

Maintenance on Treatment

In this section you will...

- Gain an understanding of the maintenance phase of treatment;
- Develop an understanding of the therapeutic dosing levels suitable for patients in the maintenance phase; and
- Be provided with the Tasmanian policy on takeaway and missed doses.

Section Contents

8	Maintenance Treatment.....	114
8.1	Methadone.....	114
8.1.1	Therapeutic dosing levels.....	114
8.1.2	Dose increases during maintenance.....	114
8.2	Buprenorphine.....	115
8.2.1	Therapeutic dosing levels.....	115
8.2.2	Dose increases during maintenance.....	115
8.3	Ongoing Review.....	116
8.4	Urine drug screening during maintenance.....	116
8.5	Takeaway Doses: general considerations.....	117
8.5.1	Safe storage of doses.....	118
8.5.2	Use of benzodiazepines and takeaway doses.....	118
8.5.3	Assessing eligibility for takeaway doses.....	119
8.6	Methadone takeaway doses.....	120
8.6.1	Weekends and Public Holidays.....	122
8.6.2	Exceptional circumstances.....	122
8.6.3	Methadone split dosing.....	122
8.7	Buprenorphine dosing schedules and takeaway doses.....	123
8.7.1	Double dosing.....	123
8.7.2	Triple dosing.....	124
8.7.3	Buprenorphine takeaway doses.....	125
8.7.4	Weekends and Public Holidays.....	126
8.7.5	Takeaway Dose Agreement.....	126
8.7.6	Interstate Transfers.....	126
8.7.7	Suspension and Temporary Removal of Take-Away Doses.....	127
8.8	Missed Doses.....	128
8.8.1	Effects on opioid tolerance.....	128
8.8.2	Following a missed dose.....	129
8.8.3	Missed doses of methadone.....	131
8.8.4	Missed doses of buprenorphine.....	133
8.9	Lost or Stolen Doses.....	134
8.10	Vomited Doses.....	134
8.10.1	Buprenorphine.....	134

8.10.2	Methadone.....	134
8.11	Continued Use of Other Drugs	135
8.12	Transferring Between Treatment Agents.....	136
8.12.1	Buprenorphine to Methadone	136
8.12.2	From Methadone (<40mg) to Buprenorphine	137

SECTION: 8

Maintenance Treatment

SECTION: 8

8 Maintenance Treatment

Once the patient has been successfully inducted into the program, maintenance treatment can begin. The following section outlines therapeutic dosing levels suitable for patients in the maintenance phase, as well as the Tasmanian policy on takeaway and missed doses.

8.1 Methadone

8.1.1 Therapeutic dosing levels

While some patients can be successfully maintained on 30-50 mg of methadone, the therapeutic dose for most patients is 50-100mg. There is little evidence to indicate that doses above 100mg are therapeutic for most patients, nevertheless, some patients may require more than 100 mg to reach a therapeutic dose. Table 8.1 provides guidelines for authorisation requirements for prescribing various methadone maintenance doses in Tasmania.

Table 8.1: Guidelines for methadone dosing and authorisation at various doses

Methadone Maintenance Dose	Expected Therapeutic Outcomes	Authorisation Requirements
30-50mg	Therapeutic range for some patients	Authorisation not required
50-100mg	Therapeutic range for most patients	Authorisation not required
100mg	Recommended maximum therapeutic dose for maintenance	Authorisation not required
>100mg <120mg	High dose for most patients, therapeutic for some	Second opinion from an ADS Addiction Medicine Specialist recommended
120mg	Maximum allowable dose, therapeutic for some	Second opinion from an ADS Addiction Medicine Specialist recommended
>120mg	High risk dose, patient likely seeking outcome that methadone cannot provide	Authorisation from ADS Clinical Director required

8.1.2 Dose increases during maintenance

Throughout the course of treatment, there are times when a patient may require a dose increase to maintain the therapeutic effects of methadone. The guidelines for dose increases during maintenance are the same as for dose increases during week two of induction, as the same risks and mechanisms for reaching a steady state apply. That is, the maximum total dose increase of methadone in any seven day period is 10mg.

The maximum total dose increase of methadone in any 7 day period is 10 mg.

All dose adjustments or adjustments to dosing arrangements must be discussed with the patient and recorded in the patient file. The pharmacist must be informed immediately with a fax of the script. The hard copy script must be posted to the pharmacist within 24 hours.

8.2 Buprenorphine

8.2.1 Therapeutic dosing levels

As outlined in Section 6, since buprenorphine doses can be increased more rapidly than methadone, most patients will reach their therapeutic dose by the end of the induction period. This is because most patients are stabilised on 24 mg of buprenorphine or less. The registration of buprenorphine in Australia specifies that a maximum dose of 32 mg of buprenorphine can be prescribed (either per day or in a double or triple dosing regimen). Prescribers should be aware of the medico legal implications for prescriber outside of recommended guidelines.

The registration of buprenorphine in Australia specifies that a maximum dose of 32 mg can be prescribed per day. This restriction applies whether it is a daily, double, or triple dose.

Patients requiring more than 24 mg per day may be seeking outcomes that the drug cannot provide. It is recommended that GP prescribers seek advice from an ADS Addiction Medicine Specialist if the patient is requiring more than 24mg of buprenorphine per day.

The Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards recommends GP prescribers seek advice from an Alcohol and Drug Services Addiction Medicine Specialist if the patient is requiring more than 24mg of buprenorphine per day.

8.2.2 Dose increases during maintenance

Patients should be at, or, close to their therapeutic dosing levels after induction into buprenorphine treatment; however, if dose increases are required, the following rules apply:

- Dose may be increased by 2-4 mg with a review in approximately 4 days;
- All dose adjustments or adjustments to dosing arrangements must be negotiated with the patient, consent obtained, and recorded in the patient file; and

SECTION: 8

Maintenance Treatment

- The pharmacist must be informed immediately by telephone of the adjustment, with an accompanying fax of the script. The hard copy script must be posted to the pharmacist within 24 hours.

8.3 Ongoing Review

Assessment is a dynamic and ongoing process that allows the clinician to gather information about the patient's current status. Patient circumstances are fluid, consequently risks status can change. Ongoing review during the maintenance phase allows the clinician to monitor these changes, evaluate the effectiveness of the treatment plan, and modify the plan accordingly.

Once stabilisation is complete and maintenance has commenced, patient reviews can be tapered to fortnightly for a further six to eight weeks. After this period, a medical review that includes a comprehensive assessment including a physical examination (as outlined in Section 5) is required at minimum 3 monthly intervals. Where there are significant changes to clinical risk indicators, a thorough review should be conducted. Any changes in medical management must be authorised by the prescribing doctor.

