidal or Suboxone/Sublocade HDWA authorisation is issued for a 5 year treatment period. This enables patients to be easily transferred between formulations if needed.

Avoiding Precipitated Withdrawal

When initiating treatment with BPN, it is important to be aware of the partial agonist profile of BPN. Buprenorphine products have caused precipitated withdrawal symptoms in opioid-dependent patients when administered before the agonist effects resulting from recent opioid use or misuse have subsided.

To avoid precipitated withdrawal:

- Short acting opioids -patients should not be acutely intoxicated at the time of depot BPN induction.

- Long acting opioids e.g. methadone – induction is best considered when objective signs and symptoms of mild to moderate withdrawal are evident.

To avoid precipitated withdrawal when patients are inducted to Buvidal *directly* from another opioid:

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

Patients require a minimum of 8mg SL BPN for 7 days prior to induction to Sublocade and should not be directly inducted from other opioids such as heroin and methadone.

Managing Depot Buprenorphine Precautions

Precautions:

- Drug-drug interactions e.g. CYP3A4 Inhibitors and Inducers, Serotonergic Drugs, QTc concerns
- Serotonin syndrome
- Respiratory depression and obstructive sleep apnoea syndrome (OSAS)
- Cardiac arrhythmias
- Severe renal impairment
- Pregnancy and lactation
- Unstable ongoing drug use
- Moderate hepatic impairment e.g. Child Pugh Class B

Contraindications:

Treatment is contraindicated where there exists any acute or chronic condition placing the patient at risk of negative consequences, such as over sedation or overdose, and includes;

- Allergy/sensitivity to Buprenorphine (or depot excipients)
- Decompensated hepatic disease e.g. Child Pugh Class C
- Patients less than 18 years of age (Sublocade)
- Patients less than 16 years of age (Buvidal)
- Severe respiratory insufficiency
- Active Alcohol Use Disorder or delirium tremens

Refer to Product Information document (PI) for more detailed information.

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 thrombo-embolic events, including life threatening pulmonary emboli, if administered intravenously.

***Do not administer intravenously or intramuscularly.**

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 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'. This product is designed to be administered by subcutaneous (SC) 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: 8mg/0.16mL, 16mg/0.32mL, 24mg/0.48mL and 32mg/0.64mL BPN as the active ingredient.
- **Buvidal Monthly** is also available in four dose strengths in prefilled syringes with a 23-gauge needle: 64mg/0.18mL, 96mg/0.27mL, 128mg/0.36mL and 160mg/0.45mL BPN as the active ingredient.

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

- Sublocade® is available in two dose strengths: 100mg/0.5mL and 300mg/1.5mL 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:

- appropriate use of the medicine
- regular clinical reviews and monitoring
- participation in psychosocial interventions
- addressing medical, mental health and social comorbidities.

Clinical tasks include:

- reviewing medication doses and patient satisfaction
- checking for adverse events
- assessment of comorbidities
- establishing therapeutic rapport
- formulation of a recovery plan
- encouraging and facilitating access to psychosocial support.

Treatment with depot BPN potentially challenges the way in which OST services are structured and delivered. The less frequent dosing with depot BPN formulations may require a different approach to structuring clinical reviews, psychosocial interventions and treatment care planning.

Options:

- Consider weekly depot when commencing treatment for the first 2-4 weeks.
- Consider weekly depot for patients requiring more frequent monitoring (e.g. unstable psychiatric and social conditions).
  Monthly formulation – schedule more frequent clinical reviews, e.g. after initiation and during periods of instability.

These issues should be discussed with individual patients when considering the choice of depot versus SL BPN treatment, and when developing treatment plans with patients. It should be emphasised that safe and effective OST is more than the provision of medication, and that regular reviews, treatment planning, and psychosocial interventions are important elements of OST and recovery.

There is minimal research evidence to guide choice between the depot formulations and SL BPN. Individual patient, clinician factors and access should be considered.

It is essential that patients are presented with 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 remove 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 not having to attend 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
- low risk of diversion and non-medical use of the medication, enhancing community safety.

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

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.

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.

Monitoring Treatment

The requirements for clinical monitoring of patients maintained on depot BPN are similar to when oral or SL formulations are used for OST. 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 CPOP Clinical Policies and Procedures for the use of methadone and BPN in the treatment of opioid dependence.

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
- treatment progress against the case formulation and treatment plan.

Urine Drug Screening (UDS)

UDS should be undertaken to corroborate opioid use history and to monitor for other drug use as appropriate.

Dosing recommendation for Buvidal®

Commencing BPN treatment with Buvidal

Direct Induction

Direct induction to Buvidal is most appropriate for patients with previous evidence of BPN use without adverse effect before exposure to long acting depot BPN products.

Patients who have not previously been prescribed BPN would benefit from induction to depot BPN via a brief period on Suboxone and should have at least one or two test doses of SL BPN prior to initiation of Buvidal to ensure tolerance and no adverse effects.

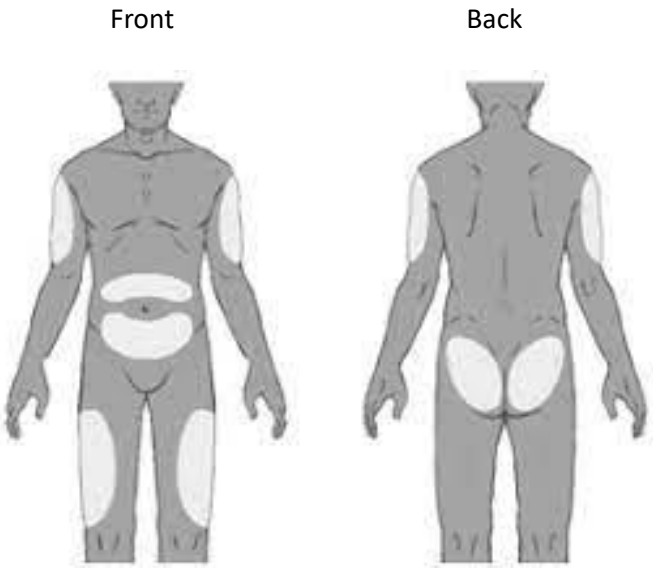
Buvidal may cause withdrawal symptoms in methadone-dependent patients if administered too early.

