Interim Clinical Guidance:

Outpatient Transfer from Methadone to Buprenorphine Using the Micro-dosing or Bridging Methods

Introduction

Clients on the NSW Opioid Treatment Program (OTP) may be transferred from methadone to buprenorphine. There are three ways for accredited health professionals to enable this transfer:

- **Direct transfer** - standard approach for transfer from methadone to buprenorphine endorsed in current *NSW Clinical Guidelines – Treatment of Opioid Dependence* (page 26). Clients transferring from methadone doses ≤30mg can transfer directly to Buvidal® without micro-dosing or bridging medication.
- **Micro-dosing** (a modified 'Bernese' method) – may be considered for clients on higher doses of methadone (>40mg). Seek specialist advice if considering transfers for clients on methadone doses higher than 150mg.
- **Bridging** with a short-acting opioid – may be considered for clients on higher doses of methadone (>40mg). Seek specialist advice if considering transfers for clients on methadone doses higher than 150mg.

When using the direct transfer method, prescribers should refer to the *NSW Clinical Guidelines – Treatment of Opioid Dependence*.

The evidence base for micro-dosing and bridging methods is still developing. Use of opioid agonist treatment (OAT) medications in this context is considered 'off-label' and must be undertaken:

- in accordance with local clinical governance procedures
- in accordance with legislation, policies or procedures that govern off-label prescribing.

Prescribers are expected to use their professional judgement to determine the most clinically appropriate transfer method on a case-by-case basis. As the evidence continues to develop, this document will be updated in line with updates to clinical evidence and practice. Please refer to Appendix 1 for the version history of this document.

Note to readers: This document is based on the prescribing procedures developed by the Alcohol and Drug Service St Vincent's Health Network Sydney and Drug and Alcohol Services, South-Eastern Sydney Local Health District.

Purpose of this document:

To provide general guidance to prescribers intending to transfer clients from higher doses of methadone (>40mg) to buprenorphine use the micro-dosing or bridging methods on an outpatient basis. Services should design their local procedures in line with this guidance.

Relevant setting:

Outpatient

Definitions:

Table 1:

Clinical Opioid Withdrawal Scale (COWS)	An eleven-item, validated measure of the severity of a client's opioid withdrawal symptoms.
Opioid Agonist Therapy (OAT)	Long-term treatment with opioid medication (usually methadone or buprenorphine) as part of the treatment of opioid use disorder.
Short Opiate Withdrawal Scale (SOWS)	A 10-item self-report scale that provides a reliable and valid means of measuring the signs and symptoms of withdrawal among clients with opioid dependence.
Withdrawal Management	The management of withdrawal from a substance in a person who is dependent on that substance. Previously known as 'detox' or 'detoxification'.
Withdrawal Syndrome	A specific group of signs and symptoms that occur when a person who has developed tolerance to a particular drug (after regular use at high doses) stops or reduces use of the drug.

Planning:

The clinical situations in which clients are considered for methadone to buprenorphine transfer may vary significantly. For example, some stable clients will present electively requesting transfer. Other clients may have clinical features (for example, long QT interval demonstrated on ECG while on methadone) which make a more urgent inpatient transfer necessary.

Wherever possible, methadone to buprenorphine transfers should be planned well ahead of time, and when other matters (physical, psychological and social) are relatively stable, to improve the likelihood of success and decrease the likelihood of adverse outcomes.

Clinicians should inform clients about buprenorphine opioid agonist treatment, how the medication (duration of action, common effects and side effects) and treatment requirements (e.g. frequency of attendance for dosing, costs) differ to methadone. Clinicians should inform clients of the different methods for transfer from methadone to buprenorphine, the risks involved (see below) and what will happen if the transfer or stabilisation is unsuccessful. The involvement of peer workers may be of benefit to assist in this process.

Clinical risk regarding transfer processes:

Transfer from methadone to buprenorphine may be associated with complications including:

- precipitating withdrawal on initiating buprenorphine
- destabilisation of the client during transfer (including opioid or other substance use, or their medical, psychiatric or social condition)
- side effects from buprenorphine
- inability to transfer and stabilise on buprenorphine.

The risk of precipitating withdrawal is greater when transferring from long-acting opioids such as methadone. Further information on principles of safe transfer from methadone to buprenorphine are set out in the *NSW Clinical Guidelines – Treatment of Opioid Dependence*.

Assessment:

Unless otherwise known, the following information should be collected as part of an initial assessment.