Within the ADS pharmacotherapy program, case management reviews should be conducted at least 6 weekly. Regular contact with the case manager can assist in identification and coordination of the patient's health needs, as well as monitoring ongoing risk status and treatment effectiveness. (Refer to Section 10 for more information).

8.4 Urine drug screening during maintenance

Urine drug screening (UDS) is an important tool to assist in the assessment and review of patients during the maintenance phase. In addition to the assessment and physical examination, a UDS can increase the efficacy and safety of treatment. While a UDS can be an important clinical tool, it does not in itself lead to a reduction in drug use.

Some of the limitations of a UDS are that:

- it generally detects drugs used recently, and may not indicate a pattern of use;
- it may not be a reliable indication of drug use if not supervised;
- false positive and false negative results do occur; and
- there are significant financial and resource costs associated with urine drug testing.

Furthermore, Medicare Australia limits the frequency of urine drug testing to 21 urine drug tests in the first year of treatment, and 15 tests in following years. Where additional testing is required, costs are not rebated by Medicare and an agreement must be reached about payment of testing.

The benefits of *supervised* and *randomised* urine drug screening include:

- useful for identifying polydrug use that may pose additional risks for patients on the program;
- provision of objective evidence of progress towards treatment goals;
- monitoring of extraneous drug use or diversion;

- an objective form of monitoring when self-report may not be reliable;
- provision of supportive evidence of stability in treatment; and
- can be useful for medico-legal purposes.

While urine drug screens are effective at detecting methadone, the detection of buprenorphine requires chromatography procedures. This procedure does not provide information about whether the patient is consuming buprenorphine as prescribed. Enzyme-linked immunosorbent assay (ELISA) or Gas Chromatography and Mass Spectrometry (GCMS) are techniques that accurately detect the presence of buprenorphine, but these are expensive and less readily accessible. Consequently, buprenorphine testing should only be requested when there is a clinical indication.

During the maintenance phase, refusal to provide a supervised UDS must be regarded as a positive test result. Consequently, the patient is requested to attend for a thorough physical examination, which may result in changes to the treatment plan.

8.5 Takeaway Doses: general considerations

In order to improve patient safety and to ensure the appropriate prescription and use of opioids, the Tasmanian Opioid Pharmacotherapy Policy is necessarily conservative and maintains that many of the patients on the program will not be suitable for take away doses.

The main focus and drivers for the Tasmanian Opioid Pharmacotherapy Policy (TOPP) are safety, meaningful clinical outcomes and, in particular, the need to address the fundamental feature of drug addiction – impairment or loss of control over drug use.

Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards maintains that many of the patients on the program will not be suitable for take away doses.

The program acknowledges that, while some patients are suitable and may benefit from takeaway doses, they can be unsafe for a large proportion of patients. Takeaway doses are highly desirable and lucrative on the illicit market and, hence, the risk of diversion is high. Therefore, the ADS estimates that only 5-10% of opioid pharmacotherapy patients will be suitable for a limited number of takeaway doses after a period of stabilisation. The Tasmanian Opioid Pharmacotherapy Program is primarily a supervised dosing program.

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It is important that takeaway doses are not provided during the commencement and induction phase of treatment, particularly methadone treatment, as this is a period of high risk for polysubstance use, drug overdose and death. Therefore, patients will be required to attend the pharmacy daily during the first two weeks of methadone induction and the first

SECTION: 8

Maintenance Treatment

week of buprenorphine induction. One exception regarding buprenorphine is supported and is outlined below.

8.5.1 Safe storage of doses

If takeaway doses are approved (according to the criteria below), then prescribers must advise patients of their responsibility for safe storage of these medications. Patients must also be informed of the risks associated with the consumption of the takeaway dose by anyone other than the patient, particularly children. The provision of this advice should be documented in the patient file.

Patients should be encouraged to purchase a lockable device that can be placed out of reach of children to store their takeaway doses. In the public system, case managers can assist patients in finding a suitable storage device. Even if clinically stable, takeaway doses should not be provided to patients in unpredictable and insecure living arrangements, in which the storage arrangements of takeaway doses may endanger public safety.

Patients should also be informed that the following are **NOT** suitable storage locations:

- anywhere within reach of children;
- transient accommodation such as motel rooms, boarding houses, caravans, tents, trucks;
- transport vehicles such as cars and motorcycle panels; and
- eskies or refrigerators.

8.5.2 Use of benzodiazepines and takeaway doses

As noted throughout this document, the concurrent use of benzodiazepines while receiving opioid pharmacotherapy treatment presents a high risk of respiratory depression for patients. Furthermore, there is little evidence to support the efficacy of long term use of benzodiazepines for the management of chronic sleep disturbances, long term anxiety difficulties, or in the context of chronic non-malignant pain management (Morin & Wooten, 1996; Chen & Lader, 1990; and King & Strain, 1990).

Indeed, the negative effects of benzodiazepines on memory and learning are well established and are exacerbated when combined with methadone treatment (Rapeli, 2009). Therefore, the TOPP only supports the short-term use of diazepam in a controlled environment during benzodiazepine withdrawal treatment, until the patient is able to benefit from alternative treatments such as cognitive behaviour therapy (CBT) or anti-depressant medication. Clinicians must consider the extent to which benzodiazepine treatment may actually be hindering effective processing of CBT strategies for managing anxiety.

Consequently the Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards advocates a strict policy for the provision of takeaway doses for patients using benzodiazepine medication. Patients treated with medium to high doses of benzodiazepines (i.e. more than 5mg per day of diazepam or equivalent) are ineligible for takeaway doses.

Patients treated with medium to high doses of benzodiazepines (>5 mg per day of diazepam or equivalent) are ineligible for takeaway doses.

This will inevitably limit the number of patients eligible to receive takeaway doses. Prescribing doctors and, in public settings, treating teams, should take this opportunity to motivate patients to reduce their benzodiazepine use in order to improve their eligibility for takeaway doses. In relation to benzodiazepine use, the goal of pharmacotherapy treatment is to safely and gradually withdraw patients from benzodiazepines.

Since receiving prescriptions from multiple sources is a common problem with patients reliant on benzodiazepines, the treating doctor is encouraged to register with the Prescription Shopping Information Service (www.medicareaustralia.gov.au). Transparency with the patient about the access to this information is imperative for maintaining a strong therapeutic alliance and ensuring the patient's safety. Patients should also be encouraged to access support (e.g. through allied health professionals) for ongoing sleep or anxiety difficulties which may perpetuate the use of benzodiazepines.

