

SESLHD PROCEDURE COVER SHEET



Health
South Eastern Sydney
Local Health District

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SUMMARY	This document provides guidance to all SESLHD clinical staff, with particular note for registered nurses, medical officers and pharmacists working in inpatient hospital settings and SESLHD Opioid Treatment Programs (OTPs) to ensure that patients/clients who miss doses of methadone (Methadone Hydrochloride 5 mg/1mL), sublingual buprenorphine and buprenorphine – naloxone , and depot injections of buprenorphine are reviewed and dosed in a manner that minimises the risk of overdose and optimises retention in treatment.

COMPLIANCE WITH THIS DOCUMENT IS MANDATORY

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1. POLICY STATEMENT

This document is based on the [NSW Clinical Guidelines: Treatment of Opioid Dependence \(2018\)](#), [NSW Clinical guidelines for use of depot buprenorphine \(Buvidal® and Sublocade®\) in the treatment of opioid dependence \(2019\)](#) and [National Policy and Guidelines for Medication-Assisted Treatment of Opioid Dependence \(2014\)](#). It provides further specific detail for use in South Eastern Sydney Local Health District (SESLHD).

2. BACKGROUND

Missed doses

Repeated missed doses (patients not taking their regular dose of methadone or buprenorphine, buprenorphine - naloxone) can be associated with reduced opioid tolerance, opioid withdrawal and/or use of other substances, which in turn impact on treatment safety and effectiveness.

There are particular safety concerns for:

- Patients recommencing methadone after missing doses on four or more days because of reduced opioid tolerance and risk of overdose on recommencement of methadone, particularly if other sedative drugs have been used.
- Patients recommencing sublingual buprenorphine, buprenorphine - naloxone after missing doses on four or more days because of precipitated withdrawal if the patient has been using opioid agonists (e.g., heroin, morphine, methadone).
- Safety concerns regarding delays in attending for doses of depot buprenorphine injected formulations (Buvidal, Sublocade) are considerably different, as these products have prolonged duration of effects, such that concerns regarding loss of tolerance or precipitated withdrawal are less of a concern.
- People released from correctional settings on weekly or monthly depot buprenorphine who do not attend initial appointment for new client assessment and dose

An assessment and calculation of a safe and appropriate recommencement dose is required in order to ensure that the risk of harm is reduced, while the goal of retaining the patient in treatment is achieved by expediting the return to a stable dose.

This document provides guidance to SESLHD clinical staff in inpatient hospital settings and outpatient Opioid Treatment Programs in the management of missed doses.

3. DEFINITIONS

Methadone: The term 'methadone hydrochloride' as referred to in this document includes all liquid brands of the drug methadone hydrochloride 5 mg per 1mL. Methadone is a synthetic opioid agonist which is rapidly absorbed from the gastrointestinal tract with measurable concentrations in plasma within 30 minutes of oral administration and peak plasma levels generally between 2 to 4 hours. It has a highly variable elimination half- life (14-58 hours). The effects of methadone are qualitatively similar to morphine and other pure agonist opioids.

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Buprenorphine is a partial opioid agonist with high receptor affinity. A partial agonist is a drug that binds to a receptor but does not produce maximum stimulation. It is used for the treatment of opioid dependence and also as an opioid analgesic. Buprenorphine is available:

- in sublingual formulations – generally requiring daily doses, or
- as subcutaneous injections – generally requiring doses either every 5-9 days (Buvidal Weekly) or approximately every 4 weeks (Buvidal Monthly (doses every 3-5 weeks) and Sublocade (doses every 26-42 days)).

Naloxone is an opioid antagonist. It is used in combination with buprenorphine sublingually to limit the abuse potential of buprenorphine by reducing the potential for injection. Naloxone has poor bioavailability when taken sublingually. It does not reduce the bioavailability of buprenorphine when taken in combination sublingually.

Precipitated Withdrawal is a state of opioid withdrawal which may be induced by poorly timed initiation of buprenorphine in the presence of full opioid agonists such as heroin, methadone or morphine. It is characterised by opioid withdrawal symptoms such as abdominal pain, diarrhoea, muscle aches, anxiety and sweating. It may be a risk if buprenorphine is administered when the patient has missed several days of scheduled buprenorphine doses, and has taken a short acting opiate (e.g. heroin) within the last six to 12 hours, or a longer acting opioid (e.g. methadone) in the past 24 to 36 hours.