- Methadone dose, dosing point, and prescriber
- Reason for requesting transfer from methadone to buprenorphine
- Past history of attempted transfers and outcome
- Past physical and psychiatric medical history
- Current medications and allergies
- Any concurrent substance use:
  - Substances being used
  - Quantity, frequency and duration of use
  - Route of administration
  - Previous withdrawal experiences, including a predicted severity of withdrawal based on recent patterns of use and past withdrawal experiences

Authority to prescribe and supply OAT:

The *Poisons and Therapeutic Goods Act 1966* (NSW) prohibits the prescribing and supply of a drug of addiction (Schedule 8 medicine) to a drug dependent person. However, a medical practitioner or nurse practitioner may apply to be authorised to prescribe or supply a drug of addiction to a drug dependent person for the purpose of opioid dependence treatment under the OTP. This authority is issued by the Pharmaceutical Regulatory Unit of the NSW Ministry of Health.

New application forms related to the management of patients under the NSW OTP may be found on the NSW Health website. These forms have been reviewed and updated to streamline the application process, improve the health practitioner experience and to align with the online process for applying for authorities which will be available to health practitioners later this year. Additionally, these forms support new treatment and transfer protocols including micro-dosing and bridging transfers and other OAT.

The new application forms replace the old OTP application forms that were on the NSW Health website and in the OTP Clinical Guidelines.

Please note that there are declarations at the beginning (except for the exit form) and end of the forms. Applicants must ensure they complete and submit both declarations.

Interim Micro-dosing Guidance

Micro-dosing involves a client continuing to take methadone while commencing small doses of sublingual buprenorphine. Buprenorphine is up titrated while methadone is down titrated over approximately one week.

Client identification and risk assessment for micro-dosing

- Most clients looking to electively transfer from methadone to buprenorphine are suitable to transfer via micro-dosing in an outpatient setting. Inpatient transfers should be undertaken in the following circumstances:
    - Doses >150mg – at this time there are no reported cases of ambulatory micro-dose transfers from methadone to buprenorphine at doses >150mg.
    - Cirrhosis – due to the potentially altered pharmacokinetics of methadone and buprenorphine metabolism for people with cirrhosis, inpatient transfer is recommended.
    - Inconsistent dosing/lifestyle pattern – micro-dosing requires either daily attendance for transfer, or unsupervised management of a variable buprenorphine regimen. For those who miss regular doses or would not be suitable for unsupervised dosing, this may not be a suitable option.
- Occasionally clients will be referred for transfer due to medical reasons (e.g. long QT syndrome, drug-drug interaction).
- Unsupervised dosing can be trialled for clients who have been assessed as able to manage the daily changes in buprenorphine dosing, but this will require careful planning, scripting and discussion with pharmacy to simplify dosing as much as possible. The following criteria should be considered on a case-by-case basis:
    - Already prescribed unsupervised methadone dosing
    - No concomitant unsanctioned substance use
    - Stable accommodation.

Micro-dosing method to transfer a client from methadone to sublingual buprenorphine

- Apply for authority using Application for Authority to Prescribe or Supply Methadone, Buprenorphine, or other Opioid Agonist Therapy (OAT) Treatment under the NSW Opioid Treatment Program (OTP). Ensure Section D *Drug and Dose Information* and Section E *Other Treatment & Transfer Protocols* are completed.
- Once approved, the authority will be granted for buprenorphine on an ongoing basis. Additionally, it grants the applicant authority to prescribe methadone for a specified time allowing for transfer treatment to occur. If they held the methadone authority for the patient prior to the transfer, the applicant is not required to submit an exit form for methadone.
- Administer COWS and SOWS each day; SOWS is based on symptoms reported in the previous 24 hours.

Table 2:

Day	Methadone dose	Buprenorphine dose	Throughout
0	X mg	0 mg	COWS Symptomatic relief* Support + encouragement
1	X mg	0.2 mg BD or 0.4 mg mane	
2	X mg	0.4 mg BD	
3	X mg	2 mg	
4	X mg	4 mg	
5	X mg	8 mg	
6	½X mg	16 mg	
7	¼X mg	16-32 mg Clients may commence depot buprenorphine weekly at this point (optional). See *Brief Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence*	

X = client's current methadone dose

*For example:

- Clonidine 50mcg up to QID PRN - clients should take while seated, and avoid if dizzy/light-headed
- Ondansetron 8mg up to BD PRN

Management of missed doses

Table 3:

	Recommended action
One day of missed methadone and buprenorphine	Recommence regimen at the most recent dosing schedule
Two-three days of missed methadone and buprenorphine	Complete COWS • If >24 – initiate onto buprenorphine • If <24 – recommence regimen at the most recent dosing schedule
Four - five days of missed methadone and buprenorphine	Complete COWS • If >13 – initiate onto buprenorphine • If <13 – commence procedure at day 6
More than 5 days of missed methadone and buprenorphine	Initiate onto buprenorphine
Note: Regardless of the number of days missed, prescribers are to discuss with clients their medication preference as they may prefer to return to methadone rather than continue with buprenorphine.	