Finally, for safety reasons and to avoid perpetuating dependence, benzodiazepine treatment should be not initiated during opioid pharmacotherapy. High risk patients presenting with complex issues related to use of high dosages of benzodiazepines should be referred to ADS as per the Tasmanian Shared Care Model (Section 2).

Benzodiazepine treatment should not be initiated during opioid pharmacotherapy.

8.5.3 Assessing eligibility for takeaway doses

When the prescribing doctor is assessing for eligibility for takeaway doses, he or she is specifically assessing for whether the patient meets criteria for clinical stability, ongoing safety, and whether providing takeaway doses will promote meaningful clinical outcomes.

Additional criteria regarding the level of clinical stability required prior to provision of takeaway doses for the specific treatment agents are described below.

Clinical stability is indicated once the patient has achieved all of the following clinical outcomes:

- no signs of injecting drug use, including no fresh or recent needle marks;
- no presentations of intoxication with alcohol or other drugs to the clinic or pharmacy;
- few (1-2 per month), if any, unexplained missed doses;
- few (1-2 per month), if any, unexplained missed appointments;

SECTION: 8

Maintenance Treatment

- no code of conduct violations;
- no traces of polysubstance use or unsanctioned opioid use in random supervised urine samples; and,
- compliance with supervised dosing requirements.

While the patient may have met the criteria for clinical stability, the doctor must also be satisfied that **ongoing safety** is likely to be maintained, which means that:

- the patient is not using more than 5 mg of diazepam or equivalent per day (as per policy above);
- the patient does not present with a risk of overdose, injecting drug use, or drug diversion; and
- the patient is able to safely store the takeaway dose. This also means that patients should be in stable living or housing arrangements.

Clinical outcomes:

- providing the takeaway dose will enhance the patient's clinical outcomes and wellbeing;
- the patient can maintain clinical stability with reduced supervision; and
- the patient will be responsible to take the dose on the day and time agreed.

In the ADS pharmacotherapy clinics, endorsement for the provision of takeaway doses is provided by the medical doctor in conjunction with the treating team. In the private system, the treating doctor is solely responsible for approving takeaway doses, although ADS should be consulted for complex clinical presentations.

Once the patient has met the criteria for eligibility for takeaway doses, all members of the treating team are responsible for ensuring that indicators of stability continue to be assessed. If the prescribing doctor is unsure that the patient is clinically stable, takeaway doses can be ceased until stability and safety is re-established. It is important to communicate this to patients prior to commencing takeaway dosing.

Takeaway doses should not be given without a thorough risk assessment.

Patients will only be given takeaway doses when there is clear evidence of clinical stability.

8.6 Methadone takeaway doses

As discussed in Section 6, patients will not be permitted to access methadone takeaway doses during the induction phase, and are therefore required to attend a pharmacy daily for the first two weeks of induction.

One methadone takeaway dose

Patients are eligible for one takeaway dose once they are clinically stable for a continuous period of 3 months.

Once 3 months of clinical stability has been achieved, the patient has a good case to request one takeaway dose per week from their prescribing doctor. In the public system, the case manager should support the patient through this process, and encourage them to be an active agent in their treatment planning. This includes supporting the patient through a medical review to assess whether providing the takeaway dose will promote positive clinical outcomes and whether the patient is likely to maintain ongoing safety.

Patients are eligible for one (1) takeaway dose once they are clinically stable for a continuous period of three months.

If the patient does not have access to a seven-day dosing pharmacy, a takeaway dose for Sundays may be given prior to 3 months. However, the patient must meet the above criteria for clinical stability and ongoing safety, and the induction phase of treatment must be complete.

As per the Gateway model outlined in Section 3, buprenorphine remains the induction agent of choice because double dosing allows prescribers to reduce many of the problems and risks associated with methadone takeaway doses. However, if patients on an interstate transfer are well established and stabilised on methadone, a switch to buprenorphine is not required.

Two non-consecutive methadone takeaway doses

After a patient has demonstrated a further 3 months of clinical stability (as defined above) on one methadone takeaway dose, he or she is eligible for two takeaway doses per week (non-consecutive). Hence, most patients will have demonstrated six months of continuous clinical stability before being eligible for two non-consecutive takeaway doses.

Most patients will demonstrate six months of continuous clinical stability before being eligible for two (2) non-consecutive takeaway doses.

As per the procedure for approving one takeaway dose, the prescribing doctor must first conduct a medical review (including risk assessment), **with the additional criteria that the patient must return a clean urine sample in the 7 days prior to commencing on two takeaway doses.** Two methadone takeaway doses per week is the maximum number approved by the Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards.

SECTION: 8

Maintenance Treatment

Two (2) methadone takeaway doses per week is the maximum number approved by the Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards.

Table 8.2: Guidelines for the provision of methadone takeaway doses

Time in treatment	Eligibility criteria	Number of takeaway doses permitted
Induction Phase	Not Applicable	No takeaway doses permitted
2 week – 3 months	Not Applicable	No takeaway doses permitted
3-6 months of continuous clinical stability	Demonstrated clinical stability Takeaway dose will facilitate meaningful clinical outcomes Ongoing safety likely to be maintained.	One takeaway dose permitted
6-9 months of continuous clinical stability	Demonstrated clinical stability on one takeaway dose Takeaway doses will facilitate meaningful clinical outcomes Ongoing safety likely to be maintained Clean urine sample in last 7 days	Two non-consecutive takeaway doses permitted

8.6.1 Weekends and Public Holidays

Whenever possible, the prescribing doctor should try to maintain current takeaway dose arrangements and avoid additional or consecutive takeaway doses during public holidays. This may require, for example, a temporary change of days. Prescribers can contact the ADS for advice or support around managing takeaway doses during holiday periods.

8.6.2 Exceptional circumstances

In exceptional circumstances, patients may be provided with additional or consecutive takeaway doses following consultation with an ADS Addiction Medicine Specialist. In this circumstance, the rationale for these additional takeaway doses, as well as the management plan, should be clearly documented in the patient file. The ADS Addiction Medicine Specialist must provide confirmation in writing to prescribers regarding exceptional takeaway dose arrangements agreed upon during consultation.

8.6.3 Methadone split dosing

It is possible that high methadone doses or split doses may benefit some patients with rapid opioid metabolism. However, the relationship between plasma methadone levels and treatment outcomes for patients on methadone programs remains contentious.

According to Eap and colleagues (2002), while there is evidence that increasing the dose can assist some patients cease using unsanctioned opioids if the trough (R)-methadone blood levels are below 250ng/mL, the majority of patients responding to treatment and not using illicit opioids, have plasma levels that are below this threshold level.

