

**Bay of Plenty Addiction Service**

**GP Shared Care Manual**



**A manual for General Practitioners who are authorised by Bay of Plenty Addiction Services to prescribe Methadone or Buprenorphine/Naloxone for addiction**

Contents

[Introduction 4](#_Toc29901734)

[Why transfer to GP Shared care? 4](#_Toc29901735)

[A harm reduction approach 5](#_Toc29901736)

[Roles and responsibilities 5](#_Toc29901737)

[Opioid Substitution Treatment (OST) 6](#_Toc29901738)

[Aims 6](#_Toc29901739)

[Reducing the methadone or Buprenorphine/Naloxone dose (as opposed to planned withdrawal) 6](#_Toc29901740)

[Increasing the methadone or Buprenorphine/Naloxone dose 6](#_Toc29901741)

[Managing missed doses 7](#_Toc29901742)

[Restabilisation 7](#_Toc29901743)

[Signs and symptoms of opioid withdrawal and intoxication/overdose 8](#_Toc29901744)

[Signs and symptoms of opioid withdrawal 8](#_Toc29901745)

[Signs and symptoms of opioid intoxication/overdose 8](#_Toc29901746)

[Indications of stability and instability 8](#_Toc29901747)

[Indicators of stability 8](#_Toc29901748)

[Indicators of instability 9](#_Toc29901749)

[Methadone facts and effects 9](#_Toc29901750)

[Absorption, distribution and half-life 9](#_Toc29901751)

[Methadone toxicity 9](#_Toc29901752)

[Metabolism and excretion 9](#_Toc29901753)

[Effects on driving ability and memory 9](#_Toc29901754)

[Side effects of methadone 10](#_Toc29901755)

[Methadone interactions 11](#_Toc29901756)

[Buprenorphine/Naloxone facts and effects 14](#_Toc29901757)

[Absorption, distribution and half-life 14](#_Toc29901758)

[The ‘precipitated withdrawal’ and ‘opiate-blocking’ effects of Buprenorphine/Naloxone. 14](#_Toc29901759)

[Dosing and maintenance treatment 15](#_Toc29901760)

[Buprenorphine/Naloxone toxicity 15](#_Toc29901761)

[Metabolism and excretion 16](#_Toc29901762)

[Effects on driving ability 16](#_Toc29901763)

[Pregnancy 16](#_Toc29901764)

[Side effects of Buprenorphine/Naloxone 17](#_Toc29901765)

[Hypersensitivity to buprenorphine 17](#_Toc29901766)

[Buprenorphine/Naloxone interactions 17](#_Toc29901767)

[Appointments 18](#_Toc29901768)

[Three monthly review 18](#_Toc29901769)

[Not attending appointments 18](#_Toc29901770)

[GP – Six Monthly Information Forms 18](#_Toc29901771)

[Methadone or Buprenorphine/Naloxone takeaway arrangements 18](#_Toc29901772)

[Variance 19](#_Toc29901773)

[Replacement doses 19](#_Toc29901774)

[Agents collecting on behalf of a patient 20](#_Toc29901775)

[Writing a methadone H572 controlled drug prescription 20](#_Toc29901776)

[H572 Prescription example 21](#_Toc29901777)

[Urine toxicology guidelines 23](#_Toc29901778)

[Serum levels 23](#_Toc29901779)

[Clinical situations where serum levels may be useful are: 24](#_Toc29901780)

[Serum level testing: 24](#_Toc29901781)

[Serum level interpretation and guidelines: 24](#_Toc29901782)

[Split methadone or Buprenorphine/Naloxone dosing 25](#_Toc29901783)

[Pregnancy and OST 25](#_Toc29901784)

[Vomiting in pregnancy 26](#_Toc29901785)

[Concurrent medical conditions 26](#_Toc29901786)

[HIV/hepatitis B and C 26](#_Toc29901787)

[Chronic liver disease 26](#_Toc29901788)

[Respiratory disorders 26](#_Toc29901789)

[Epilepsy 26](#_Toc29901790)

[Mental health disorders 26](#_Toc29901791)

[Pain management 27](#_Toc29901792)

[Acute pain: 27](#_Toc29901793)

[Chronic pain: 27](#_Toc29901794)

[Transfers between pharmacies 27](#_Toc29901795)

[Transfers to another Opioid Substitution Treatment (OST) programme 27](#_Toc29901796)

[Prescribing when GP is on leave/absent 28](#_Toc29901797)

[Prescribing for holidays/travel 28](#_Toc29901798)

[Public holidays: (Please contact BOPAS for support as required.) 28](#_Toc29901799)

[Patient holidays (within New Zealand) 28](#_Toc29901800)

[Travel overseas 29](#_Toc29901801)

[Hospitalisation 29](#_Toc29901802)

[Imprisonment/detention in Police custody 29](#_Toc29901803)

[Treatment completion 30](#_Toc29901804)

[Method of withdrawal 31](#_Toc29901805)

[Rate of withdrawal: 31](#_Toc29901806)

[Patient complaints 32](#_Toc29901807)

[Contact details 33](#_Toc29901808)

[Appendix (a) 35](#_Toc29901809)

[Appendix (b) 37](#_Toc29901810)

[Appendix (c) 38](#_Toc29901811)

# Introduction

The Tauranga Opioid Substitution Programme (OST) is one of the services offered by Bay of Plenty Addiction Service (BOPAS) that is part of Mental Health and Addiction Services, Bay of Plenty District Health Board (BOPDHB).

This manual contains information and guidelines for General Practitioners authorized by BOPAS to prescribe methadone or Buprenorphine/Naloxone to patients in the GP Shared Care Programme. BOPAS OST intends that this document will assist in the provision of a quality, safe, professionally delivered OST Service that meets the needs of patients, their family/whanau, and the wider community. GPs and their staff are encouraged to consult with the Addiction Liaison Clinician (ALC) or the Medical Officer at BOPAS OST) working in a shared-care partnership model.

BOPAS OST provides services for the management of opioid dependency from a harm reduction philosophy, supporting people towards recovery, relative to each individual and his or her own circumstances.

The OST programme is in accordance with:

* MOH New Zealand Practice Guidelines for Opioid Substitution Treatment 2014

The BOPAS OST Service manages the admission, stabilisation and specialist maintenance phases of OST treatment. Patients may then be assessed as meeting criteria for the GP Shared Care Programme where their OST is integrated with their primary health care provider who is authorised by BOPAS on a three-monthly (or with approval of MOH 6-monthly) basis to prescribe methadone or Buprenorphine/Naloxone.

