Information Bulletin

Ministry of Health, NSW
73 Miller Street North Sydney NSW 2060
Locked Mail Bag 961 North Sydney NSW 2059
Telephone (02) 9391 9000 Fax (02) 9391 9101
http://www.health.nsw.gov.au/policies/

NSW Opioid Treatment Program Clinical Guidelines - Changes Regarding Takeaway Doses

Document Number IB2015_060

Publication date 04-Nov-2015

Functional Sub group Clinical/ Patient Services - Mental Health
Clinical/ Patient Services - Pharmaceutical

Summary This Information Bulletin advises of changes to the 2006 NSW Opioid Treatment Program Guidelines regarding takeaway or unsupervised doses for methadone and buprenorphine, including indications for, risk assessment, and strategies to minimise harm.

Author Branch Mental Health and Drug and Alcohol Office

Branch contact Mental Health and Drug & Alcohol Office 02 9391 9873

Applies to Local Health Districts, Board Governed Statutory Health Corporations, Chief Executive Governed Statutory Health Corporations, Specialty Network Governed Statutory Health Corporations, Affiliated Health Organisations, Public Hospitals

Audience OTP Prescribers, GPs, Drug and Alcohol Staff, Community Pharmacies

Distributed to Public Health System, Divisions of General Practice, Ministry of Health

Review date 03-Nov-2017

Policy Manual Patient Matters

File No. 14/4604

Status Active

Director-General

INFORMATION BULLETIN

NSW OPIOID TREATMENT PROGRAM CLINICAL GUIDELINES CHANGES REGARDING TAKEAWAY DOSES

PURPOSE

The purpose of this Information Bulletin is to inform NSW Health services, opioid treatment program prescribers and community pharmacies of changes to the NSW Opioid Treatment Program (OTP): Clinical Guidelines for Methadone and Buprenorphine Treatment of Opioid Dependence (NSW Guidelines; developed 2006 and reprinted 2009) with regard to pharmacotherapy takeaway doses.

These changes result from the endorsement of the National Guidelines for the Medication-Assisted Treatment of Opioid Dependence (National Guidelines) in April 2014.

The National Guidelines should be used as the primary source of clinical guidance unless otherwise indicated. They are available at:
http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/AD14DA97D8EE00E8CA257CD1001E0E5D/$File/National_Guidelines_2014.pdf

KEY INFORMATION

The 2006 NSW Guidelines are currently being updated, with completion anticipated in December 2015. While this work is progressing, it is necessary to resolve a difference of clinical guidance between the National Guidelines and the NSW Guidelines in relation to pharmacotherapy takeaway doses. On this issue, the national guidelines indicate that reference should be made to State guidelines.

To clarify this for practitioners, this Information Bulletin has been prepared, together with current information attached about pharmacotherapy takeaway doses.

ATTACHMENTS

1. NSW Opioid Treatment Program Takeaway Dosing - Guidelines

INFORMATION BULLETIN - ATTACHMENT 1

NSW OPIOID TREATMENT PROGRAM
TAKEAWAY DOSING GUIDELINES

Definitions used in this attachment.

"*Supervised dosing*" refers to the direct observation of the patient taking their medication by the administered dose and route, by a registered nurse, pharmacist or medical practitioner.

"*Takeaways*" are defined as dispensed doses of medication to be taken from the dispensing point for later consumption by the patient.

Hence it is possible to describe three types of dosing regimens:

- *Supervised dosing regimen*: routine supervision of all doses (exceptions may apply for special circumstances)
- *Takeaway regimen*: combination of supervised and takeaway doses routinely provided
- *Unsupervised regimen*: refers to the dispensing of medication without regular or frequent (i.e. less than weekly) supervision of dosing. Unsupervised dosing is restricted to buprenorphine-naloxone.

Background

In general, treatment of opioid dependence with methadone or buprenorphine is based on daily, supervised dosing at a pharmacy or clinic, with access to takeaway or unsupervised doses according to individual patient circumstances. Supervised dosing provides:

- Greater adherence to the medication regimen, with less diversion to others and less misuse (e.g. unsanctioned dose escalations, injecting) of medication;
- Less risk of overdose, with less risk of dosing of intoxicated patients, following missed doses (lowered tolerance), or use of excessive doses; and
- Daily structure and routine that can be important for many patients early in treatment.