Eap and colleagues (2002) also point out that beside pharmacokinetic factors, pharmacodynamic parameters, such as variability in receptors and psychological or social factors, are very important for the success of methadone maintenance treatment. On the other hand, if patients are not responding to treatment and have low trough levels, these authors see no reason not to increase or split the dose.

Unfortunately, the structural and other practical barriers to observed split dosing are substantial. For some patients, there is an added concern about the veracity of the drug use history and clinical safety with split dosing arrangements. This may present a significant risk of diversion and overdose to the patient.

Regardless of these clinical effectiveness doubts, Tasmania does not have the clinical or pharmacy dispensing capacity to manage split dosing among patients registered on the opioid pharmacotherapy program. Given the high levels of problems associated with takeaway doses, including their diversion and unsanctioned use, split dosing is considered unsafe clinical practice in Tasmania.

The Tasmanian Opioid Pharmacotherapy Program cannot support methadone split dosing.

8.7 Buprenorphine dosing schedules and takeaway doses

As per the Gateway model outlined in Section 3, Suboxone® (buprenorphine-naloxone) is the preferred induction and treatment agent for the Tasmanian Opioid Pharmacotherapy Program. As well as being clinically safer than methadone, the ability to double or triple dose most patients means that buprenorphine is more convenient for many patients, requiring fewer visits to the pharmacy. It also means fewer patients will require takeaway doses. Amass et al., 1998 reported that 96% of their subjects chose alternate day dosing over daily dosing.

8.7.1 Double dosing

Once inducted into buprenorphine pharmacotherapy, patients may be trialled on double dosing. This means that the patient can be provided with twice their daily dose in one visit to the pharmacy. Patients are then maintained on this dose for two days, thus not needing to attend the pharmacy the following day. The patient only needs to attend the pharmacy four times per week, making it much more convenient than daily dosing. Double dosing works best for patients on a daily dose of eight to 16mg of buprenorphine.

SECTION: 8

Maintenance Treatment

Double dosing works best for patients on a daily dose of 8-16mg of buprenorphine.

Unfortunately, double dosing for patients on less than 8mg buprenorphine per day is often insufficient to manage withdrawal symptoms. Such patients are likely to require daily dosing. However, a trial of double dosing is appropriate.

Patients on more than 16 mg of buprenorphine per day cannot be double dosed since the maximum dose of buprenorphine that can be provided on any one day is 32mg (section 8.2). Some patients on 20mg of buprenorphine per day have reported being successfully managed on a 32mg double dose. A trial of double dosing with 32 mg double doses for such patients is appropriate.

If the patient is on a dose between 8-16mg buprenorphine per day, a double dosing trial with close observation by the treating team (including the pharmacist) of the patient's progress is appropriate.

An example of a weekly double dosing schedule for a patient on 12mg of buprenorphine is:

Monday – 24mg double dose

Wednesday – 24 mg double dose

Friday – 12 mg single dose

Saturday – 24 mg double dose

Patients living in rural and remote areas with no access to a 7 day dosing pharmacy can double dose on a Saturday during the induction phase. If a patient with limited pharmacy access is on 20 mg of buprenorphine by the end of week 2 of induction, trialling a double dose of 32 mg on the second Saturday is appropriate. However, the patient cannot access buprenorphine take-away doses during the induction phase.

8.7.2 Triple dosing

Patients who have successfully been double dosed for a period of time can be trialled on triple dosing, which requires them to attend the pharmacy only 3 times per week. Triple dosing works best for patients on a daily dose of 8-10mg of buprenorphine.

Triple dosing works best for patients on a daily dose of 8-10mg of buprenorphine.

An example of a weekly triple dosing schedule for a patient on 8mg of buprenorphine is:

Monday – 8mg single dose

Tuesday – 24mg triple dose

Friday – 24mg triple dose

8.7.3 Buprenorphine takeaway doses

Daily dosing regimens

The TOPP recommends patients on buprenorphine only be maintained on daily dosing schedules if alternative double dosing schedules within the guidelines have been trialed and were not successful.

Only patients on a daily dosing regimen are eligible to receive takeaway doses. The Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards allows for a maximum of two buprenorphine takeaway doses per week, however, takeaway doses can only be provided if the patient is unable to double dose.

Only patients on daily dosing schedules can access buprenorphine takeaway doses.

Requirements for accessing takeaway doses are the same as for methadone: that is, clinical stability is indicated, ongoing safety is likely to be maintained, and provision of take-away doses will promote meaningful clinical outcomes.

Two (2) buprenorphine takeaway doses per week is the maximum number approved by the Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards.

Buprenorphine takeaway doses can only be provided if the patient is unable to double dose.

Patients will not require access to take-away doses in the first week of buprenorphine induction as the Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards specify the maximum dose at the end of week one is 16mg daily. Hence, patients can be double dosed on the first Saturday.

Double or triple dosing regimens

Unlike methadone, with the availability of double and triple dosing buprenorphine regimens, the need for takeaway doses due to inconvenience for the patient is reduced and safety on the program enhanced.

The Tasmanian Opioid Pharmacotherapy Policy and Clinical Practice Standards does not support patients on double or triple dosing regimens receiving takeaway doses, as their dosing schedule requires them to attend a pharmacy a maximum of 4 times per week, and can be designed to fit within their weekly schedules. Only patients on daily dosing schedules can access buprenorphine takeaway doses.

SECTION: 8

Maintenance Treatment

Patients on low daily doses may display visible signs of opioid withdrawal on the second day, this may indicate the need to increase this double dose. For patients on 16-20mg buprenorphine daily, this will include trialling on a double dose of 32mg.

Table 8.3: Guidelines for buprenorphine takeaway doses for patients on daily dosing schedules

Time in treatment	Eligibility criteria	Number of takeaway doses permitted
Induction Phase (0-2 weeks)	Not applicable	No takeaway doses permitted Double dose on first Saturday permitted
2 weeks – 3 months	Not applicable	No takeaway doses permitted
3-6 months of continuous clinical stability	Demonstrated clinical stability Ongoing safety likely to be maintained Takeaway dose will facilitate meaningful outcomes	One takeaway dose permitted
6-9 months of continuous clinical stability	Demonstrated clinical stability on one takeaway dose Ongoing safety likely to be maintained Takeaway doses will facilitate meaningful clinical outcomes Clean urine sample in last 7 days	Two non-consecutive takeaway doses permitted

8.7.4 Weekends and Public Holidays

Whenever possible, try to maintain current takeaway dose arrangements and avoid additional or consecutive takeaway doses during public holidays. This may require, for example, temporary change of days or double dosing around public holidays. Prescribers can contact the ADS for advice or support around managing takeaway doses during holiday periods.