# Why transfer to GP Shared care?

OST aims to support patients to live as normal a lifestyle as possible within the parameters of treatment. GP shared care has the benefits of;

* allowing services to focus on patients in need for intensive specialist input
* improving social integration by normalising patients treatment
* instigating more comprehensive health care for patients.

The phases of treatment provide a patient pathway based on recovery principles. A person may or may not move sequentially through the phases from high intervention to low intervention, but as with any recovery process, may experience periods of higher intervention (re-stabilisation or a return to specialist maintenance) as part of their recovery.

Underpinning the practices and policies of BOPAS OST is local and international research which demonstrates the effectiveness of Opioid Substitution Treatment (OST). Treatment provided by BOPAS OST is delivered within a framework of sound medical practice, accepted standards, approved guidelines and legal requirements. BOPAS OST seek to ensure that methadone or Buprenorphine/Naloxone is prescribed and dispensed in a clinically responsible manner.

**Note:**

**This manual should be seen as an adjunct to the Ministry of Health, NZ Practice Guidelines for Opioid Substitution Treatment (2014). It is recognised this manual is unlikely to address all situations that may arise during treatment. GPs are encouraged to consult with BOPAS OST staff for information and support.**

# A harm reduction approach

All aspects of service provision are aimed at reducing harm to the individual, the family/whanau and the community.

Aims of Opioid Substitution Treatment (OST) are to:

* contribute to improving the health of patients as well as aspects of their personal and social functioning
* reduce the spread of infectious diseases associated with injecting drug use, specially hepatitis B and C and HIV/AIDS
* reduce the mortality and morbidity resulting from the misuse of opioid drugs
* assist individuals to achieve successful withdrawal from opioids
* reduce episodes of illegal and other harmful drug use
* reduce crime associated with opioid use.

To achieve these aims the service focuses on (From the Opioid Substitution Treatment New Zealand Practice Guidelines 2014):

* delivering person-centred, services that are both accessible and acceptable to patients
* maintaining a partnership approach with patients
* adopting a motivational rather than confrontational approach
* adopting prescribing practices that are evidence and strengths based
* supporting planned withdrawal from methadone or Buprenorphine/Naloxone when appropriate.

Patient confidentiality and privacy are maintained in accordance with relevant legislation and patient consent is obtained in line with the requirements of the Code of Health and Disability Services Consumer Rights Act 1996.

# Roles and responsibilities

The BOPAS OST lead medical officer as authorising medical officer retains overall responsibility for patients on the GP Shared Care programme.

GP authorisation is based on a shared care model of service delivery. BOPAS OST provide specialist support and can always be accessed for advice or assistance. Renewal of authorisation is contingent upon prescribing practices remaining consistent with BOPAS OST policy and regular review with lead clinician.

For roles and responsibilities of the patent, GP and BOPAS OST, please see the appendix documents:

* Bay or Plenty Addiction service GP Shared Care Agreement
* Authority for a general practitioner to prescribe controlled drugs for the treatment of addiction (section 24(2)(d) MODA).

# Opioid Substitution Treatment (OST)

## Aims

* suppression of opioid withdrawal and craving
* non-induction of sedation or euphoria
* reduction or elimination of opioid use as measured by self-report, by clinical assessment and by reports of others
* focus on improvements to quality of life such as education, employment, relationships with significant others.
* Maintenance doses are individualised to assist the patient to achieve their negotiated treatment goals.
* Any increase/decrease in dose should be based on a clinical assessment.

## Reducing the Methadone or Buprenorphine/Naloxone dose (as opposed to planned withdrawal)

This may be indicated where the patient is reporting unwanted sedative effects or is presenting with signs of opioid intoxication.

It may be necessary as a result of increased methadone or Buprenorphine/Naloxone levels due to dose accumulation or interaction with other medication (see methadone or Buprenorphine/Naloxone interactions). It may also be advisable in the event of continued illicit opioid use or ongoing high level use of other sedatives such as alcohol or benzodiazepines.

The dose should be titrated down until a satisfactory outcome is achieved.

**Notify the Addiction Liaison Clinician**

## Increasing the Methadone or Buprenorphine/Naloxone dose

This may be indicated when the patient is reporting that the dose is not sufficiently suppressing opioid withdrawal symptoms for the full 24 hours. The symptoms typically have their onset during the evening and overnight, are most marked in the hours before their usual dosing time and are markedly relieved within an hour or two of dose consumption. (See Signs and Symptoms of Opioid Withdrawal and intoxication/Overdose. Page…)

This may occur as the result of:

* ongoing development of tolerance to methadone or Buprenorphine/Naloxone
* interaction with other medications or alcohol (see Methadone or Buprenorphine/Naloxone interactions)
* decreased patient ability to manage previously tolerated mild withdrawal symptoms because of increased stress
* cessation of illicit opioid use.

Where continued, or relapse to illicit opioid use is reported:

* check for signs of injecting
* check for signs of opioid intoxication
* get a urinalysis done (full drug screen)
* enquire about triggers/stressors.

***Note;***

* ***once a stable, comfortable dose has been achieved, it is not usual that the dose needs to be repeatedly adjusted upwards because of increasing tolerance***
* ***patients may report craving without significant physical withdrawal. If in doubt, prescribers can defer a decision and advise patients to discuss with the Addiction Liaison Clinician***
* ***in the situation of risky alcohol use (or other CNS depressants), methadone or buprenorphine/naloxone dose increase may actually increase clinical risk. Seek advice if necessary.***

Where, after careful clinical assessment, the decision is to trial an increase in dose, they should contact the Addiction Liaison Clinician. Dose increases should be titrated up at no more than 5 to 10mg at intervals of 5 to 7 days.

Any changes in dose will require an updated GP shared care authorization.

We recommend whilst the dose is increased a temporary return to daily or more frequent consumption is implemented – this will allow the pharmacist to support the client during the re-stabilisation phase. If there is evidence of injecting, provide harm reduction information related to safer injecting practices and access to needle exchange. Notify Addiction Liaison Clinician.

There are occasions when patients request an increase in dose to manage acute or chronic pain. We advise consultation with the Addiction Liaison Clinician before increasing the dose for pain relief. It is generally advised to add short-term additional medication for pain relief rather than altering OST medication.