Consideration should be given to the types of opioid used (that is short or long-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 last use of opioids. The patient should also not display any signs or symptoms of acute opioid intoxication.
- For patients receiving methadone, the dose of the methadone should be reduced to a maximum of 30mg/day before starting treatment with Buvidal Weekly, which should not be administered until at least 24 hours after the patient last received a methadone dose and clear signs and symptoms of withdrawal are present.

A longer period of SL BPN treatment may be required if the patient reports adverse events, drug-drug interactions or is finding it difficult to stabilise on a dose of BPN. For example, following a transfer from methadone (which can take 1-2 weeks to stabilise).

Buvidal injections should be rotated and alternated between sites in the buttock, thigh, abdomen, or upper arm. Injections on the waistline or within 5 cm of the navel should be avoided.



The recommended starting dose is 16mg of Buvidal Weekly, with one or two additional 8mg doses at least 1 day apart, to a target dose of 24mg or 32mg 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 Buvidal Monthly can be started after treatment initiation with Buvidal Weekly, in accordance with the dose conversion in Table 1.

Direct initiation of Buvidal Monthly from heroin or other opioids is not recommended and requires prior stabilisation on sublingual buprenorphine or Buvidal Weekly .

Transferring from SL BPN

Patients stabilised on SL BPN may be transitioned directly to Buvidal Weekly or Buvidal Monthly starting on the day after the last daily SL treatment dose. See Table 1 for conversion recommendations.

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

Daily SL BPN dose	Buvidal Weekly depot dose	Buvidal Monthly depot dose
≤6mg	8mg	No monthly equivalent
8-10mg	16mg	64mg
12-16mg	24mg	96mg
18-32mg	32mg	128mg
		160mg

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

* Where the maximum dose of 160mg Monthly Buvidal is administered and fails to prevent withdrawal effects or cravings, administration can be scheduled 3 weekly, or an alternative treatment option considered (e.g. Sublocade 300mg or SL BPN). It is extremely uncommon that patients will experience subtherapeutic effect when receiving

160mg. Patients may benefit from counselling and psychological support regarding expectations, or additional aetiologies for the reported symptoms should be considered. Additional supplemental doses or further increases in Buvidal Monthly doses to achieve a monthly dose exceeding 160mg is not permitted.

Transferring from methadone

There is limited experience and no documented evidence regarding the transfer of patients from methadone directly to depot BPN products. Patients should be on a methadone dose not greater than 30mg prior to transferring to Buvidal Weekly, which should not be administered until at least 24 hours after the patient last received a methadone dose and clear signs and symptoms of withdrawal are present.

Transferring patients directly from methadone to Buvidal Monthly or Sublocade is not recommended. Longer periods of SL BPN treatment may be required if the patient reports adverse events, drug-drug interactions or if finding it difficult to stabilise on a dose of BPN.

Transferring patients on a higher dose of methadone (>30-40mg) to depot BPN products is considered off-label practice, with no convincing published evidence. Contact CPP or CAS to discuss options.

Flexible dosing schedule

Patients may switch between Buvidal Weekly and Buvidal Monthly if needed in accordance with transition recommendations (see Table 1). Individual dose adjustment may be required.

- Buvidal Weekly doses may be given up to 2 days before or after the weekly time point (days 5-9).
- Buvidal 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.

Maintenance treatment and dose adjustments

Buvidal Weekly

Should be administered according to individual patient's needs as well as clinical judgement and at doses established after switching from sublingual buprenorphine. A maximum of one supplemental Buvidal Weekly 8 mg dose may be administered at an unscheduled visit between the regular weekly doses. The maximum dose per week for patients who are on Buvidal Weekly treatment is 32 mg with an additional 8 mg dose.

Buvidal Monthly

Should be administered according to individual patient's needs as well as clinical judgement and at doses established after switching from other buprenorphine formulations. A maximum of one supplemental Buvidal Weekly 8 mg dose may be administered at an unscheduled visit between the regular monthly doses. The maximum dose per month for patients who are on Buvidal Monthly treatment is 160 mg.

Supplemental or 'top up' BPN doses

Supplemental Buvidal injections may be used if clinically indicated (patient is experiencing opioid withdrawal, cravings or persists with unsanctioned opioid use).

Comprehensive discussion and counselling regarding expected timeframes to reaching steady state may assist patients during the first few months of treatment in continuing with the chosen formulation.

If supplemental Buvidal Weekly doses cannot be administered due to supply or access issues, supplemental doses of SL BPN (up to 8mg daily) may be used until the next depot injection can be organised if a current authorisation remains in place.

Buvidal and pregnancy

There is limited data regarding the effect of use of BPN on human fertility and in pregnant women.
Buvidal is listed with special precautions for use in pregnancy and lactation. Patients should be advised of other options, provided special precautionary information and informed consent obtained before prescribing to women planning pregnancy or who are already pregnant. As with any medication use in pregnancy, use of Buvidal depot BPN could be considered for continued use only if the potential benefit justifies the potential risks to the mother and baby. The CPOP CRC must be consulted if depot BPN continuation is to be considered during pregnancy.