8.7.5 Takeaway Dose Agreement

ADS patients, including patients transferred from interstate are required to sign a Takeaway Agreement (Appendix XX) prior to accessing takeaway doses. This agreement includes information about limitations and eligibility for takeaway doses.

8.7.6 Interstate Transfers

Patients being transferred from interstate will need to meet the same criteria prior to accessing takeaway doses and double or triple dosing arrangements as locally established patients. That is, they will need to demonstrate the same length of continuous clinical stability in Tasmania before being eligible for takeaway doses. This is regardless of their previous takeaway dose arrangements interstate.

8.7.7 Suspension and Temporary Removal of Take-Away Doses

If the prescriber or treating team identifies changes in clinical risk factors for the patient and that takeaway doses are no longer suitable, then the provision of takeaway doses should be suspended. The removal of takeaways doses can be challenging for both the clinician and the patient. Patients may perceive the removal of takeaway doses as a form of punishment and this may lead to overt expressions of frustration and anger. It is also important to remember that many patients experience feelings of powerlessness and low self-worth and in this context they may interpret the removal of takeaways as confirmation of failure or inadequacies.

For this reason it is very important to talk to patients at the commencement of treatment about the reasons for the restrictions relating to access to takeaway doses and the circumstances that may lead to the removal of takeaway doses. When takeaway doses are to be suspended, it is important to discuss this with the patient and outline the rationale for the suspension. Clear advice should be provided about the conditions under which takeaway doses will be reinstated (e.g. 3 clean urines and no missed doses for a period of 3 months).

In some instances, the patient may attend the pharmacy for dosing before they have been informed of changes to their treatment plan, and is denied their takeaway dose by the pharmacist. This scenario can place the pharmacist at increased risk of verbal abuse (or worse).

Procedure for Removing or Temporarily Suspending Takeaway Doses

When a clinical decision is made to remove or suspend takeaway doses:

- communicate this change to patient immediately or as soon as possible;
- carefully explain of the reason for the removal of takeaway doses and how long this change in their treatment will be in-place (it can be very helpful to provide the patient with this information in writing);
- emphasise that their clinical safety is always a priority and if necessary review the with the pharmacotherapy treatment agreement;
- ensure that the patient understands what changes need to occur to increase their clinical safety or program compliance (i.e. clean urine drug screens; regular attendance at appointments) and offer strategies and assistance to the patient to support them with these changes;
- always try to explain any changes in the patients treatment with them in-person at the time of their assessment (or review) or when the need for a change to their treatment has been identified;
- if a decision is made to remove takeaway doses in the absence of the patient, every attempt should be made to contact the patient in person and inform them of this change to their treatment;
- if the patient is unable to be contacted then a message should be left for them to contact the prescriber prior to dosing at pharmacy;

SECTION: 8

Maintenance Treatment

- if the prescriber or treating team are unable to contact the patient directly about suspension of takeaway doses, this information should be provided to the patient in writing and a copy sent to the pharmacist;
- if the patient has no fixed abode, then two copies should be sent to the pharmacist. The pharmacist can then provide this letter to the patient and request that they contact their prescriber or treating team regarding their treatment plan;
- the pharmacist/dosing site should also be informed immediately of any changes to dosing arrangements and of any identified clinical or safety risks (or behavioural/treatment contracts and requirements); and
- document in the clinical notes the rationale for the removal of takeaway doses and the ongoing management plan.

It is important **NOT** to place the pharmacist/dosing site in the position of having to inform a patient that their takeaway doses have been removed. This is the responsibility of the prescriber or treating service.

It is the responsibility of the prescriber to inform patients of any changes to their takeaway dose arrangements.

These changes must be communicated as soon as possible.

8.8 Missed Doses

The key to effective outcomes for patients receiving opioid pharmacotherapy is supervised dosing. This supports the patient to manage one of the key features of opioid dependence – impairment of control over drug use. Therefore, patients are required to consume the prescribed dose at the time (hours) and location specified in the treatment plan.

Patients are required to consume their prescribed dose at the time and location specified in their treatment plan.

While patients may miss doses due to personal circumstance, regular unexplained missed doses (i.e. more than three times a month) are often an indication of either clinical instability or unsuitability of the treatment plan and dosing arrangements. Frequently missed doses can have a significant impact on the effectiveness of the treatment, for a more detailed discussion of this issue see Section 12.

8.8.1 Effects on opioid tolerance

Missed doses can have a significant effect on the patient's opioid tolerance. This places the patient at an increased risk of overdose, particularly if they continue unsanctioned opioid use. These risks are significantly higher for patients receiving methadone than those receiving buprenorphine.

For example, a patient's methadone blood levels can drop by 25% in one day after missing just one dose. Re-establishing a steady state of methadone levels can take between 2-3 days, during which time the patient is more likely to relapse into unsanctioned opioid use and be at risk of multiple drug toxicity. Figure 8.1 below demonstrates the effects of missing one dose on methadone blood levels. This is discussed in greater detail in Section 4.