# Managing missed doses

The pharmacy should notify you if the patient misses any doses. Three or more consecutive missed doses as under National protocols the patient must be assessed before dispensing can resume. The GP needs to contact the Addiction Liaison Clinician, who will be able to discuss a plan with the OST service medical officer, and appropriately advise the GP. Opioid tolerance rapidly changes, so several days without opioids can significantly alter tolerance to methadone or buprenorphine/naloxone.

# Restabilisation

* restabilisation is indicated when a patient’s biopsychosocial functioning becomes unstable (see indications of stability and instability), requiring more frequent treatment monitoring
* where the level of illicit drug use is of concern or fails to reduce/cease with supported intervention by the Addiction Liaison Clinician, then referral back to BOPAS, is likely appropriate. Such a transfer may be temporary or permanent, depending on the patient’s progress and situation.

# Signs and symptoms of opioid withdrawal and intoxication/overdose

### Signs and symptoms of opioid withdrawal

* lacrimation
* rhinorrhoea
* dilated pupils
* abdominal cramps
* anorexia
* nausea
* diarrhoea
* perspiration
* weakness
* hot and cold flushes
* muscle aches/leg cramps
* joint pain/backache
* fatigue
* restlessness
* yawning
* gooseflesh
* drug seeking behaviour

The onset of Methadone or Buprenorphine/Naloxone withdrawal starts at 24 to 48 hours after the last dose. The duration of Methadone or Buprenorphine/Naloxone withdrawal is up to 21 days. Psychological and neurological (including pain receptors) adjustments can last up to six months. Research indicates withdrawal symptoms from Buprenorphine/Naloxone are less than from Methadone.

### Signs and symptoms of opioid intoxication/overdose

* sedation
* pinpoint pupils
* bradycardia
* hypotension
* pulmonary oedema
* scratching of skin
* seizures
* respiratory depression
* coma

In cases of overdose ensure that the airway is clear and perform emergency cardiopulmonary resuscitation as necessary.

*Transfer to hospital as soon as possible where treatment with an infusion of naloxone can be commenced.*

# Indications of stability and instability

The following indicators may be considered when determining patient stability:

## Indicators of stability

* defined and progress towards treatment goals
* no problematic, harmful or hazardous use of alcohol or drugs
* no evidence of criminal activity
* responsible management of number of takeaways
* schedules and attends appointments
* rarely requests changes to dispensing
* social stability as evidenced by relationships with others, stable and healthy housing, employment/occupation
* any co-existing mental or physical health problems are well managed
* participates in primary health care
* complies with programme requirements.

## Indicators of instability

* problematic, harmful or hazardous use of alcohol or other drugs
* engages in or supports criminal activity
* signs of intoxication at clinic or pharmacy
* evidence of intravenous injecting
* irregular dosing
* poor attendance at appointments
* avoidance of urinalysis or blood tests
* behavioural problems such as aggression
* frequently requests changes to dispensing
* requests to replace lost or stolen doses
* any co-existing mental or physical health problems are difficult to treat or are not well managed

# Methadone facts and effects

### Absorption, distribution and half-life

* Methadone or Buprenorphine/Naloxone is rapidly absorbed after oral administration with detectable plasma levels after 30 minutes
* it undergoes considerable tissue distribution and crosses the blood brain barrier
* peak level is 3 to 4 hours after consumption
* with regular doses the half-life is 6 to 96 hours with a mean of 25 hours
* steady state plasma levels are reached after approximately 4 hours
* Methadone accumulates on repeated administration therefore doses **should not be increased more often than every 4 days.**

### Methadone toxicity

Methadone causes respiratory depression and coma in overdose. There can be a narrow margin between a safe and a fatal dose especially in the presence of other CNS depressants (prescribed or illicit) or if there is no opioid tolerance established.

* for non-tolerant adults oral or parenteral doses of 50 mg or less have been fatal. Potentially fatal dose for children under 14 years is 10 mg
* potentially lethal overdoses can occur within 0.5 to 6 hours after ingestion by non-tolerant or partially tolerant individuals
* a child consuming any quantity of Methadone or Buprenorphine/Naloxone must be taken to an accident and emergency department immediately.

This is one of the major underlying reasons behind the emphasis on safety and the limitations on takeaway doses in OST patients.

### Metabolism and excretion

* methadone is primarily metabolized in the liver and is excreted in urine and bile
* a small amount is excreted unchanged by the kidneys and this amount increases with increased urinary acidity.

### Effects on driving ability and memory

* individuals on an appropriate stable dose will not have impaired reaction time. In this situation there is no evidence to suggest that Methadone on its own decreases ability drive a vehicle or operate machinery
* care should be taken during the induction phase of treatment and patients should be advised not to drive until a stable dose of Methadone has been achieved
* subtle recall differences may appear on rigorous testing but clinically no memory deficit can be identified.

BOPAS OST service prescribes the **5mg/ml formulation** of methadone. This is in accordance with National Guidelines. The 5mg/ml formulation is a clear liquid, with no additives, which makes it less likely to be attractive to children than coloured formulations. As it has no additives, it also reduces the likelihood of causing harm to veins when injected. Tablets are not to be used (unless for travel purposes) – these are easier to divert, and makes adequate observation of observed doses difficult.

# Side effects of methadone

Some of these side effects may be confused with withdrawal symptoms and may be experienced even when the dose is appropriate.