However, many patients find the requirements of daily supervised dosing intrusive and not compatible with community re-integration through activities such as work or study. The provision of takeaways and unsupervised dosing may:

- Improve patients' reintegration into normal daily activities and routines by reducing the inconvenience of regular pharmacy or clinic attendance (particularly for workers, or in regional or rural areas)
- Reduce the cost of treatment to patients by reducing dispensing fees (for unsupervised Buprenorphine/Naloxone treatment) and travel costs
- Facilitate treatment engagement by enabling patients with travel difficulties, work or other commitments to maintain regular dosing
- Enhance treatment outcomes, in which positive behaviours (e.g. regular attendance for appointments or dosing, cessation of other substance use) are linked to increased access to takeaway doses, consistent with the principles of contingency management
- Greater patient self-autonomy in the management of their medication and treatment in general, consistent with the principles of chronic disease management, and
- Reduce stigma associated with regular attendance at pharmacies or clinics, particularly where there are concerns regarding confidentiality for the patient.

However, there are also potential harms associated with unsupervised or takeaway doses of opioid medication to the patient, to others intentionally or accidently (e.g. children) using opioid medication, and to the broader opioid treatment program (assessment considerations for takeaways are further

outlined in A10.4 of the National Guidelines). These potential harms, and the relative risk profile of methadone, buprenorphine and buprenorphine-naloxone medications are shown in Table 1.

Table 1. Potential harms associated with takeaway doses

Activity	Safety concerns	Methadone	BPN	BNX
Patient using takeaway dose whilst intoxicated on other drugs.	Further intoxication, sedation, overdose	+++	++	++
Patient being dosed after period of several missed doses	Intoxication or overdose (if has reduced tolerance) on recommencing	++	+	+
	Precipitated withdrawal if recommencing BPN/BNX after recent opioid agonist use (e.g. heroin).	-	++	++
Poor medication adherence: (taking higher or lower doses than prescribed)	Intoxication and overdose Increased tolerance	++	+	+
	Reduced treatment effectiveness (e.g. running out of medication early, relapse to other substance use, destabilised other conditions)	++	++	++
Use by non-prescribed routes (injected, intranasal)	Intoxication, overdose (higher peak plasma concentration)	+++	++	+
	Vein damage, infections, BBV	++	+++	++
Intentional or accidental use of opioid medication by person for whom not prescribed.	Intoxication and overdose risk. Particular concern with children and others with low opioid tolerance	+++	++	++
	Opioid related harms, including adverse drug effects, route of administration, economic, legal and psychosocial consequences	++	++	++
Regular use of opioid medication by person for whom not prescribed.	Development of dependence to medication	++	++	++
Illegal activities associated with selling, diverting or possession of medications not prescribed to patient.	Regulatory and legal and consequences	++	++	++
Poor reputation of opioid treatment from misuse of unsupervised medication	Stigma against patients and treatment services	++	++	++
	Reduces attractiveness of treatment to target population, health providers and community	++	++	++

Takeaway and unsupervised dosing guidelines

Takeaway guidelines reflect the need to individually tailor dosing conditions according to the relative benefits and risks for the patient, the service and the broader community. **Decisions regarding the level of supervised dosing should reflect:**

1. *Indication for takeaway or unsupervised dosing*. This may include need for travel, participation in employment, study, care of others, or other activities that enhance social and community reintegration
2. *Risk assessment of the potential harms* of unsupervised doses to the patient, to others (particularly children), and to the broader opioid treatment program, and
3. *Strategies that aim to minimise potential harms* associated with unsupervised doses (risk mitigation strategies).

The guidelines aim to strike a balance between recognition of patients' rights to autonomy, practitioners' duty of care, and public concerns about diversion of medication.

Dosing during induction and stabilisation phases of treatment

Recommendation: Induction and stabilisation phase of treatment should involve a supervised dosing regimen, with routine supervision of all doses. Exceptions may apply for special circumstances. This period usually refers to the first 3 months for methadone, and 1-3 months for buprenorphine/naloxone treatment.

Periods of induction and stabilisation of opioid substitution treatment are associated with frequent dose adjustments, the development of tolerance to medications, development of a treatment care plan, and changing patterns of substance use, general health and living conditions.