Key points to consider include the following:

- Patients should be involved in decision making regarding their treatment and a **Patient Consent for Depot Buprenorphine Treatment During Pregnancy and Breastfeeding** signed. (see appendix 1)
- BPN should be used during pregnancy only if the potential benefit outweighs the potential risk to the foetus.
- Optimal ante-natal care for pregnant women who are on opioid agonist treatment includes regular liaison between their opioid treatment team and the ante-natal care team.
- A neonatal opioid withdrawal syndrome is considered likely to occur if buprenorphine is continued late in pregnancy as has been reported with the sublingual formulations.
- BPN and its metabolites are excreted in human breast milk and Buvidal should be used with caution during breast-feeding.

Discontinuing Buvidal

Currently, no studies have been performed to examine discontinuation of Buvidal. 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 achieved. Therefore, withdrawal signs and symptoms may be delayed for days to weeks. Withdrawal is likely to emerge within 1 to 4 weeks following regular dosing with the Weekly depot or 4 – 12 weeks following the Monthly depot injection.

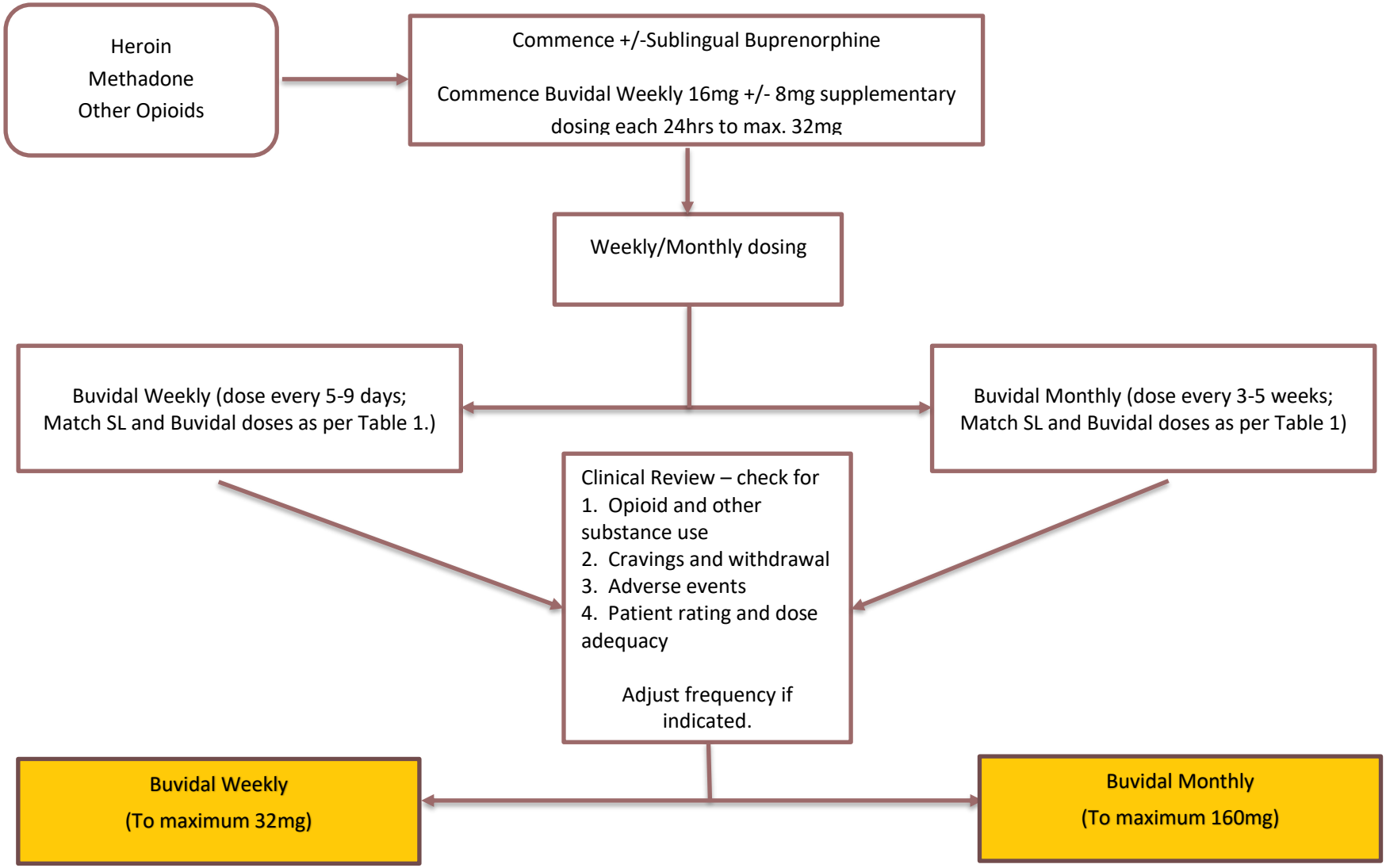
There are multiple dose formulations of Buvidal so a slow reducing titration can be provided by using successively lower dose depot injections. At the end of such a discontinuation procedure, some patients may still require continued buprenorphine weaning with transfer to SL Suboxone or Subutex. Transfer to a SL formulation may require a new HDWA authorisation. Discontinuation of treatment may result in a withdrawal syndrome that may be delayed in onset.

It is good practice to document why a patient (or prescriber) has decided to discontinue treatment and to always provide relapse prevention education together with follow up support and access to Naloxone (e.g. Nyxoid nasal spray or Prenoxad Solution for Injection).

Transferring from Buvidal to SL BPN

Initiate SL BPN dosing at the time of the next scheduled injection (e.g. 5-9 days after Buvidal Weekly, or 3-5 weeks after last Buvidal Monthly injections). Dose conversion tables should be used to guide the initial SL BPN dose, with frequent clinical reviews and titration of the SL dose over subsequent days.