|  |  |  |
| --- | --- | --- |
| **Side effects** | **Notes** | **Interventions/advice** |
| Aching muscles and joints | Some individuals report rheumatic type pains and ‘bone pain’ - uncommon | Medical examination for any underlying pathology. Hot Epsom salts bath may ease symptom |
| Analgesia and hypo- analgesia | Systemic analgesia, long term can lead to opiate receptor saturation and hypo- analgesia or increased pain sensation | Advise patient to discuss chronic pain with GP |
| Constipation | A common side effect | Increase water, fiber and increase exercise. If necessary take regular Lactulose/Movicol  |
| **Side effects** | **Notes** | **Interventions/advice** |
| Galactorrhoea | Due to mildly/moderately increased prolactin levels | Check prolactin level and rule out pathology. Seek specialist endocrinologist advice if uncertain |
| Irregular menstrual cycle/amenorrhoea | Common in women who take opioids | Educate women about the risk of pregnancy despite menstrual irregularity/amenorrhoea |
| Lowered sex drive and impotence | Common with all opioid use | Reduce dose but needs to be weighed against compromising outcomes on OST |
| Oedema | Fluid retention, puffiness, swelling, particularly of feet & ankles - uncommon | Usually resolves within a few weeks of starting treatment |
| Other G.I effects | Include:Nausea and vomiting reduced gastric emptyingElevated pyloric sphincter toneBiliary tract outflow effects (can result in biliary spasm)Loss or increased appetite | To reduce nausea and vomiting, suggest patient eat before consuming dose and drink dose slowlyOther symptoms may be reduced by reducing the dose |
| Increased Perspiration | Common especially at peak serum levels |  |
| Q-T prolonging effect |  Potential for QTc prolongation, especially if combined with other drugs with similar effect | Annual ECG tests recommended. See medications also with QT prolonging effects |
| Sedation | Drowsiness may be experience at peak serum level (3 to 4 hours after dose) especially duringinitial stabilisation | Check serum levelsReduced dose or split dose may be necessary – see relevant sections |
| Shallow breathing | From the respiratory depressive action of opioids | Reduce dose |
| Skin rash/itching |  | Appropriate skin lotion, e.g. BK lotion or similar emollient, antihistamine |
| Tooth decay/dry mouth | Opioids reduce the production of saliva | Increase fluid intake, chew sugar- free gumRegular flossing and tooth brushingRegular dental checks |
| Weight gain | Occurs in small number of patients | Assistance with weight management strategies |
| Weight loss | Lack of appetite, may be associated with mood | Assistance with weight management strategies |

# Methadone interactions

* Synergism of actions with consequent toxicity and death has occurred as a result of mixing methadone with some drugs. When more than one drug is used with methadone the effects can be unpredictable. Substances that alter liver metabolism may increase or decrease the metabolism of methadone
* Medications with a QT prolonging effect

Some interactions are listed below but please also see the NZ Formulary

|  |  |  |  |
| --- | --- | --- | --- |
| **Drug** | **Status of interaction** | **Effect** | **Mechanism** |
| **Alcohol** | Clinically significant | Increased sedation & Increased respiratory depression(? Increased hepatotoxic potential) | Additive CNS depression(NB Chronic alcohol use leads to increased hepatic metabolism of methadone → decreased methadone levels; acute consumption leads to decreased metabolism→ increased methadonelevels) |
| **Antacids** | Significant | Decreased plasma levels of methadone | Decreased absorption of methadone |
| **Anti-arrhythmics** Quinidine Sotalol Amiodarone DisopyramideProcainamide |  Significant | Potentially fatal *Torsade de Pointes* arrhythmia | Dangerous QT prolongation is likely if they are used together. |
| **Antibiotics** Clarithromycin Azithromycin Erythromycin Roxithromycin Metronidazole Moxifloxacin | Potentially clinically significant | Possible increase in serum methadone concentrations.Possible *Torsade de Pointes* arrhythmia | QT prolongation is theoretically possible if they are used together |
| **Antidepressants** Amitriptyline Imipramine Clomipramine DothiepinDoxepin | Potentially clinically significant | Potential increased risk of developing serotonin syndromePotential *Torsade de Pointes* | QT prolongation is theoretically possible if they are used together |
| **Antifungals**Fluconazole Ketoconazole | Significant | Potential *Torsade de Pointes* | QT prolongation is theoretically possible if they are used together |
| **Antimalarials**Mefloquine Chloroquine | Theoretical | Potential *Torsade de Pointes* | QT prolongation is theoretically possible if they are used together |
| **Antipsychotics** Risperidone Fluphenazine Droperidol Haloperidol Thioridazine Pimozide ClozapineOlanzapine | Clinically significant | Additive sedation Increased risk of hypotension & ventricular arrhythmias *Risperidone: case reports of precipitation of opioid withdrawal* | Additive CNS depression*Unknown* |
| **Benzodiazepines** | Clinically significant | Increased sedation | Additive CNS depression |
| **Buprenorphine, Pentazocine** | Clinically significant | Precipitation of opioid withdrawal. Increased sedation and respiratory depression | Partial opioid agonists |
| **Carbamazepine, Phenobarbitone, rifampicin, Phenytoin** | Clinically significant | **Decreased plasma levels of methadone** (Phenobarbitone: increased sedation, additive CNS depression also) | Hepatic enzyme induction leading to increased metabolism of methadone |
| **Cimetidine, Fluconazole\*, Isoniazid, Ritonavir\*, Idinavir, Ketonazole\*, Erythromycin, Ciprofloxacin, SSRIs,****Grapefruit juice** | All potentially Clinically significant. (Biological variation)**\*** = Clinically significant | **Increased plasma levels of methadone or Buprenorphine/Naloxone** Fluconazole: found to decrease methadone or Buprenorphine/Naloxone clearance by 24%SSRIs: Fluvoxamine decreases clearance by 20 – 100%. Known effect with Fluoxetine. Caution with other SSRIs. | Hepatic enzyme inhibition leading to decreased metabolism of methadone |
| **Cyclizine, other Sedating antihistamines** | Clinically important | Reports of ‘buzz’ when injected with opioids. Even high oral doses can cause euphoric effect with methadone | Additive psychoactive effects |
| **Disulfiram** | Clinically significant | Conflicting reports: Increased clearance/decreased clearance/no interaction | Avoid in combination with methadone preparations containing alcohol |
| **MAOIs** | No known cases,but severe interaction occurs with Pethidine | CNS excitation, delirium, hyperpyrexia, convulsions, hypotension, respiratory depression, serotonin syndrome | Unclear. Avoid combination if possible |
| **Other Opioids** | Clinically significant | Increased respiratory depression. Increased sedation | Additive CNS depression |
| **Tricyclic anti- depressants** | Clinically significant with desipiramine. Theoretically possible with other TCAs | Increased sedation **Desipiramine: Plasma levels increased by 100% when given with methadone** | Additive CNS depression Methadone causes decreased hepatic metabolism of desipiramine (Other TCAs) |
| **Urinary acidifiers** | Clinically significant | Decreased plasma levels of methadone | Increased renal clearance of methadone |
| **Urinary alkalinisers** | Clinically significant | Increased plasma levels of methadone | Decreased renal clearance of methadone or Buprenorphine/Naloxone *NB One study found half-life of methadone to be 19.5 hours with acidified urine & 42.1 hours with alkalinised urine* |
| **Zidovudine (AZT)** | Clinically significant | Increased plasma levels of Zidovudine | Decreased hepatic metabolism of Zidovudine |
| **Zopiclone** | Clinicallysignificant | Additive sedation | Additive CNSdepression |

# Buprenorphine/Naloxone facts and effects

Buprenorphine/Naloxone became Pharmac approved in 2013 as an alternative treatment in OST. Its qualities include less likely to be injected as compared to methadone and other opioids, (thus lowering ‘street’ value), low over-dose risk, blockade effect on other opiates and less emotionally sedating as methadone. This is a negative for some patients who find methadone better controls anxieties.