Due to the increased risk of harms from takeaway doses during this stage of treatment, it is recommended all opioid substitution treatment is supervised during the period of induction and stabilisation. Takeaway doses should only be provided for exceptional (e.g. necessary travel) or special circumstances, such as the usual dosing site not being open 7 days a week. Other arrangements that avoid takeaway doses (e.g. alternative dosing sites, or alternate day dosing for buprenorphine) should be considered before authorising takeaway doses. Treatment with buprenorphine enables a faster and safer induction and stabilisation phase than methadone, accommodating earlier access to takeaways and unsupervised dosing of buprenorphine-naloxone[1].

Maintenance phase of treatment

Recommendation: Decisions regarding the level of supervised dosing should reflect (a) indications for takeaway or unsupervised dosing; (b) risk assessment of the safety of unsupervised doses; and (c) risk mitigation strategies.

The maintenance phase of treatment is characterised by the patient having engaged in the treatment program, being on a stable dose, addressing their substance use, and other medical, psychiatric or social problems. This period usually commences approximately 3 months after commencing methadone treatment, and 1 to 3 months after commencing buprenorphine treatment, however individual patients may take more or less time to achieve these conditions. In particular, patients with poor treatment adherence (e.g. missed doses, missed appointments), and/or complex health and social problems may take longer to achieve these goals. Patients with fewer problems (e.g. no history of injecting drug use, stable psychosocial state) may achieve stabilisation more rapidly.

The following table summarises the recommendations regarding supervision and unsupervised dosing conditions in NSW program.

Table 2. Takeaway framework for NSW OST

<table>
<tr><td colspan="3">Methadone</td></tr>
<tr><td>Induction & stabilisation: usually first 3 months of treatment</td><td colspan="2">Supervised dosing. No takeaway doses except in special circumstances, which should be qualified and clearly documented in the patient medical record.</td></tr>
<tr><td rowspan="3">Maintenance phase: takeaway availability based on risk assessment</td><td>High risk</td><td>Supervised dosing. No takeaway doses except special circumstances.</td></tr>
<tr><td>Moderate risk</td><td>0-2 takeaways per week</td></tr>
<tr><td>Low risk</td><td>2-4 takeaways per week</td></tr>
<tr><td colspan="3">Buprenorphine mono (Subutex)</td></tr>
<tr><td>Induction & stabilisation period: Usually</td><td colspan="2">Supervised dosing. No takeaway doses except special circumstances.
Consider alternate day dosing to reduce attendance requirements.</td></tr>
</table>

[1] Stable and effective buprenorphine doses (usually 12 to 24mg daily) should be reached within the first week of treatment with buprenorphine, compared to usually four to eight weeks to achieve effective methadone doses associated with reduction in other opiate use for most patients (60 to 100mg).

first 1-3 months of treatment		
Maintenance phase: takeaway availability based on risk assessment	High Risk	Supervised dosing. No takeaway doses except special circumstances
	Moderate or Low Risk	0-4 takeaways. Unsupervised dosing may be considered for moderate or low risk pregnant or breastfeeding women.
Buprenorphine-naloxone (Suboxone)		
Induction & stabilisation period: Usually first 1-3 months of treatment	Supervised dosing. No takeaway doses except in special circumstances. Consider alternate day dosing to reduce attendance requirements.	
Maintenance phase: Takeaway availability based on risk assessment	High risk	Supervised dosing. No takeaway doses except special circumstances.
	Moderate risk	0-4 takeaways.
	Low risk	Unsupervised (1 to 4 week dispensed)

Decisions regarding the level of supervised dosing should reflect (a) indications for takeaway or unsupervised dosing; (b) risk assessment of the safety of unsupervised doses; and (c) risk mitigation strategies. These are described in detail below.

1. Indications for takeaway or unsupervised dosing

The prescriber should consider the reasons for issuing takeaway or unsupervised doses. These may include:

- Need for travel e.g. for employment or other family or personal reasons e.g. carers (for further detail refer to the *National Guidelines A10.1 – Jurisdictional Issues*)
- Participation in activities that enhance social and community reintegration (e.g. study, employment, care of others, sporting, religious or recreational pursuits)
- Associated costs of travel for supervised dosing, and
- Accessibility of dosing and/or transport options (e.g. pharmacies or transport may not be available 7 days a week).