Figure 1: Overview dosing with Buvidal

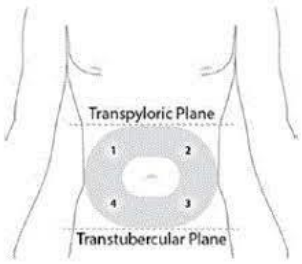


Dosing recommendations with Sublocade®

Commencing Sublocade treatment

Sublocade treatment requires preceding treatment with ≥8mg daily BPN for at least 7 days. Sublocade is generally **not recommended for patients on daily SL BPN doses <8mg**.

Sublocade injections are to be given on the abdomen between the transpyloric and transtubercular planes with adequate subcutaneous tissue that is free of skin conditions (e.g. nodules, lesions, excessive pigment). Ideally the patient should be in the supine position.



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 with a 300mg dose each month for the first 2 months, providing '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 relating to high BPN plasma levels (e.g. severe hepatic disease, DDIs). Induction at lower doses is considered "off-label" and the CPOP CRC should be consulted for support.

Following the initial two monthly Sublocade 300mg doses, for most patients 100mg Sublocade maintenance doses every 4 weeks thereafter will be adequate for maintaining plasma levels at steady state equilibrium.

300mg monthly doses may be considered thereafter for those patients who had previously stabilised on high dose SL BPN (e.g. 24mg daily) or who continue to experience cravings, withdrawal or unsanctioned opioid use during the first 2-month period of Sublocade dosing. This dosing regimen may also be considered for patients who continue to experience cravings, withdrawal or unsanctioned opioid use whilst receiving maintenance 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 via SL BPN pathway may be required if more than eight weeks has elapsed between Sublocade doses. Prescribers can contact CPP or CAS for advice.

Discontinuing Sublocade

Where a patient's treatment plan includes pharmacist administration of depot buprenorphine, the prescriber should inform the pharmacist as soon as practicable when treatment is to be discontinued. If Sublocade is discontinued, its modified-release characteristics should be considered, and the patient should be monitored for several months for signs and symptoms of withdrawal or BPN effects and treated appropriately. Importantly, the half-life of Sublocade is approximately twice the half-life of Buvidal and therefore peak withdrawal features may emerge 8-24 weeks after the last dose is administered. After steady-state has been achieved (4-6 months) patients discontinuing Sublocade may have detectable plasma levels of BPN for 12 months or longer.

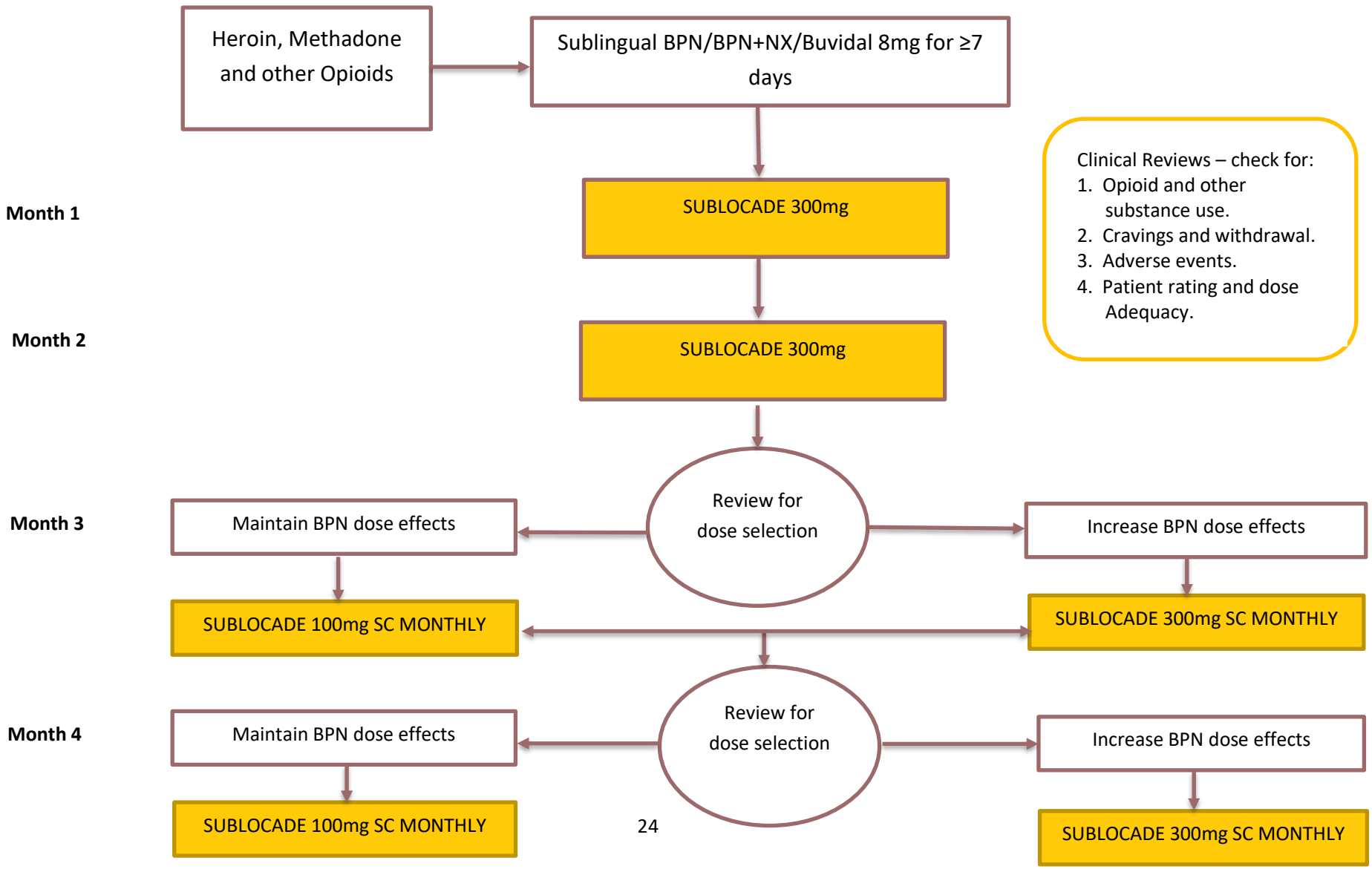
Transfer to SL preparations might need to be considered. If transfer to a sublingual formulation is considered necessary, the conditions of the current authorisation should be reviewed, and a new application submitted if required. Discontinuation of treatment may result in a withdrawal syndrome that may be delayed in onset.