Interim Bridging Guidance

This procedure involves stopping methadone and allowing several days of 'wash out' before commencing buprenorphine. A short acting opioid (e.g. oxycodone) is administered in the intervening period from last methadone dose to first buprenorphine dose to prevent the onset of severe withdrawal on stopping methadone.

Client identification and risk assessment for bridging using oxycodone

As the bridging method involves providing some unsupervised doses of a drug of dependence (oxycodone) to a drug dependent person, it is important to consider the suitability of the client to complete the transfer in an outpatient setting. Part of that assessment involves a detailed risk assessment around concomitant substance use, physical and mental health comorbidities, and social situation.

The criteria to be used to identify suitable clients are:

- Methadone doses 40-150mg daily. Clients transferring from high methadone doses (80-150mg) may benefit from an inpatient admission to undertake the transfer, as they are at greater risk of precipitated withdrawal, and often have more physical and mental health comorbidities that can complicate management.
- Methadone dose >150mg daily, should attempt to reduce their dose to 150mg. If this is not possible, then seek specialist advice and consider inpatient admission to undertake the transfer.
- Has previously been prescribed buprenorphine without severe adverse events.
- No history of allergy or anaphylaxis to buprenorphine or any other component of Buvidal®.
- Risk assessment (particularly important for assessing suitability for outpatient transfer setting)
    - Minimal unsanctioned opioid use (<1 day per week)
    - No illicit intravenous use of pharmaceutical opioids in the last month
    - No excessive use of other sedating substances: alcohol (excessive use defined as >4 standard drinks per day more than once a week), benzodiazepines (excessive use defined as >10mg diazepam equivalent daily)
    - Stable social situation: not at risk of coercion, no domestic violence, not experiencing homelessness, consider childcare arrangements if applicable.

Bridging method using oxycodone to transfer a client to Buvidal® (a form of Long-Acting Depot Buprenorphine)[1]

Oral oxycodone can be used as a 'bridge' between last methadone dose and initiation of Buvidal® to alleviate opioid withdrawal symptoms which are likely to follow cessation of methadone. The rationale for using oxycodone (rather than morphine) is:

[1] Advice in this document is directed at Buvidal® transfers specifically, as undertaking this process with Sublocade® is not advised. For information on transferring from Buvidal® to Sublocade®, see p 32 in the *Clinical guidelines for use of depot buprenorphine (Buvidal® and Sublocade®) in the treatment of opioid dependence*.

- Modified release oxycodone (OxyContin®) is a tamper-resistant product (very difficult to inject), making it safer to supply as take-home medication
- any additional heroin use can be differentiated from oxycodone use in urine drug screens.

A conversion rate of oxycodone to methadone of 3-4:1 should be used, supplied in two divided doses per day (BD) using the Modified Release OxyContin® formulation. On the first day without methadone, the conversion rate will usually be 3:1. On the second day without methadone, the dose may be titrated up to 4:1 (administered in 2 divided doses) if required. On the day in which Buvidal® Weekly injection is commenced, a dose of immediate release oxycodone (Endone®) (one third of total dose administered on previous day) is administered immediately before the Buvidal® dose. The rationale is that Buvidal® takes 3 to 6 hours after the injection to start to have effect, and 12-24 hours to have full effect; a dose of immediate release oxycodone prevents onset of opiate withdrawal until onset of Buvidal® effect. Oxycodone dosing is summarised below.

Note: Clinicians should explain to clients that dispensed medications for use at home will not be replaced in the event of any mishap (e.g. through loss or theft).

Table 4:

Day	Oxycodone formulation and dose calculation
1	Oxycodone MR (OxyContin®) 3:1 conversion e.g. for 50mg methadone, give total daily dose of 150mg OxyContin® as divided dose i.e. 75mg OxyContin® BD
2	Oxycodone MR (OxyContin®) 3-4:1 conversion (depending on clinical presentation, COWS/SOWS/local drug and alcohol review form) E.g. for 50mg methadone, give total daily dose of between 150mg-200mg OxyContin® as divided dose i.e. between 75mg-100mg OxyContin® BD
3	Oxycodone immediate release (Endone®) 4:1 conversion and give one-third of that dose as a single supervised dose immediately prior to Buvidal® administration E.g. for 50mg methadone, give 200mg/3 = ~65mg oxycodone immediate release

Buvidal® dosing

For clients transferring from >40mg methadone, an initial Buvidal® Weekly dose of 24mg is recommended. For clients transferring from <40mg, administer Buvidal® Weekly 16mg dose. The clients should be reviewed daily on subsequent days to monitor for withdrawal symptoms. If required, additional Buvidal® Weekly 8mg doses can be administered (up to 24 hours apart, and to a maximum of 32mg total dose in the first week).