Consider alternatives to takeaway doses (e.g. alternative dosing sites, 2- or 3-day buprenorphine dosing), or the engagement of others (e.g. carers) in overseeing and enhancing medication adherence where the treatment team have concerns regarding the safety of takeaway doses.

2. Risk assessment of the potential harms of unsupervised doses to the patient, to others, and to the broader opioid treatment program

Prescribers are responsible for conducting and documenting regular risk assessments regarding the suitability of takeaway or unsupervised doses. A risk assessment for takeaway dosing can be generally performed using clinical information routinely obtained as part of regular reviews by the treating team. The use of structured clinical outcome instruments (e.g. the Australian Treatment Outcomes Profile - ATOP) can assist in this process. Risk assessments require communication and exchange of relevant clinical information between service providers, particularly between OTP providers in prescribing, dosing, psycho-social support and case co-ordination roles, and in some cases with other health, correctional or welfare agencies as required.

Risk assessment involves consideration of the following patient factors:

- Stability of opioid medication. Consider stability of dose (changing doses that require close monitoring, missed doses, interruptions to dosing, or doses withheld due to intoxication) and aberrant medication behaviours, particularly of takeaway opioid and/or other medications. Examples include using higher doses, alternate route (e.g. injecting), diverting medication to others and doctor shopping

- Adherence to other conditions of treatment. Attendance and frequency of patient review and monitoring, including urine drug tests. Poor attendance prohibits appropriate risk assessment of patient conditions
- Use of other substances, including alcohol, illicit or pharmaceutical drugs. Use of sedatives (e.g. alcohol, opioids, benzodiazepines, sedating antidepressants or antipsychotic medications) is associated with increased risk of overdose. Psychostimulant use (e.g. **amphetamine-type stimulants** (ATS), cocaine) can be associated with erratic behaviours; and
- Other medical, psychiatric or social factors that may impact upon medication adherence and/or safety of takeaway doses. Medical (e.g. respiratory or liver failure, other medications, mobility), psychiatric conditions (e.g. suicidal, severe anxiety or depression, psychosis), or impaired cognition (e.g. impaired memory). Ability to safely store and control medication. Examples include unsafe storage (e.g. homelessness), children in the care of patient, relationships with others (abusive relationships, domestic violence).

These issues are described further in Table 3.

Table 3 Risk assessment for takeaway or unsupervised dosing regimens

Risk factor	Low risk	High risk
Stability of opioid medication and adherence with medication, particularly of takeaway opioid and/or other medications	Stable dose with good attendance for dosing No significant aberrant medication behaviour	Recent induction (within 1 – 3 months for methadone, 1- 4 weeks for buprenorphine) Frequent missed doses or interruptions to treatment Significant aberrant behaviour, such as using higher doses than authorised, alternate route of administration (e.g. injecting), diversion to others
Adherence with other treatment conditions	Good adherence with appointments, and UDS monitoring	Poor adherence with appointments and UDS monitoring
Use of alcohol or other drugs	No significant use alcohol or other drugs	Frequent and heavy use of alcohol, illicit or pharmaceutical drugs, particularly sedatives.
Other health or social conditions that impact upon medication adherence and/or safety of takeaway doses	No significant medical, psychiatric, cognitive or social conditions that impair medication adherence or safety of takeaway doses.	Medical (e.g. respiratory or liver failure), psychiatric conditions (e.g. suicidal, severe anxiety or depression, psychosis), impaired cognition (e.g. impaired memory), homelessness, child safety concerns.

After considering each of these factors, the prescriber should identify the overall risk rating for takeaway dosing, with three levels proposed:

- High Risk: presence of one or more significant risk factors
- Moderate Risk: presence of some risk factors, but no significant high-risk factors
- Low Risk: no significant risk factors identified.

The global risk rating for takeaway dosing recognises that each individual patient may have different levels of risk for different factors. It is recommended that prescribers should tend towards conservative takeaway prescribing, and where prescribers seek to prescribe a greater number of takeaways than is suggested within these guidelines, they should seek specialist advice, and clearly document their decision making.