It is good practice to document why a patient (or prescriber) has decided to discontinue treatment and to always provide relapse prevention education and follow up together with access to Naloxone (e.g. Nyxoid nasal spray or Prenoxad Solution for Injection).

Transferring from Sublocade to SL BPN

Recommended practice is to initiate SL BPN with low doses at approximately the time of the next scheduled depot BPN injection – usually commencing with 8mg SL BPN four weeks after the last Sublocade® dose, and to titrate the dose upwards over subsequent days or weeks according to clinical need as the depot BPN concentrations gradually subside, aiming to achieve the expected SL dose based on clinical assessment and patient report. Frequent clinical reviews are recommended. CPP or CAS can be contacted for advice.

Figure 2: **Overview dosing with Sublocade**



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, pregnancy and lactation, cardiac arrhythmias, and respiratory depression (see Product Information for details).

Adverse events (AEs).

Depot products can be associated with local injection site adverse reactions – redness, pain, tenderness and swelling in 5-10% of 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 are as per SL BPN (e.g. nausea, headache, constipation).

*Please note that all suspected adverse events relating to the Buvidal formulations should also be reported to safety@camurus.com

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 there are concerns, stabilise on SL BPN and monitor DDI before transferring to depot BPN products.

Transfer to methadone

Since there are no published studies and little clinical experience, patients seeking to transfer from depot BPN to methadone should transition via SL BPN, commencing at the time the next scheduled depot dose is due. **Once stabilised on a dose of SL BPN for at least 2 weeks (for Buvidal Weekly) and 4 weeks (for Buvidal Monthly or Sublocade), transition to methadone can occur.**

Methadone initiation should be at low doses (20-25mg) daily with regular review and careful titration of doses. Patients should be observed for sedation since residual BPN from depot BPN doses may be present for between 2 and 6 months after long-term treatment.

Transferring between depot products

Currently there are no studies to provide evidence about transferring between BPN products. There are very limited anecdotal reports of transfer between BPN products and while 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 transfer until the withdrawal process can be reasonably established following which induction to the other depot BPN could commence. In some circumstances the new depot BPN injection may not be available at a time when withdrawal has commenced, in which case

the patient may also be temporarily provided SL BPN to manage withdrawal until the new depot BPN can be initiated.

However, there may be situations where transfer between the products may be clinically preferable to transferring back to SL BPN formulations. This may include suboptimal clinical effect on the maximum dose, supply issues, or lack of availability of the current treatment formulation. Where transfer is required, the following is recommended.

Transfer from Buvidal to Sublocade

Patients receiving Buvidal Weekly or Buvidal Monthly should be transferred to 100mg Sublocade doses in most cases since the patient should already have adequate plasma levels. However, where patients receiving the maximum dose of Buvidal Weekly or Buvidal Monthly experience suboptimal effect with significant cravings or withdrawal symptoms, they should be transferred to a 300mg Sublocade dose.

Transfer from Sublocade to Buvidal

Patients stable on Sublocade 300mg monthly doses for greater than two months should transfer to the maximum dose of Buvidal Weekly (32mg) or Buvidal Monthly (128mg). Patients may experience a decrease in plasma BPN levels and develop opioid withdrawal and/or cravings following transfer to Buvidal, although given the long half-life of Sublocade this is unlikely to occur. Patients experiencing withdrawal and/or cravings following transfer to Buvidal 128mg can be considered for an increase in dose to the maximum of 160mg monthly with the addition of a single 32mg weekly dose within the treatment period. Patients receiving Sublocade 100mg monthly doses, or who have only received one or two Sublocade 300mg injections for initiation, should not experience a significant decrease in plasma BPN levels when transferring to Buvidal Weekly or Buvidal Monthly. Commencing Buvidal Weekly 24 mg or Buvidal Monthly 96 mg and titrating doses up or down as clinically indicated thereafter will assist a problem-free transfer.

In some circumstances the new depot BPN injection may not be available at a time when withdrawal has commenced, in which case the patient may also be temporarily provided SL BPN to manage withdrawal until the new depot BPN can be initiated. CPP should be contacted for assistance in these circumstances as a new HDWA authorisation for SL formulation may be required.

Pregnancy and breastfeeding

The Product Information for use of Buvidal Weekly, Buvidal Monthly and Sublocade in pregnancy and lactation recommends cautionary use.

While 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 or transferred to a depot formulation if the potential benefit justifies the potential risks to the mother and baby. A continuation/transfer to depot buprenorphine consent form is required and is available

for use with these Guidelines and from CPP. The signed consent form should then be forwarded to the CPOP CRC along with any supporting information for their consideration and endorsement.

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, intradermally, intravenously or intraarterially.* For this reason, depot formulations must be administered by a suitably qualified health care professional and must never be dispensed or supplied directly to the patient or a carer.