Subsequent Buvidal® doses (Weekly or Monthly, as selected by patient and prescriber) can be administered 5 days after the first Buvidal® Weekly dose.

Reviewing clients during transfer procedure

Clients undertaking outpatient transfers should attend each morning on days 1-3 during the transfer process. Morning reviews will take place in person, and afternoon reviews will generally be scheduled via telehealth for between 2-4pm. The client's address, contact number, and emergency contact details should be confirmed on the first day of the transfer. This is outlined in Table 5 below.

Table 5:

Day	Clinical procedures	Medication	Admin tasks
(At least one week prior to transfer)	Client review to discuss transfer procedures and ensure all necessary arrangements in place	• Continue usual methadone dosing • Day prior: continue usual methadone dosing or reduce methadone dose by up to 50%	Submit PRU application *Application for Authority to Prescribe or Supply Methadone, Buprenorphine, or other Opioid Agonist Therapy (OAT) Treatment under the NSW Opioid Treatment Program (OTP).* Ensure Sections D and E are completed.
1	**Morning review** (in-person): Check with client s/he ceased methadone dose previous day and has had nil dose today • Use local Drug & Alcohol Review Form • COWS and SOWS* • Discuss with addiction medicine specialist or on-call AOD medical officer if concerned e.g. intoxication. **Afternoon review** (structured telehealth): • Use local Drug & Alcohol Review Form • SOWS* • Discuss with addiction medicine specialist or on-call AOD medical	• Oxycodone MR (OxyContin®)** ○ First dose supervised administration ○ Second dose given as individually packaged takeaway ○ Dose conversion: usually 3:1 • Consider need for other medications e.g. antiemetics, simple analgesia, buscopan. **NB provision of benzodiazepines is not recommended.** • Provide overdose response with take home naloxone and overdose brief intervention	• Confirm methadone last dose details with dosing point and confirm methadone script inactivated. • Provide SOWS form to client, instruct to complete in the afternoon before next oxycodone

Day	Clinical procedures	Medication	Admin tasks
	officer if concerned e.g. intoxication.		
2	**Morning review** (in-person): • Use local Drug & Alcohol Review Form • COWS and SOWS* • Discuss with addiction medicine specialist or on-call AOD medical officer if concerned e.g. intoxication. **Afternoon review** (structured telehealth): • Use local Drug & Alcohol Review Form • SOWS* • Discuss with addiction medicine specialist or on-call AOD medical officer if concerned e.g. about intoxication.	• Oxycodone MR (OxyContin®)** ○ First dose supervised administration ○ Second dose given as individually packaged takeaway dose ○ Dose conversion: up to 4:1 • Consider need for symptomatic medications as for Day 1.	• Review self-completed SOWS from previous day and file in medical record • Provide SOWS form to client, instruct to complete in the afternoon before next oxycodone.
3	**Morning review** (in-person): • Use local Drug & Alcohol Review Form • COWS and SOWS* • Discuss with addiction medicine specialist or on-call AOD medical officer if concerned e.g. intoxication. **Afternoon review** (structured telehealth): • Use local Drug & Alcohol Review Form • SOWS* • Discuss with addiction medicine specialist or on-call AOD medical	• Oxycodone IR** ○ Give single supervised dose immediately prior to Buvidal® administration ○ Usually administer 1/3rd of total day 2 dose • Buvidal® Weekly subcut injection.	• Review self-completed SOWS from previous day and file in medical record. • Provide SOWS form to client, instruct to complete in the evening.

Day	Clinical procedures	Medication	Admin tasks
	officer if concerned e.g. intoxication.		
4	**Morning review** (structured telehealth): • SOWS* • Discuss with addiction medicine specialist or on-call AOD medical officer if concerned e.g. about intoxication. *(Clients should be given the option of an in-person review if preferred.)*	• Advise client about the option of a top-up Buvidal® injection over next few days if required. • Organise next scheduled Buvidal® dose 7 days after first dose.	• Review self-completed SOWS from previous day and file in medical record

***SOWS:** Clients should complete 2 SOWS forms per day. The first is completed on-site prior to the first dose of oxycodone, and the second should be completed at home before taking the second dose of oxycodone. Clients should be asked to return the forms to the clinic the following day. Forms can be located at: https://www.asam.org/docs/default-source/education-docs/sows_8-28-2017.pdf

****Dose calculation oxycodone:** see Table 4 for suggested dose conversions and administration considerations.

Appendix 1

Version	Date updated	Summary of changes made
1	April 2023	Published

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