3. Strategies that aim to minimise potential harms associated with unsupervised doses (risk mitigation strategies)

- *Clear communication with the patient and relevant others* (e.g. carers, family members) regarding the conditions for unsupervised doses, and their responsible storage and use of their medication.
- *Clear and regular communication between service providers*, particularly where there are concerns regarding the safety of unsupervised doses.
- *Use of safer opioid preparations*:
  - Takeaway doses of buprenorphine are generally associated with fewer safety concerns than methadone, due to the lower risks of overdose and respiratory depression, the greater flexibility of dosing (e.g. safety of 'double dosing' with buprenorphine), and the fewer concerns regarding interactions with other drugs. (see www.opioiddruginteractions.com/ or Appendix 1 below).
  - The reduced injecting risk profile of buprenorphine-naloxone compared to buprenorphine-mono or other opioids more safely enables unsupervised doses to be dispensed on a weekly, fortnightly or four weekly basis.
  - Patients with a history of injecting buprenorphine-mono tablets should consider transfer to buprenorphine-naloxone or to methadone (with greater capacity for supervised dosing) in order to access takeaway doses.
  - Patients with a history of methadone injecting may have their risk mitigated by dilution of takeaway doses. (For further detail on diluting takeaways refer to A10.4 in the National Guidelines).
- *Regular clinical reviews*.

  Patients receiving takeaways or unsupervised doses should have a formal clinical review, further outlined in A4.3.2 of the National Guidelines, at least every three months by a member of the multidisciplinary team (e.g. prescriber, nurse), and more frequently for patients with more complex treatment needs. Patients in receipt of (or being assessed for) takeaway or unsupervised doses should also have regular urine drug screening as part of the risk assessment process. Structured reviews using instruments such as the ATOP enable clear documentation of key risk factors (e.g. recent substance use, injecting practice, social and health status). Patients who routinely miss scheduled appointments should have their dosing conditions reviewed.
- *Addressing aberrant use of medications*.

  Clinicians have a responsibility to address aberrant medication behaviours, such as missed doses, 'running out early', using doses additional to those prescribed, 'lost' or 'misplaced' medications, diversion to others, unauthorised routes (e.g. injecting), intoxicated presentations, or obtaining opioids from multiple doctors or other sources . These behaviours or incidents require a review of the patient's dosing conditions, and are generally markers of the need for greater levels of supervised dosing and monitoring.
- *Clear documentation in medical records* regarding the indications, risks and strategies put in place to mitigate identified risks.

Roles and responsibilities regarding unsupervised doses

Prescribers are responsible for
- Authorising takeaway doses and clearly documenting dosing instructions on the prescription and communicating with dosing sites
- Regularly reviewing dosing conditions for each patient, involving regular assessment and documentation of the indications, risks and risk mitigation strategies
- Communicating takeaway guidelines and conditions to patients, enabling patients a clear understanding of decision-making processes regarding access to takeaway or unsupervised doses, and
- Regularly communicating with the patient regarding safe use and storage of unsupervised doses of medication.

Patients are responsible for
- Using their medications as prescribed and according to the instructions on dispensed medication
- Safe storage of their medication, and ensuring that medication is kept out of reach of children
- Notifying their treatment providers of any issues or concerns regarding their medication (including lost or misplaced doses, consumption by others, or use of the medication not as prescribed), and

- Seeking emergency medical assistance in the event that their medication is consumed by others, particularly children or adults with low opioid tolerance, due to the risk of overdose and death.

Pharmacists and other dosing staff (e.g. nurses in clinics)

- Ensuring supervised and unsupervised doses are administered as per prescription, unless there are safety concerns (such as providing unsupervised doses to intoxicated patients, or where patients have been routinely missing doses), in which case they should communicate with the prescriber
- Keeping accurate records regarding dispensed medications
- Regularly communicating with the prescriber or other members of the multidisciplinary team regarding factors that impact upon the safety of unsupervised doses, including intoxicated presentations, missed doses, attempts at not consuming supervised doses, or evidence of diversion to others, and
- Regularly communicating with the patient regarding safe use and storage of unsupervised doses medication.

Patients with takeaway doses who are admitted to hospital

Patients' own takeaway supplies of methadone and buprenorphine should not be administered to inpatients.