Pain Management

- Prescribers are advised to contact CPP/CAS where there is an intention to prescribe opioids for a patient who is also receiving depot BPN treatment or other OST.
- Prescribers should consider seeking pain specialist advice prior to prescribing opioids for patients receiving OST.
- Any prescribing of S8 medications will require the involvement of the CPOP CRC and authorisation from the DoH.

Acute pain management

Patients receiving OST often require acute pain management which can be complicated by buprenorphine treatment. It is important that patients have access to effective pain management. BPN has high mu receptor affinity and reduces the effects of most full opioid agonists such as morphine or oxycodone. NSAIDs or paracetamol and physical therapies may be considered for use with mild acute pain conditions, however BPN can complicate routine opioid analgesia in the management of severe acute pain (e.g. in acute/emergency situations such as trauma, renal stones). In such circumstances, the National Guidelines for Medication-Assisted Treatment of Opioid Dependence (2) recommend the following approaches:

(a) Use of higher doses of traditional opioids such as morphine (with careful titration of effects)

(b) Use of mu opioid reception super agonists such as fentanyl, that themselves have similar or higher mu intrinsic activity than BPN
(c) Use of parenteral BPN (e.g. Temgesic®) for breakthrough pain; and/or
(d) Non-opioid analgesic approaches such as ketamine infusions or regional analgesia.

Similar approaches can be used for patients with depot BPN treatment to achieve analgesia in acute/emergency situations. It is not possible to cease BPN in clients treated with depot BPN formulations. When a patient on depot BPN presents to a general practitioner with severe acute pain, they may need to be referred to an emergency department or the GP can consult with an Addiction Medical Specialist. Persistent pain should be managed with an emphasis on psychosocial and non-opioid pharmacological approaches. Non-pharmacological strategies can include patient education about healthy lifestyle modifications including a daily routine of structured activities incorporating sleep, nutrition, adequate exercise, social interaction and rest. Patient education regarding the links between tobacco and pain may be indicated with discussion about quitting. Non-opioid pharmacological options might include simple analgesia like paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and/or adjuvant medications, such as anticonvulsants and antidepressants. Benzodiazepines can exacerbate pain in the longer term and should only be considered for extremely short episodic use.

Chronic pain management

It is estimated that between 30 to 60% of patient on OST experience chronic pain which is often masked by the high doses of methadone or BPN used to treat opioid dependence. Whilst current evidence does not identify the most effective strategies for treating chronic pain in clients in methadone or BPN treatment, general principles of chronic pain management should be followed. This includes education and engagement in the treatment process, appropriate use of opioid and non-opioid medications (e.g. antidepressants, NSAIDs, paracetamol, gabapentinoids), physical (e.g. exercise, physiotherapy) and psychosocial (e.g. Cognitive Behavioural Therapy) interventions. BPN itself is a powerful opioid analgesic, and extended release BPN formulations (e.g. 7-day topical patches) have historically been incorporated into treatment plans for clients with concurrent chronic pain. It is expected that depot BPN formulations will also be effective as part of the treatment plan in managing comorbid chronic pain in dependent opioid users, however this should not be used in conjunction with other opioid analgesics (e.g. morphine, fentanyl, codeine) in chronic pain management, given its 'blockade' effect.

The use of depot BPN products in certain patient populations and treatment settings (correctional facilities, hospitals, residential rehabilitation), and in the management of clinical scenarios (acute and chronic pain management, overdose, intoxicated presentations) is described in the *Clinical guidelines for use of depot Buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence (2019).* Centre for Alcohol and Other Drugs. NSW.

CPP should be contacted for advice and assistance when patients receiving depot buprenorphine require treatment support within hospitals, residential rehabilitation facilities and other accommodations/locations which are not generally part of the Program and requiring special consideration.

Table 2. Overview of Buprenorphine products available for treatment of opioid dependence in Australia.

	SL Suboxone® and Subutex®	Buvidal® Weekly and Monthly	Sublocade®
Formulations	Suboxone contains Buprenorphine (BPN) and naloxone in 4:1 ratio 2/0.5mg and 8/2mg sublingual film Subutex contains Buprenorphine in 0.4mg, 2mg and 8mg sublingual tablets	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 Buvidal Weekly: 8mg/0.16mL, 16mg/0.32mL, 24mg/0.48mL; 32mg/0.64mL Buvidal Monthly: 64mg/0.18mL, 96mg/0.27mL; 128mg/0.36 mL; 160mg/0.45mL	Sublocade contains BPN in the ATRIGEL® Delivery System SC injections in prefilled syringes with 19-gauge needle administered into the abdomen Monthly doses: 100mg/0.5mL or 300mg/1.5mL
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 28 days before use. Remove from cold storage for at least 15 minutes prior to SC injection.
Clinical pharmacology	Bioavailability 10-30% Onset effects within 1 hour, with peak effects 2-4 hours after dose Duration effects usually last for 24 hours but is dose dependent and can vary from 8 to 72 hours	Bioavailability = 100% Time to peak plasma level (Tmax) • Buvidal Weekly = 24hrs • Buvidal Monthly = 6-10hrs Half life • Buvidal Weekly = 3-5 days • Buvidal Monthly = 19-25 days. Steady-state equilibrium reached by 4th dose	Bioavailability = 100% Time to peak plasma levels (Tmax) = 24hrs Half-life = 43 to 60 days Steady-state equilibrium reached by 2nd (300/100mg) to 6th dose (300/300mg)
Frequency of dosing	Daily, two or three day doses. Take-aways and unsupervised dosing available for patients considered low risk	Buvidal Weekly dose can be administered every 7±2 days (5-9 day schedule) Buvidal Monthly dose can be administered every 4±1 week (3-5 week schedule)	Sublocade dose administered every 4 weeks (26-42 day schedule)