DARF (Drug & Alcohol Review Form) is an electronic form in the eMR which includes:

- Clinical observations including pulse, respiratory rate, pupil size, oxygen saturation (if available), blood pressure and breath alcohol reading.
- History of drug use since last dose, patient's reasons for missing their dose, and any other relevant clinical issues (e.g. medical, psychiatric or social).
- As directed in the DARF, clinicians should complete the COWS (electronic version in the eMR) or other clinical instruments as clinically indicated.

4. RESPONSIBILITIES

Employees will:

- All clinical staff involved in patient care of people in opioid pharmacotherapy treatment will act in accordance with this procedure.

Line Managers will:

- Implement and monitor the management of patients who miss consecutive doses of Opioid Agonist Treatment (OAT)

District Managers/ Service Managers will:

- Facilitate discussion about the implementation of this procedure.
- Work with authors to implement relevant policies, procedures and guidelines in their teams and ensure their staff's compliance with them.
- Develop strategies to manage non-compliance.

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Agonist Treatment in Inpatient and Outpatient settings****SESLHDPR/411****5. PROCEDURE****A. Inpatient Hospital Settings: Assessment of clients who have missed consecutive doses of methadone or sublingual buprenorphine, buprenorphine – naloxone**

All inpatients on methadone or sublingual buprenorphine, buprenorphine – naloxone treatment programs must be assessed for suitability of dosing in the event that they have missed four or more consecutive days. Doses may have been omitted prior to hospital admission, early in admission or interruptions occurred during admission (e.g. nil by mouth, surgery etc.).

Staff in inpatient settings should observe the patient ingesting oral/sublingual treatment doses of OAT to ensure safety and medication adherence (and prevent diversion of medication).

Missed doses will be identified using the **Details of Inpatient on Opioid Treatment Program Form** (Form No. SEI060.136 Stock order code s0339).

Inpatient and Emergency Department staff must consult with SESLHD Drug and Alcohol medical officer on-call for advice regarding further assessment and management.

**SESLHD DRUG AND ALCOHOL MEDICAL OFFICER ON CALL via
Sydney Hospital Switchboard: 9382 7111**

B. Outpatient settings: Assessment of patients who have missed consecutive doses of methadone or sublingual buprenorphine, buprenorphine – naloxone

Repeated missed doses (patients not taking their regular dose of methadone or buprenorphine) can be associated with reduced opioid tolerance, opioid withdrawal and/or use of other substances, which in turn impact on treatment safety and effectiveness. There are particular safety concerns for:

- Patients new to, or early in opioid treatment;
- Patients recommencing methadone after missing doses on four or more days because of reduced opioid tolerance and risk of overdose on recommencement of methadone, particularly if other sedative drugs have been used;
- Patients recommencing buprenorphine after missing doses on four or more days because of the risk of precipitated withdrawal if the patient has been using opioid agonists (e.g., heroin, morphine, methadone).

Patients who miss 1, 2 or 3 consecutive missed doses should be reviewed by a clinician prior to dosing, and may require escalation to a senior clinician or medical officer if there are concerns.

When a patient misses more than three consecutive doses, a review or consultation with the prescriber or the on-call SESLHD Drug and Alcohol Medical Officer if the prescriber is not available, must occur before the next dose of medication is administered.

The following procedures are recommended for missed doses, and summarised in Appendix 1 and 2.

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B.1 – Patients who have missed 1, 2 or 3 doses

A clinician experienced in the treatment of drug and alcohol problems needs to review the patient prior to dosing.

Normal dosing can be resumed if there are no concerns regarding intoxication, significant withdrawal or other clinical issues.

If the patient presents intoxicated, in severe withdrawal or if there are other significant medical or psychiatric concerns, the clinician should complete the eMR *Drug and Alcohol Review Form* (DARF) and consult with a senior clinician or medical officer. An altered dose of methadone or buprenorphine may be indicated according to the clinical circumstances (e.g. split or reduced dose), following communication between dosing staff and prescribing doctor.

B.2 – Patients who have missed 4 or 5 consecutive doses

All patients who present for a methadone or buprenorphine, buprenorphine - naloxone dose after missing four or more consecutive days must be assessed for suitability for dosing by a clinician using the eMR *Drug and Alcohol Review Form* (DARF) and then the clinician should consult with the prescriber or on-call SESLHD Drug and Alcohol Medical Officer.

If there is to be a change in the administered dose, a prescription or telephone order from the Medical Officer must be obtained prior to dosing.