Patients who have takeaway doses for the days they are in hospital should hand the takeaway doses to the ward staff on admission along with all other patient own medication. All inpatient medication including methadone or buprenorphine should be supplied or dispensed through the hospital pharmacy or from patient care area stock. This allows closer monitoring of their clinical condition and certainty about the dose an inpatient is receiving.

A patient's own takeaway medications handed over by the patient on admission must only be returned to the patient on discharge when both the prescriber and dosing point have been authorised accordingly.

The patient perspective

During treatment, patients are assessed for suitability for takeaway doses. Patients should expect the rules for takeaway doses to be explained in detail, in particular the time points at which access to more frequent takeaway doses can be assessed, the criteria used to assess takeaway access on an ongoing basis, and the process for stopping takeaways if the patient is no longer assessed as suitable.

Patients should appreciate that safe storage of their takeaway doses is an important criteria for ongoing access to further takeaways.

Patients should be informed that under the Drugs Misuse and Trafficking Act 1985, giving or selling ("on-supplying") methadone or buprenorphine (including dispensed takeaway doses) to another person constitutes an indictable (ie more serious) offence, and that they could be charged by police for such conduct.

Urine screening is a controversial issue for many patients and the requirements in place at each clinic and dosing point must be clear and performed on a basis to avoid a perception that an individual is being punished.

(Appendix 1 on following page)

Appendix 1

Clinically significant interactions between methadone, buprenorphine and other medications

This appendix lists some prescription medications that are known to, or may potentially result in clinically significant interactions when used in combination with methadone or buprenorphine. The list is not exhaustive; if in doubt, specialist advice should be sought.

The listing draws on information from www.opioiddruginteractions.com/.

In the tables ++ indicates a strong clinical interaction, + indicates an interaction of less significance, ? indicates the potential for interaction with limited supporting evidence. All interactions should be avoided if possible, or patients should be monitored and drug regimens adjusted if necessary.

1. Increased sedative effects

The medications in this group may increase the risk of overdose through additive CNS depression, or increased plasma levels of methadone or buprenorphine resulting from decreased metabolism or decreased urinary clearance.

Clinical significance for:		Medication
Methadone	Buprenorphine	
++	++	Amitriptyline
	++	Atazanavir
++	++	Benzodiazepines (alprazolam, diazepam, triazolam)
?		Ciproflaxin
++		Citalopram/escitalopram
?		Erythromycin
++	?	Fluconazole
+	?	Fluoxetine
++	+	Fluvoxamine
+	?	Indinavir
?	?	Ketoconazole
+		Moclobemide
?		Omeprazole
?	?	Ritonavir (avoid using in combination with atazanavir)
?		Sertraline
+		Urine alkalisers e.g. sodium bicarbonate
++	+	Zopiclone

2. *Withdrawal symptoms or adverse effects*

The medications in this group may cause decreased plasma levels and withdrawal symptoms due to increased metabolism of methadone or buprenorphine, or may cause adverse effects through other mechanisms.

Clinical significance for:		Medication
Methadone	Buprenorphine	
++		Carbamazepine
+	?	Cimetidine
+		Disulfiram (if used in conjunction with methadone formulations containing alcohol)
+	?	Hypericum perforatum (St Johns Wort)
+		Moclobemide (may cause serotonin toxicity)
+		Nevirapine
	?	Nifedipine
++	?	Phenytoin
++	?	Rifampicin
++	++	Rifabutin
+	+	Urine acidifiers e.g. ascorbic acid

3. *Prolongation of QTc interval*

These medications may be contraindicated by the manufacturer for use in combination with methadone or buprenorphine due to their capacity to cause prolongation of the QTc interval.

Clinical significance for:		Medication
Methadone	Buprenorphine	
+	+	Domperidone
+		Citalopram/escitalopram
?	?	Erythromycin
+	?	Thioridazine

4. *Effects on other medications*

Methadone and buprenorphine may also impact adversely on the other medications that may be used in combination.

Clinical significance for:		Medication
Methadone	Buprenorphine	
++		Atazanavir (methadone may decrease serum levels)
++		Desipramine (metabolism decreased leading to increased plasma levels of desipramine)
++		Nifedipine (methadone may inhibit metabolism)
++		Zidovudine (metabolism is decreased leading to increased plasma levels of zidovudine. Symptoms of zidovudine toxitiy can be misinterpreted as opioid withdrawal)