### Absorption, distribution and half-life

Buprenorphine/Naloxone is a combination of buprenorphine (a semi-synthetic partial opiate agonist) and naloxone (a full opiate antagonist). It is used in opioid substitution treatment as an alternative to methadone.

Both buprenorphine and naloxone are rapidly metabolised in the small intestine and liver and both have very poor bioavailability when taken this way. For this reason Buprenorphine/Naloxone is taken sublingually: buprenorphine has rapid absorption and good bioavailability via this route, whereas bioavailability for sublingual naloxone remains poor. Once absorbed, buprenorphine undergoes rapid distribution and readily crosses the blood-brain barrier. Although the serum half-life of buprenorphine is only around 3 hours, it has a very high affinity for the mu-opioid receptor, and once across the blood-brain barrier it will exert a clinical effect for 24-36 hours.

The naloxone in Buprenorphine/Naloxone is to discourage intravenous use. If taken intravenously, naloxone has good bioavailability and exerts a strong antagonist effect at the opioid receptors. This is likely to cause unwanted symptoms of opiate withdrawal in those who are opiate tolerant.

As a partial opiate agonist, buprenorphine exhibits a plateau effect with increasing dose and this makes it far safer in overdose than a full agonist such as methadone. As the risk of accumulating a toxic dose is reduced, doses can be increased more frequently during the induction/ titration phase of treatment, and with specialist drug service supervision, daily increases in dose are possible until stability is achieved.

### The ‘precipitated withdrawal’ and ‘opiate-blocking’ effects of Buprenorphine/Naloxone.

Buprenorphine has an extremely high affinity at the mu-opioid receptor but exerts only a moderate effect at the receptor. Consequently, if the initial Buprenorphine/Naloxone dose is taken too soon after the last use of another opiate, buprenorphine will both displace that opiate and cause a marked reduction in overall opiate effect. This is the so- called ‘precipitated withdrawal’ effect, which can be both unpleasant and frightening for opiate-dependent patients. Precipitated withdrawal is not reversible once triggered, although the effects will pass within a few hours and symptomatic relief during this time may be useful.

To avoid precipitated withdrawal, care must be taken to ensure that sufficient time has elapsed since the last opiate dose, usually at least 12-24 hours for a short-acting opioid such as dihydrocodeine. Checking that a patient is in at least mild opiate withdrawal before starting Buprenorphine/Naloxone, eg by using the Clinical Opioid Withdrawal Scale, can be useful. Transition to Buprenorphine/Naloxone from longer-acting opioids, eg methadone, can be done using a micro-dosing regime. Transition from any opioids to buprenorphine/naloxone is best carried out under the supervision of specialist alcohol and drug services.

Once successfully inducted onto Buprenorphine/Naloxone, the strong affinity of buprenorphine for the mu-receptor means that the consequences of the patient subsequently using prescribed opiates are unpredictable. Usually, the buprenorphine will prevent the opiate from accessing the receptors and the user will feel that the opiate has had no effect at all – this is the so-called ‘blocking effect’. In some cases however; using another opiate may trigger a precipitated withdrawal event. Some patients have been known to try to override the blockade effect of buprenorphine by taking very large doses of opiates; such behaviour is extremely risky in terms of accidental overdose and if such behaviour is suspected treatment should be reviewed, including the suitability of Buprenorphine/Naloxone as a treatment choice.

### Dosing and maintenance treatment

Initial dose is usually 2-4mg Buprenorphine/Naloxone on the first day with subsequent doses titrated upwards against withdrawal symptoms in 2-4mg increments, to a maximum daily dose of 32mg. For most patients, good compliance can be achieved in the range 8-16mg daily. Unlike methadone there are no Buprenorphine/Naloxone ‘fast metabolisers’ and once-daily dosing is appropriate for the vast majority of patients.

For some patients who have had a suitable period of stabilisation at a regular daily dose, the frequency of dosing may be reduced to alternate-days at twice the titrated daily dose, with no reduction in clinical effect. For example, a patient stable at 8mg Buprenorphine/Naloxone daily may be prescribed 16mg on alternate days. However; the maximum dose given on any one day should never exceed 32mg and alternate-day dosing should only be done with the full informed consent of the patient.

### Buprenorphine/Naloxone toxicity

Buprenorphine is a partial opiate agonist and unlike full agonists (morphine, methadone), the pharmacological effects of buprenorphine exhibit a “ceiling effect” with increasing doses. This makes Buprenorphine/Naloxone safer in overdose than, say, methadone, as the negative opiate effects (eg: respiratory depression) are also constrained by this ceiling effect. Nevertheless, certain groups may be particularly vulnerable to respiratory depression, eg children, those who are opiate-naïve or individuals with chronic obstructive pulmonary disease, and care should be taken to consider these factors when prescribing.

Although buprenorphine is far safer than full opiate agonists in overdose, there have been some reports of fatalities in adult users, and in particular where there have been contributing factors including:

* opiate-naïve users
* co-use of other substances (alcohol, benzodiazepines)
* use by crushing and snorting (although this risk is reduced with Buprenorphine/Naloxone due to the presence of naloxone).

Children who accidentally ingest Buprenorphine/Naloxone are particularly at risk of toxic effects:

* toxic effects are more pronounced in children under 2 years of age
* in retrospective studies, effects below 2mg dose were unlikely to be severe but at least some effects (lethargy, nausea, vomiting) occurred in all children who ingested 4mg or more
* respiratory depression occurred in 7% of paediatric overdoses, and coma in 3%.

Immediate hospital treatment must be sought in every case where a child or a non-tolerant adult has ingested Buprenorphine/Naloxone. Similarly, those who are prescribed Buprenorphine/Naloxone must be medically assessed if overdose or co-use of other respiratory depressants (alcohol, benzodiazepines) is suspected.