Key Drug – Drug Interactions (DDIs)	Systemic BPN DDIs include: – Opioid agonists: can reduce effects of other opioids (blockade); BPN may precipitate withdrawal on induction – Sedatives (e.g. benzodiazepines, alcohol, TCAs, antipsychotics, gabapentinoids): sedation, respiratory depression, overdose Several 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 cardia arrhythmias). 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.		
Recommended dosing regimen	SL Suboxone® and Subutex®	Buvidal® Weekly and Monthly	Sublocade®
Commencing Rx	**From heroin, morphine:** Commence 4-8mg, with possible addition of further 4mg if needed (maximum 12mg) Day 1 when patient is in early / mild opioid withdrawal (COWS score 5-12, usually >8-12hrs after last dose or use). Titrate upwards on daily basis as required. **From methadone:** Initiate BPN when patient in moderately severe withdrawal (e.g. COWS score ≥13) e.g. 1-2 days after last methadone dose) Day 1: initial dose of 2mg, followed by an additional dose of 4 - 6mg after 1-2 hrs, if there is no precipitated withdrawal with the initial dose. The suggested target dose for Day1 is 8-16mg with dose supervision and frequent monitoring.	**From heroin, morphine:** Direct initiation of Buvidal from short acting opioids should not be undertaken when there are signs or symptoms of acute opioid intoxication. Starting dose of Buvidal Weekly is 16mg with 1 or 2 additional 8mg doses at least one day apart to max. dose of 24mg or 32mg during the first treatment week. Recommended dose for week 2 is the total dose administered during week 1. Buvidal Monthly can be commenced after patients have stabilised on Buvidal Weekly. **From SL BPN:** Buvidal dose should be determined according to patient's SL BPN dose (see Table 1). Transition to Buvidal Weekly after the patients last SL BPN dose. Titrate subsequent doses after clinical review.	Initiate transfer to Sublocade after BPN treatment (minimum dose 8mg for 7 days), **Recommended induction:** *Months 1 and 2*: 300mg monthly injections *Month 3 onwards*: 100mg monthly doses (if patient 'stable' on initial 2 x 300mg doses) or 300mg monthly doses if requiring additional BPN effects (e.g. cravings, withdrawal, continued opioid use). Patients may be initiated with 100mg Sublocade (after at least 7 days BPN treatment) doses if safety concerns (e.g. severe hepatic disease). DDI concerns: e.g. overdose risk from polysubstance use There is no published safety data for initiating Sublocade in patients on low dose SL BPN (<8mg) and referral to CPOP

	Day 2 onwards: titrate BPN dose daily as required.	Note increasing effects during first few doses (accumulation to steady state after about 4 doses). **From methadone:** Reduce methadone to maximum of 30mg daily. Commence Buvidal Weekly not less than 24hrs after last dose and when clear signs of mild/moderate withdrawal are present.	CRC for advice and support is required. Buvidal should be preferred for such patients.
Maintenance phase	– Adjust dose to achieve treatment goals (reduced use of other opioids, reduced withdrawal and cravings; blockade effects). – Range 2 – 24mg daily (or 32mg 2nd or 3rd 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 to 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.	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.
Key adverse events	Systemic BPN adverse events	Systemic BPN adverse events Local injection site: – Redness, pain, tenderness, swelling in approximately 5-10% patients. – Usually mild and transient and resolves spontaneously	

Appendix 1

Western Australian Community Program for Opioid Pharmacotherapy (CPOP)

Patient Consent for Depot Buprenorphine Treatment During Pregnancy and Breastfeeding

I, (Name)_____DOB_____

am currently authorised to receive _____ for the management of opioid dependence and wish to transfer to/continue treatment with depot buprenorphine during my pregnancy/period of breastfeeding rather than a sublingual buprenorphine preparation.

The risks and benefits of depot buprenorphine during pregnancy or when breastfeeding have been explained to me by my prescribing doctor.

In making this decision, I understand that:

- the safety of depot buprenorphine during pregnancy or breastfeeding remains uncertain at this stage
- pregnancy appears under "special precautions" when considered for use of depot Sublocade® or depot Buvidal® in Australia by the Therapeutic Goods Administration
- the decision to continue with depot buprenorphine is based on an assessment that the risks of transferring to sublingual treatment outweigh the potential benefits
- I will need to attend regularly (and as directed) for antenatal care at _____Hospital
- I will need to attend regular appointments with my treatment team/prescribing doctor
- I give permission for my prescribing doctor to be notified of my outcome Yes ☐ No ☐
- I have been provided with written information about depot buprenorphine and my questions have been answered.

This treatment plan will be considered for endorsement by the CPOP Clinical Review Committee.

Patient's Signature:_____ Date:____/____/____

Prescriber's Name: _____
(BLOCK LETTERS)

Prescriber's Signature:_____ Date:____/____/____

CPOPCRC review date_____ Supported ☐

Chair _____ Not Supported ☐

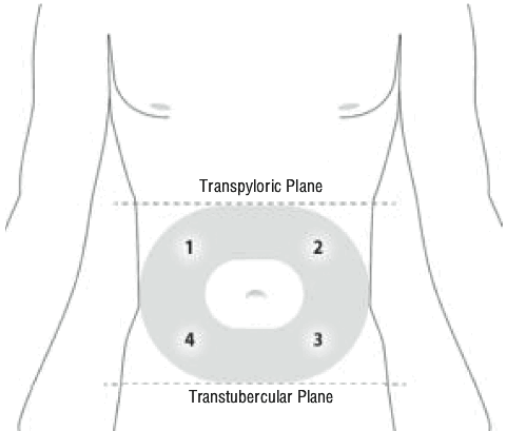
Appendix 2

Western Australian Community Program for Opioid Pharmacotherapy (CPOP)