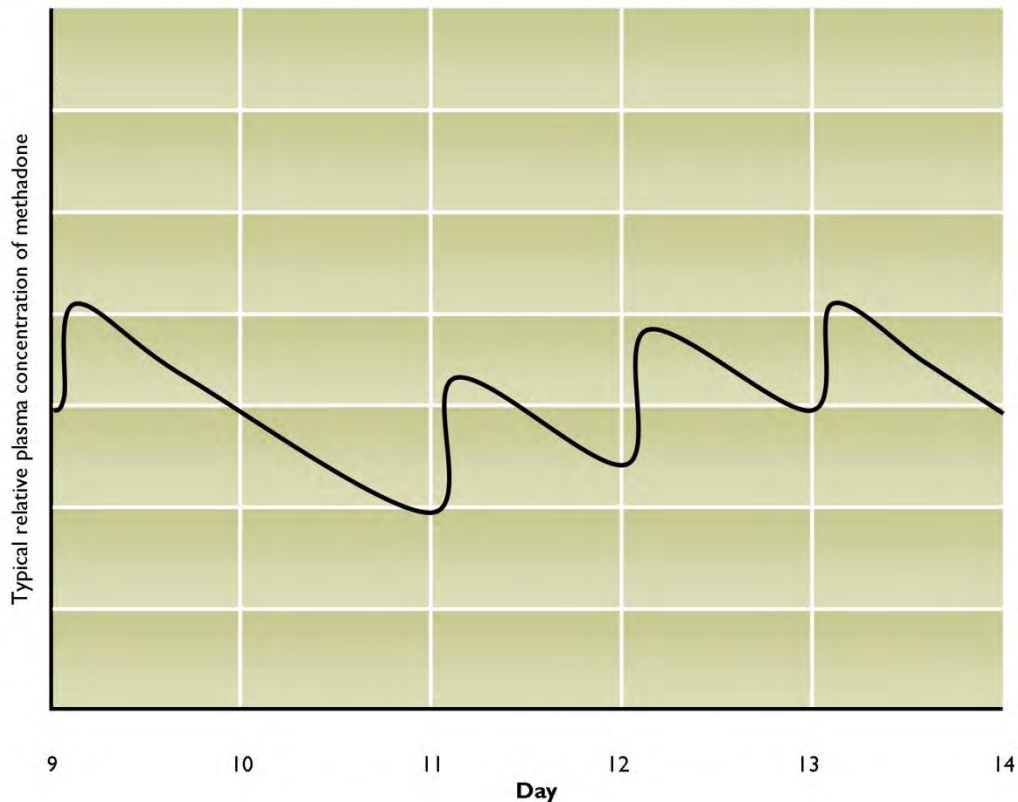


Figure 8.1: Three day recovery to steady state from missed dose at day 10

Note: Reproduced from "Guidance for the use of methadone for the treatment of opioid dependence in primary care.(1st ed.)." By Ford et al, 2005, RCGP, p.11. Substance Misuse Unit, SMMGP, RCGP Sex, Drugs and HIV Task Group and The Alliance: England.

Missing one day of buprenorphine is unlikely to affect the patient as much as missing one day of methadone. However, the time it takes to re-establish a steady state will depend on the treatment agent, dose, and patient.

After 3-4 missed days of either treatment agent, the patient will have a significantly reduced tolerance to opioids. Patients who have missed 3-4 days of treatment require titration back up to their previously therapeutic dose.

Missing 5 days or more will require the patient to be inducted back onto the program.

Intermittent consumption of opioid pharmacotherapy and its associated risks of reduced tolerance and overdose is potentially more hazardous than no treatment at all.

8.8.2 Following a missed dose

Ensuring the safety of the patient while in opioid pharmacotherapy treatment is the responsibility of all parties involved: this includes the treating team and pharmacist, as well as the patient themselves. The treating team should communicate to the patient the

SECTION: 8

Maintenance Treatment

consequences of a missed dose, including the increased risks to safety. The following subsection outlines the responsibilities that the patient, the prescriber, and the pharmacist have following a missed dose.

The patient

Patients must share the responsibility for the choices and decisions they make relating to their treatment in the program. Hence, the patient is an 'active partner' in his or her treatment. Patients are asked to:

- Let the prescriber and pharmacist know ahead of time if they cannot attend for dosing due to a predictable life circumstances. The patient may arrange either a temporary transfer or request an exemption to miss the dose for that day;
- Contact the prescriber (or ADS case manager) and reaffirm their safety if they miss 1 day of treatment;
- Contact the prescriber (or ADS case manager) and negotiate a review if they miss 2 days of treatment; or
- Attend a review set at a mutually suitable time by their prescriber if they miss 3 or more days of treatment.

The Pharmacist

The following guidelines apply to dispensing pharmacists.

One missed dose:

- assess patient suitability for dosing;
- if the patient is not intoxicated, and no other risks or concerns are identified, proceed with dosing; and
- notify the prescriber (or case manager in ADS) of the missed dose.

Two consecutive missed doses:

- do not dose the patient;
- notify the prescriber (or case manager in ADS) of the consecutive missed doses;
- inform the patient that you cannot dose them without further approval from their prescriber (or case manager in ADS); and
- inform the patient to contact their treating service and request a review from their prescriber (or case manager in ADS).

Three or more consecutive missed doses:

- do not dose the patient;
- notify the prescriber or treating service of the consecutive missed doses;
- inform the patient that you cannot dose them without further approval from their prescriber only;
- inform the patient to contact their treating prescriber or service and request a review from the prescriber; and

- if the patient is pregnant, refer them to the hospital as they are at risk of miscarriage.

If in doubt, the safest approach is to decline dosing the patient and contact the prescriber.

The Prescriber

The prescriber (including input from the treating team in ADS) must ensure that the patient is safe to continue providing treatment to after missed doses. This requires consideration of circumstances surrounding both a missed dosing period and ongoing patterns of missed doses, as well as evidence of clinical stability (or instability). The prescriber (and treating team) must carefully consider the circumstances of the missed dose(s) and determine the cause. Potential causes regularly observed by ADS clinicians include:

- predictable life circumstance, which will have ideally been communicated by the patient prior to the missed dose;
- unpredictable life circumstances, which may require verification from a family member, significant other, or other treatment agency;
- a planned attempt to engage in unsanctioned drug use;
- unplanned or spontaneous engagement in unsafe practices, such as using alcohol and other drugs;
- unsuitability of the patient's treatment plan and dose scheduling; and
- unsuitability of the opioid pharmacotherapy program for the patient.

Once the most probable cause has been determined and the history of the patient's attendance to the program is considered, the prescriber can decide to either:

- approve continuation of the patient's treatment plan, with appropriate adjustments to dosing (described below) until tolerance is re-established;
- re-negotiate the patient's treatment plan and dosing arrangements, including the cessation of takeaway doses if the criteria for clinical stability are no longer being met; or
- withdraw the patient from treatment (see Section 9 for guidelines on withdrawing from treatment).

The following are guidelines for prescribers (and case managers in ADS) for recommencement doses and requirements for reviews after a missed dose.

8.8.3 Missed doses of methadone

One missed dose:

- pharmacy will assess if the patient is suitable for dosing and notify prescriber (or ADS case manager) of missed dose; and
- record missed dose in patient file.

SECTION: 8

Maintenance Treatment

Two consecutive missed doses:

- pharmacy will not dose and inform the patient that he or she needs to contact the prescriber (or ADS case manager);
- prescriber (or ADS case manager) will review patient;
- if no evidence of intoxication or other risk factors, patient may have the usual daily dose;
- confirm with the pharmacy that it is safe to dose as per usual; and
- record missed doses and reason in patient file.

Three consecutive missed doses:

- pharmacy will not dose and will inform the patient that he or she needs to contact the prescriber;
- prescriber will review patient;
- if no evidence of intoxication or other risk factors, recommence on half the previous dose and re-titrate back up to therapeutic dose according to withdrawal symptoms displayed over subsequent days (or weeks). This will require further reviews of the patient;
- confirm the new arrangements with the pharmacy;
- document the new arrangement in the patient file, including reasons for missed doses; and
- if the patient is pregnant, refer them to the hospital as they are at risk of miscarriage.