### Metabolism and excretion

Buprenorphine is primarily metabolised via the cytochrome P450 pathway in the liver. Care should be taken when co-prescribing medications which induce this pathway (carbamazepine, phenytoin, phenobarbital, rifampin, reverse-transcriptase inhibitors) or inhibit it (azole antifungals, macrolide antibiotics, protease inhibitors). Buprenorphine metabolites are primarily (70%) eliminated in the faeces by biliary excretion, with the remainder excreted in the urine. Naloxone is eliminated via the urine.

### Effects on driving ability

Individuals on an appropriate stable dose will not have impaired reaction time. In this situation there is no evidence to suggest that Buprenorphine/Naloxone on its own decreases driving ability. Care should be taken during the induction phase of treatment and patients should be advised not to drive until a stable dose of Buprenorphine/Naloxone has been achieved.

### Pregnancy

Buprenorphine/Naloxone should be used in pregnancy only when the potential benefit justifies the potential risk to the fetus. Buprenorphine crosses the placental barrier and the neonate should be monitored for a withdrawal syndrome. Due to the long half-life of buprenorphine, this monitoring should continue for several days. Buprenorphine is excreted into human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for buprenorphine/naloxone and any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.

### Side effects of Buprenorphine/Naloxone

**Very common (reported in at least 10% of patients):**

* headache, withdrawal syndrome (usually during induction phase of treatment)
* constipation
* insomnia
* increased perspiration

**Common (reported in at least 1% of patients)**

* chills/flu-like symptoms
* tiredness/malaise
* reduced appetite/weight loss
* nausea and vomiting
* abdominal cramps
* diarrhoea
* hypertension
* vasodilation
* reduced libido
* impotence
* dental caries
* leg cramps/myalgia
* back pain
* chest pain
* peripheral oedema
* parasthesia
* somnolence
* abnormal liver function
* depression/ increased anxiety
* cough/ pharyngitis/ rhinitis
* rash/ pruritus/ urticaria
* lacrimation disorder
* amblyopia
* irregular menstrual cycles

Many of these symptoms will resolve within a few days of commencing treatment. Other, longer term concerns may be managed by changes in behaviour and lifestyle, eg the increased incidence of dental cares can be managed by improved oral hygiene, dental visits and dietary changes.

### Hypersensitivity to buprenorphine

Some patients can have a hypersensitive reaction to buprenorphine, symptoms of which include rashes, hives and itchy skin. Rarely, this hypersensitivity reaction can trigger full anaphylactic shock. Hypersensitive patients should be considered for methadone as an alternative treatment.

### Buprenorphine/Naloxone interactions

Consideration should be given to the potential interactions with Buprenorphine/Naloxone before the following medications are prescribed:

* CNS depressants, narcotics
* General anesthetics
* MAOIs
* Mitochondrial toxins (aspirin, isoniazid, valproate, amiodarone, antiviral nucleoside analogues)
* CYP3A4 inhibitors (protease inhibitors, azole antifungals, calcium channel blockers, macrolides)
* CYP3A4 inducers (phenobarbitone, carbamazepine, phenytoin, rifampicin).

# Appointments

Initially the patient will see his/her GP every 28 days when a new script is needed. This is recommended to occur for at least 3 months when the patient is new to your practice. Where there is an established relationship with the patient or there are other indications for less frequent appointments this can be negotiated between the GP, patient and Addiction Liaison Clinician.

After this initial time the patient must be seen by the GP once every 3 months for a review. The patient usually collects their script from the GP, practice nurse or receptionist at their review and in the two months between the three monthly appointments.

### Three monthly review

Check for:

* adequacy of dose
* stability on OST (as appropriate includes; urine drug screen and checking for signs of IV track marks)
* any co-existing mental or physical health problems or social problems
* write a new script if all is well. If any concerns consult with Addiction Liaison Clinician.

### Not attending appointments

If a patient consistently does not attend appointments, the GP may refrain from writing any further scripts until the patient is seen, or may write a short-term interim prescription until a new appointment can be scheduled. The GP should also contact the case manager and or the Addiction Liaison Clinician.

### GP – Six Monthly Information Forms

The Addiction Liaison Clinician will contact your practice at least every six months to update information. Please provide any additional information you may wish to raise at this time or any time between contacts. It is essential for BOPAS OST to have current information for continued GP prescribing authorisation.

# Methadone or Buprenorphine/Naloxone takeaway arrangements

A takeaway dose of Methadone or Buprenorphine/Naloxone is any dose that is not consumed under observation at the dispensing pharmacy.

Takeaway arrangements in the GP Programme continue to be based on clinical safety and within the National Practice Guidelines. All GP prescribing is notified to BOPAS, via the required six monthly information form.

***Note: the National Practice Guidelines recommend that Methadone or Buprenorphine/Naloxone should be observed to be consumed at the pharmacy or other dispensary on at least three non-consecutive days per week.***

### Variance

Where the authorised GP and the patient assess that less frequent dispensing is appropriate, this is notified to Addiction Liaison Clinician for BOPAS OST team review.

Following the review any variance from the above policy needs to be documented and referenced in relation to the indicators of stability and instability.

***Note: no more than four takeaway doses of methadone or Buprenorphine/Naloxone per dispensing can be prescribed at any one time with at least three doses being observed to be consumed at the pharmacy in any seven- day period***

***In exceptional circumstances, for example to support employment, with the agreement of the BOPAS OST team, up to 6 takeaway doses per week can be considered. All clients MUST consume their doses observed in the pharmacy at least once per week.***

***GPs are advised to refrain from making any changes to takeaway arrangements during the first 3 to 6 months in the GP programme to enable time to fully assess the patient and their safety with further takeaways.***

# Replacement doses

**BOPAS policy is not to replace doses under any circumstances. E.g. lost, stolen, spilt, damaged, retched.**

If in exceptional circumstances that can be verified (i.e. by a police report, eye witness by professional), the GP may offer to assess the patient 48 hours or more after their last dose was consumed and if there are signs of opioid withdrawal (see p.13) then part of subsequent doses may be replaced. When requests are made for replacement doses the GP should review the person’s takeaway arrangements and notify the case manager and or Addiction Liaison Clinician.

BOPAS policy is to replace 50% of a vomited dose when the patient vomits within less than 30 minutes of consuming the dose, the vomiting was witnessed by a professional and the replacement is clinically appropriate, eg pregnancy.

If a second replacement dose for vomiting is requested within a short time, or there are regular requests for replacement doses, no further replacement doses should be authorized until the patient has been assessed by the GP and any underlying cause for the vomiting assessed and treated.