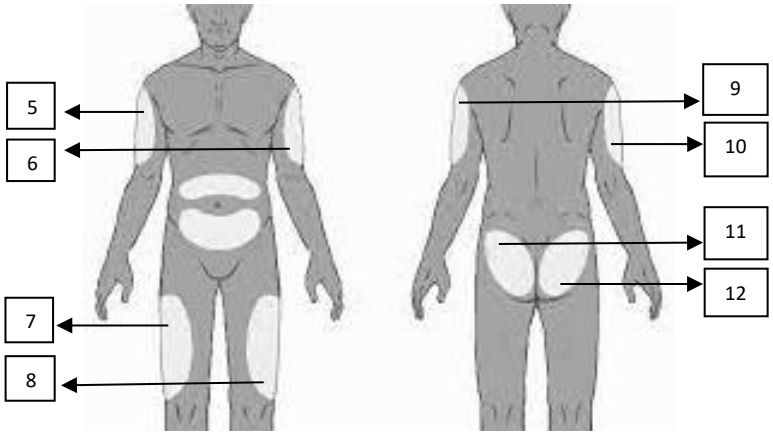
DEPOT BUPRENORPHINE ADMINISTRATION RECORD FOR PHARMACISTS **PHARMACY** _____	**Client Name:** **DOB:** **Prescriber:**

Date	**Formulation and dose administered**			**Injection site (1 to 12)** ***sites should be rotated**	**Depot**		**Administered by**		**Client sign**	**Next review appt scheduled**	**Notes**
	Buvidal		**Sublocade**		**Batch No.**	**Expiry date**	**Name**	**Sign**			
	Weekly	**Monthly**									

Appendix 3



Sublocade injection sites



Buvidal injection sites

Consent for Pharmacist Administration of prescribed Depot Buprenorphine

I (Name) _____consent to pharmacist administration of depot buprenorphine as prescribed by my prescriber. I understand that the pharmacist providing this treatment has undertaken the required training and is approved within the CPOP program to provide this service to patients under the direction of my prescriber.

I have signed a consent to receive opioid substitution treatment within the CPOP and my prescriber has explained the treatments available to me.

I understand that my prescriber is responsible for reviewing my treatment plan and progress, which should occur within the week preceding my dose administration whilst receiving depot buprenorphine. The pharmacist may choose to refer me back to the prescriber for further review prior to administering my dose should there be any concerns regarding my presentation, timing, or the treatment to be administered.
I understand that it is my responsibility to ensure that I schedule an appointment with my prescriber one week before my next dose becomes due.

Patient signature _____ Date_____ Pharmacist signature _____Date_____

Appendix 3

Western Australian Community Program for Opioid Pharmacotherapy (CPOP)

Depot Buprenorphine Administration - Advice to Prescriber

Pharmacy _____ Date_____ Doctor _____

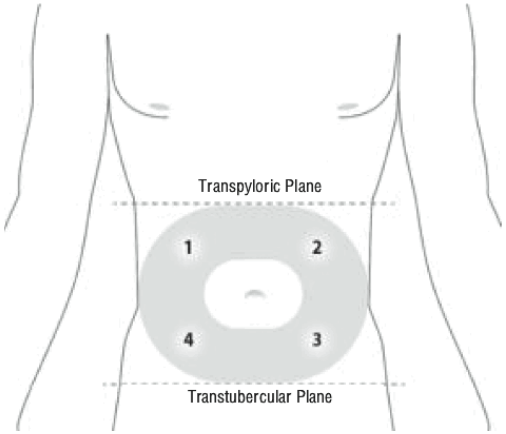
Patient _____ (DOB) _____ Formulation (tick) ☐ Buvidal ☐ Sublocade HDWA _____

Date	1. Admin 2. Refused 3. Missed	Dose	Weekly or monthly	Injection Site (e.g.1,2,3)	Next Pharmacist Appointment	Comment (e.g. site pain, withdrawal, intoxication, concerns)	Pharmacist Signature

Appendix 3

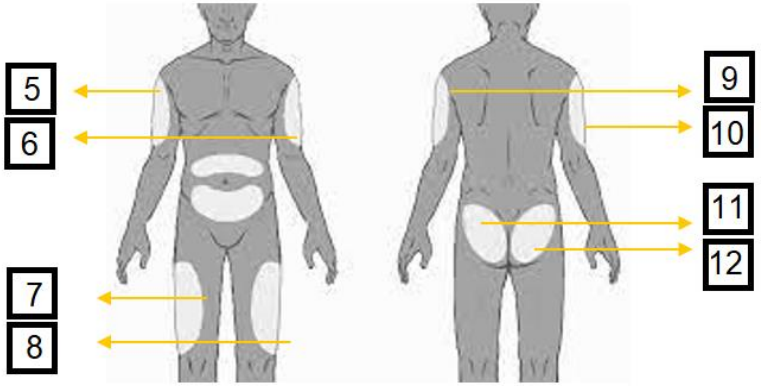
Sublocade injection sites

Front



Buvidal injection sites

Front Back



Getting support & more information

Community Pharmacotherapy Program (CPP) Tel: 9219 1913

The following numbers are for health professionals only and should not be given to patients.

- CPOP Advice and Support (CAS) Tel: 9442 5042
- Drug and Alcohol Clinical Advisory Service (DACAS) Tel: 6553 0520
- Medicines and Poisons Regulation Branch (MPRB)
  1) Tel: 9222 6883 (main) or
  2) Tel: 9222 6812 (CPOP specific)

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

Clinical guidelines

- Western Australia. Community Program for Opioid Pharmacotherapy (CPOP). Clinical Policies and Procedures for the use of Methadone and Buprenorphine in the Treatment of Opioid Dependence
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