As a guide for prescription:

- Patients on methadone less than 40mg: may recommence on regular dose.
- Patients on methadone 40 mg or more: may recommence on 40mg or half regular dose, whichever is higher. Patients should be assessed by a clinician on subsequent days prior to dosing (using the DARF), aiming to return to the regular dose within five to seven days, usually in increments of up to 20mg per day. Regular assessment should occur until the patient's dose has stabilised.
- Patients on buprenorphine 8mg or less: may recommence up to regular daily dose.
- Patients on buprenorphine 8mg or more: may recommence on 8mg or half regular daily dose whichever is higher. Patients should be assessed by a clinician on subsequent days prior to dosing (using the DARF), aiming to return to the regular daily dose within two to three days, usually in increments of up to 8mg per day. Regular assessment should occur until the patient's dose has stabilised.

In the event that the prescriber cannot be contacted or is unable to provide a valid prescription, the patient cannot be dosed.

B.3 – Patients who have missed more than 5 consecutive doses

The patient **must** be reviewed by the prescriber or on call doctor prior to recommencing treatment. Methadone dose induction should generally commence low (less than or equal to 40mg/day) with careful subsequent titration. Buprenorphine dose induction should generally commence on 8mg/day with subsequent titration.

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A minority of patients have poor attendance for dosing. This may be due to ambivalence about treatment, access issues (e.g., transport, work, limited dosing hours) or medical issues (mobility problems, cognitive impairment).

Clients who regularly miss doses should be reviewed by their treating team, examining reasons for missed doses and consider options with the patient for enhancing treatment adherence, such as changes in dosing sites, take-away conditions or organise altered dosing hours.

Some patients who repeatedly miss doses may report that their methadone or buprenorphine doses are inadequate. Regular attendance should be encouraged prior to any dose increases.

**C. Assessment of patients who have missed doses of subcutaneous depot
buprenorphine injections**

There is considerable flexibility in the scheduling of depot buprenorphine injections. If a client presents beyond the recommended dosing period (i.e. >9 days after last Buvidal Weekly; >5 weeks after last Buvidal Monthly; >6 weeks after last Sublocade):

- a clinical assessment should be conducted using a DARF and
- treating medical staff contacted regarding further instructions.

The medical officer should issue a new prescription, with the following general principles, recognising that individual patient factors (e.g. medical history, social conditions, other substance use) need to be taken into consideration,

- Buvidal Weekly: the same dose of Buvidal Weekly can be continued if the dose is to be administered within 14 days of the last Buvidal Weekly injection. If the client presents more than 14 days after their last injection, the patient should recommence on a dose not greater than 24mg Buvidal Weekly. A test dose of 4mg sublingual buprenorphine-naloxone may be recommended as an initial dose, at least 1-2 hours prior to Buvidal injection to test for opioid tolerance and precipitated withdrawal.
- Buvidal Monthly. The same dose of Buvidal Monthly can be continued if the dose is to be administered within 8 weeks of the patient's last Buvidal Monthly injection. If a client presents more than 8 weeks after their last injection, then re-induct onto treatment with either sublingual buprenorphine (up to 8mg initial dose); or Buvidal Weekly injection (up to 24mg Weekly dose).
- Sublocade: The same dose can be administered if within 8 weeks of their last Sublocade injection. If a client presents more than 8 weeks after their last Sublocade injection, then re-induct onto treatment with sublingual buprenorphine (up to 8mg initial dose), and transfer back to Sublocade after 7 days of dosing with sublingual buprenorphine.

If there are concerns that a patient being assessed to resume depot buprenorphine treatment may have used methadone (causing precipitated withdrawal), an 'instant' urine drug screen, specifically testing for the presence of methadone can be conducted.

If the client cannot be contacted and does not present to the service within 4 weeks for Buvidal weekly and 8 weeks for Buvidal Monthly, the client should be reviewed by their treating team for

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treatment / discharge planning. If the client does not respond or re-engage with the service within one week, then discharge is to be arranged.

D. Patients/Clients released from custody who have missed initial assessment and dose of subcutaneous depot buprenorphine injection

Clients received from correctional settings are provided with a script to provide one additional Monthly depot buprenorphine injection or two (2) Weekly injections as per NSW Health Policy Directive (PD2021_027). Clients who miss booked appointments for initial assessment and dose will be followed up as per Medium Risk in DASBR_03 Follow-up pathway after DNA. Once the script from correctional setting has expired and contact cannot be made with the client, they will be discussed at MDT handover meeting and discharged. Clients can return to the service via Intake if required.