All replacement doses must be prescribed on a new H572M prescription and must be consumed in the pharmacy.

**Note: repeatedly seeking replacement dose is likely instability indicator.**

# Agents collecting on behalf of a patient

A GP can authorise an agent to collect methadone on behalf of a patient in extraordinary circumstances where the patient is unable to attend the pharmacy when they are house-bound due to illness. Circumstances necessitating the authorisation of an agent must be verified with the patient and the agent. Authorisation of an agent is limited to a maximum of 3 doses of Methadone or Buprenorphine/Naloxone dispensing.

The GP can get a copy of the agent authorisation form from the addiction liaison clinician.

Authorisation must be made in writing and faxed to the appropriate pharmacy and include;

* Name and address of the agent
* Type of identification provided by agent
* Number of doses the agent is authorised to collect
* Signature of the authorising GP

The authorised agent must provide suitable identification.

**Note: The GP must feel confident that the authorised agents can responsibly manage and administer the Methadone/Buprenorphine/Naloxone(s). Discussion about safety of takeaways is essential e.g. storage away from children, no replacement of lost or stolen doses.**

# Writing a methadone H572 controlled drug prescription

The use of H572M controlled drug prescription forms is restricted to prescribing methadone for patients under the authority conferred by Section 24(2)(d) Misuse of Drugs Act 1975 (i.e. where BOPAS has authorised a prescriber for a specific patient). The form is not used for prescribing of methadone to other patients in other circumstances (e.g. pain relief for a non-BOPAS client); in these cases the general H572 controlled drug prescription is used.

See example following page.

### H572 Prescription example

**Numbered instructions on following page**

|  |
| --- |
| H572M 324071 Item Count**MINISTRY OF HEALTH** PHARMACY STAMPCONTROLLED DRUG PRESCRIPTION FORMCircle Y J A P 1 2 3 ZPrescription Date ……. /...**1**…/…….Patient …………………………………………………………………. NHI No. ……..**3**…………..Address **2**……………………………………………………….…….. Use safety Caps for Takeaways R: **METHADONE MIXTURE** Pharmacy use |
| Daily dose of **4**…… milligrams per day |  |
| Starting on …………/…..**5**……/………. |  |
| Total period of supply ………..**6** days |  |
| Daily dosage to be reduced by …………..**7**………………. |  |
| …………………………………………………………………………….. |  |
| Daily doses of methadone are to be consumed on the pharmacy premises |  |
| Takeaway doses are authorised for the following days |  |
| ………………………………**8**…………………………………………………… |  |
| …………………………………………………………………………………….. |  |
| Prescription to be dispensed at |  |
| …………………………….**9**…………………………………… |  |
| Practitioner’s signature ……………………………**10**…………………………….. |  |
| NZMC Reg No: …………………………. PIN No: ……………………………. |  |
| Practitioner’s Name: ………………………………..**11**……………………………… |  |
|  | **12** |
| Address: **…………………………………………………………………………………** | PHARMACY COPY |
|  |  |

1. Date prescription written to be no more than 7 days from prescription starting date (point 5).
2. Name and current residential address of patient. It is not acceptable to use the pharmacy address as the patient address.
3. Patient's NHI number.
4. Written dose, in numeric and word form e.g. 80 (eighty) mg.  Note, if a patient is undertaking any type of withdrawal from methadone, then the new prescription should state the current dose as the starting dose.  The script should then be annotated "adjust for reduction" to allow pharmacist to adjust the starting dose. Annotate with formulation of methadone to be used - BOPAS authorises 5mg/ml (consider using a stamp to pre-populate scripts). (2mg/ml can be used in doses under 20mg).
5. Start date (actual date pharmacist is to begin dispensing).  Check that the commencement date is a consumption day.
6. Total period of supply up to a maximum of 30 days, however a 28 day cycle is routine to ensure ease of keeping to a regular cycle.
7. Maximum rate of any withdrawal regimen (if any) is specified. eg. Reduce 1mg/week at request.
8. Days for which takeaways are authorised.  For example, 'Tuesday, Wednesday, Friday, Saturday and Sunday' for a patient on twice weekly dispensing who collects and consumes doses on Mondays and Thursdays.
9. Name of pharmacy.
10. Prescriber's signature.
11. Prescriber's stamp or print NZMC Reg. No., doctor name and address.  Each copy must be stamped.
12. Top three copies to pharmacy (via patient or post). Note: Bottom copy (blue) to be kept on patient file; please do not send to the pharmacy.

|  |  |
| --- | --- |
| **Ordering**:  | These CD pads are requested 3-6 monthly by GPs based on their current number of authorised patients.Orders are faxed to the Ministry of Health using the approved order form (refer to Forms section). On receipt of the pads, sign the enclosed verification of delivery form and fax to the Ministry of Health as soon as possible.Ministry of Health contacts:MedSafe Office – ph. 09 441-3670 |
| **Storage**:  | These CD pads must be stored in a secure place as for other CD prescription pads. You are advised to keep the receipt for the pads as a record of the prescription pad numbers. |
| **Theft of prescription forms** | If the prescription numbers are known, inform the Ministry of Health MedSafe office. If the prescription numbers are unknown, inform the Ministry of Health and request the prescription numbers of the pads recently sent to the practice. Inform the MOH MedSafe office of the numbers. |
| **Ceasing to prescribe:** | Notify the Ministry of Health that you no longer require these pads. |
| **Receipt of excess pads:** | Notify the Ministry of Health that you no longer require these pads.Destroy or return any unused pads to the Ministry of Health |

# Urine toxicology guidelines

International evaluation of urinalysis shows that it is not in itself instrumental in reducing harm related to illicit drug use. Urinalysis provides information only about a patient’s recent drug use and not about quantity, frequency or route of drug use and is a supplement to patient self-report. With these limitations in mind, urinalysis results are integrated into the clinical assessment.

Research has consistently indicated that where patients do not have to be concerned that they will be punished for disclosure of illicit drug use the reliability of self- reported drug use increases.

However; urinalysis may be indicated or useful in the following situations:

* where the patient or GP wishes to verify self-report of drug use
* where there is doubt regarding the accuracy of reported drug use or methadone or Buprenorphine/Naloxone consumption
* where the GP or pharmacist is concerned that a patient is intoxicated. Here a full drug screen is indicated
* as supportive information for monitoring by other services e.g. Community Corrections, Child Youth and Family Service
* for use in overall programme evaluation. Essential factors to promote reliability include:
* random sampling
* observed by Medical Officer
* requests must be on an appropriate laboratory request form.