Four consecutive missed doses:

- pharmacy will not dose and will inform the patient that he or she needs to contact the prescriber;
- prescriber will review patient;
- if no evidence of intoxication or other risk factors, recommence 40 mg OR half of usual dose (whichever is lower), and re-titrate back up to therapeutic dose according to withdrawal symptoms displayed over subsequent days (or weeks). This will require further reviews of the patient; and
- document the new arrangement in the patient file, including reasons for missed doses.

Five or more consecutive missed doses:

- pharmacy will not dose and will inform the patient that he or she needs to contact the prescriber; and
- prescriber will review patient and manage as a new induction.

8.8.4 Missed doses of buprenorphine

Daily dosing

One or two consecutive missed doses:

- follow the same procedures as for methadone.

Three or four consecutive missed doses:

- pharmacy will not dose and will inform the patient that he or she needs to contact the prescriber;
- prescriber will review patient;
- if no evidence of intoxication or other risk factors and there are clear signs of withdrawal, recommence half to two thirds of the usual daily dose up to a maximum of 16 mg. Re-titrate back up to therapeutic dose according to withdrawal symptoms displayed over subsequent days. This will require further reviews of the patient;
- confirm the new arrangements with the pharmacy; and
- document the new arrangement in the patient file, including reasons for missed doses.

Five or more consecutive missed doses:

- pharmacy will not dose and will inform the patient that he or she needs to contact the prescriber; and
- prescriber will review patient and manage as a new induction.

Double or triple dosing

Whether the patient is on daily or triple dosing will need to be taken into account when determining recommencement dose. Determine where in their schedule they are in relation to dose, and then follow the same regulation as daily dosing. Some examples are presented below:

Example 1: If a patient on a **double dose** attends the day after their scheduled dosing day, this means they have missed one dose and they can receive their **daily dose**.

Example 2: If a patient on a **double dose** does not attend on the scheduled dosing day, and attends 2 days later on their next regular scheduled day, this means they have missed two doses and will need to contact their prescriber (or ADS case manager) before they can receive their **double dose**.

Example 3: If a patient on a **triple dose** attends the day after their scheduled dosing day, this means they have missed one dose and they can receive a **double dose**.

Example 4: If a patient on a **triple dose** attends two days after their scheduled dosing day, this means they have missed two doses and will need to contact their prescriber (or ADS case manager) before they can receive a **daily dose**.

If in doubt, the safest approach is to decline dosing the patient and contact the prescriber.

SECTION: 8

Maintenance Treatment

8.9 Lost or Stolen Doses

Lost doses or stolen doses pose a significant risk to the community (see Section 12). There is a very high risk of overdose and death should another individual (other than that for whom the medication is prescribed) consume the methadone or buprenorphine dose. Patients who report lost or stolen doses should be asked to make a formal report to the police. When the patient does not comply with this request or the notification to police does not occur in a timely manner, the matter should be reviewed by the clinical team and a notification made to Tasmania Police.

Patients who report lost or stolen doses should be asked to make a formal report to the police.

Prescribers and case managers should discuss with the patient the circumstances of any lost doses. As the secure storage of medication is a requirement for access to takeaway doses, the patient's suitability for unsupervised dosing should be reviewed. A return to daily supervised dosing is recommended until the patient is able to demonstrate improved stability following a trial period.

8.10 Vomited Doses

In general vomited doses are not replaced. However, if this occurs it is important to consider the time that has elapsed and the possibility that some or all of the dose has been absorbed. The treatment agent of choice (i.e. methadone or buprenorphine) will have a direct impact on how vomited doses are managed.

8.10.1 Buprenorphine

Replacement after a vomited dose of buprenorphine is not required because buprenorphine is rapidly absorbed sublingually.

Replacement after a vomited buprenorphine dose is not required because buprenorphine is rapidly absorbed sublingually.

8.10.2 Methadone

After oral consumption, methadone takes approximately 20 minutes to be absorbed. Therefore, if a patient vomits more than 20 minutes after the dose is administered, the patient can be reassured that the dose has been absorbed. The following guidelines apply to partial replacement doses in certain circumstances.

During the induction phase (two weeks):

- if a patient reports vomiting within 20 minutes, the prescriber (or ADS case manager) should consider reviewing the patient 4-6 hours after the initial dose. If

withdrawal symptoms are present then a supplement dose of a maximum of half their original dose may be administered.

During the maintenance phase:

- if the patient is observed vomiting by the pharmacist within 20 minutes of the dose, the pharmacist may administer a half dose;
- after administration, the patient must wait in the pharmacy for at least 20 minutes, to monitor for risk of overdose; and
- pharmacist must contact the prescriber for approval before the dose is administered.

Pregnant patients

- if a patient reports vomiting, the prescriber (or ADS case manager) should review the patient within 4-6 hours. If there are signs of withdrawal, consider a small supplementary dose of no more than half their usual dose up to a maximum of 40 mg.

8.11 Continued Use of Other Drugs

Use of other drugs, both prescription and illicit, is common amongst opioid pharmacotherapy patients. Polysubstance use is also common, particularly in the early phase of treatment. In many cases, it is safer to continue with opioid pharmacotherapy than to withdraw the patient from treatment. However, consideration needs to be given to patient safety on the program. Information about the patient's concurrent drug use while on the program can be obtained from several sources, including:

- *Patient Self Report:* Developing a good therapeutic rapport that promotes information sharing and emphasises the patient as an active agent in their treatment planning is essential. Encouraging patients to disclose their drug use and responding to it in a non-punitive manner is also essential.
- *Random Supervised Urine Drug Screens:* This can be a useful tool in detecting unsanctioned opioid and other drug use. Although screening will not provide information about patterns of drug use, they can provide an objective report about the patient's recent drug use.
- *Changes in Clinical Condition or Behaviour:* This can be a good indication of unsanctioned drug use, for example, presenting while intoxicated, overdoses, chaotic behaviour, deteriorating medical or mental state. Ongoing communication between members of the treating team (for example, between the pharmacist and the prescriber) is also required.
- *Regular Review:* As stated in Section 8.2, a medical review is required at a minimum of 3 monthly intervals. While private prescribers may have limited capacity to communicate with service providers external to the treating team and family and friends, case managers in ADS have the capacity to link in and communicate with alternative service providers, particularly where there are concerns about patient and community safety.