6. DOCUMENTATION

Outpatient settings

- The registered nurses administering the dose will refer to the current prescription.
- The actual dose administered will be recorded on the medication chart or the computerised dosing system with details of client history and presentation documented in the client clinical notes. Missed doses will be recorded in the OTP Dosing Card and computerised dosing system in SESLHD OTP settings.
- Methadone and buprenorphine/ buprenorphine – naloxone are Schedule 8 (S8) drugs and the usual requirements for recording S8 drugs must be complied with.
- The *Drug and Alcohol Review Form (DARF)* is completed on the eMR. As directed in the DARF, clinicians should complete the COWS (electronic version on the eMR) or other clinical instruments as clinically indicated which is to be filed in the client's medical record.
- Details of Inpatient on Opioid Treatment Program Form (Form No. SEI060.135, Stock Order Code s0156), once completed, is to be filed in the client's medical record.

Inpatient settings

- Consider inpatient documentation processes such as eMEDS and Best Possible Medication History (BPMH)

Clients who are admitted to hospital after missed doses should be managed as per this procedure and PD2006_049 Opioid dependent Persons admitted to Hospitals in NSW – Management. The eMR form 'Inpatient on Opioid Treatment' form should be completed on admission.

7. AUDIT

- Medication audits of OTP and inpatient medication charts by registered nurses and pharmacists.
- ims+ recording of medication errors within SESLHD DAS e.g., non-compliance with this Procedure.

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8. REFERENCES

- [NSW Clinical Guidelines: Treatment of Opioid Dependence \(2018\)](#)
- [National Policy and Guidelines for Medication-Assisted Treatment of Opioid Dependence \(2014\)](#)
- [NSW Clinical guidelines for use of depot buprenorphine \(Buvidal® and Sublocade®\) in the treatment of opioid dependence \(2019\)](#)
- [NSW Health Policy Directive – Opioid Dependent Persons Admitted to Hospitals in NSW – Management \(PD2006_049\)](#)
- [NSW Health Policy Directive – Priority Access to Public Opioid Treatment Program Services for Patients Released from Custody \(PD2021_027\)](#)

9. VERSION AND APPROVAL HISTORY

Date	Version	Version and approval notes
October 2014	0	Authors SESLHD OTP NUM's Approval: A/Prof Nicholas Lintzeris, Director SESLHD D&A Service
April 2015	1	Approval: A/Prof Nicholas Lintzeris, Director SESLHD D&A Service
April 2016	2	Reviewed by Opioid Treatment Program Clinical Specialty Group Approval: Prof Nicholas Lintzeris, Director SESLHD D&A Service
April 2018	3	Changes: <ul style="list-style-type: none"> • Wording changed to be consistent with draft NSW OTP guidelines – no substantive change to process. Reviewed by Opioid Treatment Program Clinical Specialty Group Approval: Prof Nicholas Lintzeris, Director SESLHD D&A Service
May 2018	3	Endorsed by Executive Sponsor
June 2018	3	Endorsed by SESLHD Quality Use of Medicines Committee
April 2019	4	Review by Opioid Treatment Program Clinical Specialty Group Reference included: <ul style="list-style-type: none"> • NSW Clinical Guidelines: Treatment of Opioid Dependence (2018) Approval: Prof Nicholas Lintzeris, Director SESLHD D&A Service
Jul-Aug 2020	4	Review by Opioid Treatment Program Clinical Specialty Group Review by D&A Clinical Leadership Team Approval: Prof Nicholas Lintzeris, Director SESLHD D&A Service <ul style="list-style-type: none"> • Revised Risk rating to High (from Extreme) • Inclusion of depot buprenorphine • Clarification of different management between buprenorphine sublingual and subcutaneous injection formulations
Jul-Aug 2020	5	Commencement of review by Opioid Treatment Program Clinical Specialty Group Review by D&A Clinical Leadership Team Approval: Prof Nicholas Lintzeris, Director SESLHD D&A

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		<p>Service</p> <ul style="list-style-type: none"> • Revised Risk rating to High (from Extreme) • Inclusion of depot buprenorphine • Clarification of different management between buprenorphine sublingual and subcutaneous injection formulations
October 2020	5	Draft for comment period. No feedback received.
April 2021	6	Final version approved by Executive Sponsor. To be tabled at Quality Use of Medicines Committee.
May 2021	7	Approved at QUMC pending replacing the abbreviation “SL” with “sublingual” throughout the document.
May 2021	7	Abbreviation amended. To be tabled at Clinical and Quality Council.
June 2021	7	Endorsed by Clinical and Quality Council.
13 October 2023	7.1	<p>Minor review by Opioid Treatment Program Clinical Stream, Hospital D&A Consultation Liaison Clinical Stream, PACH Quality Manager</p> <ul style="list-style-type: none"> • Include text in title and throughout in reference to the procedure’s application in inpatient and outpatient settings • Include more detail on management of missed doses of long acting/subcutaneous/depot buprenorphine, particularly in reference to discharge process; and release from custodial settings. <p>Approved at October 2023 District Drug and Therapeutics Committee meeting.</p>

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APPENDIX 1

SUMMARY OF PROCEDURE FOR MISSED DOSES IN SESLHD OTP SETTINGS METHADONE AND SUBLINGUAL BUPRENORPHINE

<p>1, 2 or 3 days consecutive missed days</p>	<ul style="list-style-type: none"> • Assessment by experienced clinician. • Administer normal dose as per script if there are no concerns regarding intoxication, significant withdrawal or other clinical issues. • If there are concerns regarding intoxication, significant withdrawal or other clinical issues, complete the DARF and consult with senior clinician or medical officer. A split or reduced dose may be considered.
<p>4 or 5 days consecutive missed days</p>	<ul style="list-style-type: none"> • Assessment by experienced clinician, including DARF • Consult with prescriber, or on call D&A MO • Provision of new prescription or telephone order if the dose is to be altered. • Document on Dosing Card, patient clinical record and computerised dosing system <p>Prescribing guide for recommencing methadone:</p> <ul style="list-style-type: none"> – Patients on less than or equal to 40 mg: may recommence up to regular dose. – Patients on more than 40 mg: may recommence at 40 mg or half dose, whichever is higher. – Aim to return to regular dose within 5 to 7 days at increments of up to 20 mg per day. <p>Prescribing guide for recommencing sublingual buprenorphine:</p> <ul style="list-style-type: none"> – Patients on less than or equal to 8 mg: may recommence up to regular daily dose. – Patients on more than 8 mg: may recommence at 8 mg or half regular daily dose, whichever is higher. – Aim to return to regular daily dose within 2 to 3 days at increments of up to 8 mg per day.
<p>6 or more consecutive days</p>	<ul style="list-style-type: none"> • Assessment by experienced clinician, including DARF • Patient to be assessed by medical officer for re-induction. • Prescribing guide for methadone: recommence on less than or equal to 40 mg. • Prescribing Guide for sublingual buprenorphine: recommence on less than or equal to 8 mg.

Complete relevant documentation on OTP Dosing Card, patient clinical record and computerised medication system.

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APPENDIX 2

SUMMARY OF PROCEDURE FOR MISSED DOSES IN SESLHD OTP SETTINGS SUBCUTANEOUS DEPOT BUPRENORPHINE

<p>Buvidal weekly (>9 days)</p>	<ul style="list-style-type: none"> • Assessment using DARF by experienced clinician and contact medical officer • Patient presents between 9-14 days of last injection: administer normal dose if there are no concerns regarding intoxication, significant withdrawal or other clinical issues. • Patient presents >14 days of last dose: recommence on a dose not greater than 24mg Buvidal Weekly. • Consider sublingual tests dose and instant UDS if concerns re: opioid tolerance or precipitated withdrawal
<p>Buvidal Monthly (> 5 weeks)</p>	<ul style="list-style-type: none"> • Assessment using DARF by experienced clinician and contact medical officer • Patient presents between 5-8 weeks of last injection: administer normal dose if there are no concerns regarding intoxication, significant withdrawal or other clinical issues. • Patient presents >8 weeks of last dose: recommence on Buvidal weekly (16 or 24mg) or sublingual BPN treatment, prior to transitioning to Monthly injections. • Consider sublingual test dose and instant UDS if concerns re: opioid tolerance or precipitated withdrawal
<p>Sublocade (>6 weeks)</p>	<ul style="list-style-type: none"> • Assessment using DARF by experienced clinician and contact medical officer • Patient presents between 6-8 weeks of last injection: administer normal dose if there are no concerns regarding intoxication, significant withdrawal or other clinical issues. • Patient presents >8 weeks of last dose: recommence on sublingual BPN treatment (for 7 days), prior to transitioning to Sublocade injections. • Consider sublingual test dose and instant UDS if concerns re: opioid tolerance or precipitated withdrawal