SECTION: 8

Maintenance Treatment

Strategies for addressing the risks associated with concurrent drug use include:

- Regularly providing information about the risks of other substance use in combination with prescription opioids, including written information;
- Using motivational interviewing to discuss what the patient experiences as the positive and not-so-positive aspects of combining other drug use with opioid pharmacotherapy;
- Regularly discussing and encouraging harm minimisation strategies;
- Supporting access to psychosocial interventions and supports;
- Developing strategies for coping with withdrawal from other drugs;
- Discussing strategies for relapse prevention;
- Encouraging the use of non-drug strategies, such as sleep hygiene and relaxation training, to help manage psychological stressors;
- Consider changes in opioid pharmacotherapy treatment, for example, alterations to the dose or the dosing schedule (e.g. going from double day to daily supervised dosing for buprenorphine, removing or suspending takeaway doses);
- Consider change in treatment agent, for example, a switch from methadone to buprenorphine, which is the generally safer medication;
- Consider changes in dosing location; and
- If the risks of other drug use outweigh the benefits of remaining on the program, consider withdrawal from treatment.

Continued high risk drug use is challenging to manage and can seriously compromise the safety and efficacy of opioid pharmacotherapy. Section 12 discusses this in detail and presents strategies for managing this complex issue.

8.12 Transferring Between Treatment Agents

When transferring a patient between pharmacotherapy agents, private prescribers should seek specialist advice from ADS.

When transferring between pharmacotherapy agents, private prescribers should seek specialist advice from the Alcohol and Drug Service.

8.12.1 Buprenorphine to Methadone

As per the Gateway model outlined in Section 4, buprenorphine is the induction agent of choice for a number of reasons, one of which is that it is safer to switch from buprenorphine to methadone than the reverse. Nevertheless, a switch from buprenorphine to methadone should only occur if remaining on buprenorphine is contraindicated: that is, the side effects are intolerable (as reported by the patient and

observed by the treating team) or the response to treatment is inadequate after a trial period of several weeks.

When switching, the first methadone dose can commence 24 hours after the last dose of buprenorphine, with a maximum initial dose of 25 mg. If the patient is on a low dose of buprenorphine (e.g. 4 mg or less) then a lower dose of methadone should be given (e.g. 20 mg or less). Subsequent titration up (if required) should occur slowly, as if there is buprenorphine in the system it may diminish the effects of methadone.

8.12.2 From Methadone (<40mg) to Buprenorphine

Transferring from methadone to buprenorphine is more complicated than the reverse, as buprenorphine can displace the methadone from the opioid receptors, leading to precipitated withdrawal. Therefore, there is an increased risk of destabilisation during transfer.

To minimise the likelihood of precipitated withdrawal, patients on methadone are advised to reduce their dose to 40mg or less (preferably 30 mg) if possible, and be stable on this lowered dose for one to two weeks before transferring to buprenorphine. The larger the methadone dose, the longer the wait to transfer.

Patients are reviewed more frequently during this period to monitor risk and plan for the reduction and cessation of methadone. One week before switching, a urine drug screen should be conducted. Since commencing buprenorphine during pregnancy is contraindicated (see Section 11), female patients must also complete a pregnancy test.

Patients must present in some degree of mild methadone withdrawal on the day they start buprenorphine, and therefore must cease methadone at least 24 hours before the buprenorphine is initiated. Patients must also be reminded not to take any opioids during this period, including those that contain codeine phosphate (e.g. Panadeine and Panadeine Forte). Patients are also advised not to use other drugs and medications, including alcohol and benzodiazepines. Some patients may have to wait up to 48 hours to be in withdrawal.

If the last dose of methadone was between 10 – 40 mg:

- initial buprenorphine dose may be up to 4 mg;
- review 2-4 hours after the first dose or early the next day; and
- an increment of 0.8-4 mg may be given if some withdrawal present.

If the last dose of methadone was between 1-10 mg:

- initial buprenorphine dose may be up to 2 mg;
- review 2-4 hours after first dose or early the next day; and
- the dose may be increased by up to 4 mg on day two.

Following the switch, review the patient daily for 2-6 days. The following dose increases may be given:

- if buprenorphine dose is less than 16 mg, dose may be increased by 2-4 mg per day; or

SECTION: 8

Maintenance Treatment

- if buprenorphine dose is greater than 16 mg, dose may be increased by 4-8 mg per day.

From Methadone (>40mg) to Buprenorphine

The preference is to reduce methadone to 30 mg prior to switching to buprenorphine: however, some patients may suffer consider withdrawal discomfort when attempting to reduce their methadone. This type of switch is more safely conducted in an inpatient setting.

The general principle is to cease methadone dosing (or other prescribed opioids) and delay the initiation of buprenorphine treatment until the patient experiences significant, observable features of opioid withdrawal. This generally means that buprenorphine is not commenced until 48–96 hours after the last dose of methadone, and 16-32 hours after the last dose of other opioids (e.g. MS Contin, OxyContin, Kapanol or MS Mono).

The first dose of buprenorphine is generally 4mg, but in the absence of substantial opioid withdrawal signs, it may be appropriate to give 2mg as the first dose. The patient should be reviewed later the same day, approximately 3-4 hours after the first dose. If the patient is experiencing no increase in withdrawal severity, either subjectively or objectively, another 2 or 4mg of buprenorphine is administered. If the patient is experiencing a worsening of withdrawal, no further dose is administered that day. Clonidine and symptomatic withdrawal medication may be required for the rest of the day. Peak withdrawal discomfort is experienced during the first day of buprenorphine treatment.

The patient is reviewed daily and the dose titrated until stable. Patients may continue to describe mild withdrawal features for one to two weeks after transfer. It is important to inform the patient that withdrawal symptoms are a normal part of this process and to provide support and strategies to assist them through this transition.

Completing Treatment

In this section you will...

- *Learn how to complete treatment and exit patients from the opioid pharmacotherapy program.*

Section Contents

9	Completing Treatment	141
9.1	Planned and Voluntary Withdrawal from Opioid Pharmacotherapy	141
9.2	Withdrawal from Treatment Plan	141
9.2.1	Managing Withdrawal Symptoms	142
9.2.2	Review and Monitoring	143
9.2.3	Planned Methadone Dose Reductions	143
9.2.4	Planned Buprenorphine Dose Reductions	144
9.2.5	Switching from Methadone to Buprenorphine	144
9.2.6	Involuntary Withdrawal	145
9.3	Rapid Withdrawal from Opioid Pharmacotherapy	146
9.4	Avoiding secondary problems with alcohol, sedative or hypnotic drugs...	147
9.5	Exiting patients	148
9.5.1	Notifying the Dosing Site/Pharmacy	148