***Note: If a patient does not complete a requested urinalysis further investigation is required.***

# Serum levels

Methadone serum levels are indicated when the clinical picture does not agree with expected/typical responses to a given dose of methadone and when this additional clinical information would be of use in making decisions regarding changes in the methadone dose.

The serum methadone level for a given dose will vary between individuals because of individual tolerance and the influence of other factors (e.g. other medications, pregnancy, individual variations in hepatic metabolism and renal clearance).

***Research to date on the clinical application of serum methadone levels is inconsistent, generally indicating that the overall clinical picture must be the foundation for any decisions regarding adequacy of methadone dose. Serum levels may not provide conclusive information.***

**Consult with BOPAS OST prior to any serum level testing.**

### Clinical situations where serum levels may be useful are:

* when dose increase beyond 120mg/day is being considered (only to be done in conjunction with BOPAS).
* when there is doubt about the clinical indications for a dose increase.
* if there is a suspected drug interaction.
* when determining the need for split dosing (only to be done in conjunction with BOPAS).
* when there is doubt regarding the accuracy of reported methadone consumption-comparison of serum levels taken on the same individual within the last 6-12 months, may assist in determining compliance).
* in pregnancy.
* when a client has a serious liver or other physical disease and there may be methadone accumulation.

### Serum level testing:

This procedure should be undertaken in liaison with the dispensing pharmacist and the BOPAS OST service:

* The patient must consume their methadone at the pharmacy at approximately the same time for 4 days (usually Mon-Thurs) prior to the blood test/s (on Fri). This is to ensure they reach a steady state for a known dose consumed daily under observation.
* On the day of the blood test the patient presents to the laboratory for their trough blood level to be taken before they consume their dose and at the same time they have been consuming for previous four days.
* If clinically indicated (see split dosing) a peak blood level is taken 3 ½ to 4 hours after the patient has consumed their dose, and before any takeaway doses are dispensed.
* Serum methadone levels can be measured using capillary blood samples when venous access is difficult. A 1ml SST tube is sufficient.

### Serum level interpretation and guidelines:

**Serum methadone trough level:**

Level to provide 24-hour relief of withdrawal symptoms is 650-1950 ngm/ml. Where a client presents with a higher trough level then 1950, this must be discussed with the OST specialist service.

**Serum methadone or buprenorphine/naloxone trough and peak levels:**

Where the peak: trough ratio is 2 or 2.5:1 or greater then split dosing may be indicated in a stable patient. Consult with the BOPAS OST Service, prior to instituting split dosing. See Split methadone or buprenorphine/naloxone dosing.

# Split Methadone or Buprenorphine/Naloxone dosing

For the vast majority of patients adequate stability can be achieved on a once daily dose of methadone or Buprenorphine/Naloxone.

Note: BOPAS is reluctant to institute split dosing of methadone or Buprenorphine/Naloxone without strong indications. Split dosing may initially involve twice daily consumption at the pharmacy or where increased takeaways are given, an increased risk of diversion of methadone or Buprenorphine/Naloxone. There must be clinical evidence that split dosing is indicated for a particular patient. (See serum levels). However where patients are stable this may be a positive and safe intervention in some situations (as outlined below).

If the peak/trough serum level ratio is greater than 2 or 2.5:1 then the patient may be considered to have fast metabolism and/or elimination of methadone or Buprenorphine/Naloxone and split dosing should be considered. (The patient will often complain of post-dose sedation and poor sleep plus marked withdrawal symptoms for some hours pre- dose.) A natural fast metaboliser is likely to remain so.

Partial splitting of the dose may also be considered for stable pregnant patients in the latter half of pregnancy in order to avoid the necessity for increase in the dose, especially for those on doses below 60mg. A single daily dose should be reinstituted following delivery (see Pregnancy and OST).

Note: A small number of women become fast metabolisers of methadone or Buprenorphine/Naloxone in pregnancy. Where this is suspected, obtain trough and peak serum levels and discuss with the BOPAS before instituting split dosing. These women are at greater risk of destabilisation in pregnancy and timely assessment and management can prevent this.

Split dosing may also be considered for stable patients in the latter part of a planned withdrawal from methadone or Buprenorphine/Naloxone (usually at doses of 30mg or less) in order to reduce pre-dose withdrawal symptoms and to increase the likelihood of successful completion of withdrawal from methadone or Buprenorphine/Naloxone.

Split dosing may be considered for stable patients to better manage physical pain symptoms by twice-daily peak serum levels.

Note: Split dosing (including the proportions of each dose) requires the approval of the BOPAS OST team.

# Pregnancy and OST

In recognition of the potentially complex issues associated with methadone or Buprenorphine/Naloxone treatment in pregnancy, BOPAS prefer to provide specialist care to the patient and additional support to the GP once a patient’s pregnancy is confirmed.

The Addiction Liaison Clinician will contact the GP to discuss appropriate management and support during the pregnancy.

**Note**: Most pregnant women require one or more dose increases (usually a total increase of 5 to 20 mg) in the second half of the pregnancy. This is due to decreasing serum levels from the increased circulating blood volume and the metabolism of Methadone or Buprenorphine/Naloxone by the foetal liver. (See also split Methadone or Buprenorphine/Naloxone dosing.) Following delivery the dose will usually need to be decreased again. The requirement for a dose decrease is based on the patient’s report of increased sedation and clinical assessment.

### Vomiting in pregnancy

Replacement of a vomited dose may be arranged when the pregnant woman vomits within less than 30 minutes of consuming the dose and replacement is considered to be appropriate. The range of replacement for vomited doses is between 50% and 100%. When deciding the replacement dose the full clinical picture should be taken into consideration. (See replacement doses p18)

# Concurrent medical conditions

## HIV/hepatitis B and C

Issues for the GP managing a patient on Opioid Substitution Treatment (OST) are:

* testing for HIV, Hepatitis A, B and C (including Hep C PCR RNA test).
* preventing infection/transmission.
* monitoring LFTs in those with chronic Hepatitis B & C.
* Where possible the GP or BOPAs can provide treatment for Hep C, or refer to the liver specialists where indicated
* offering Hepatitis A & B vaccination to those who are HAV & HBV antibody negative.

## Chronic liver disease

Patients with chronic liver disease on long-term opioid maintenance usually do not require alterations in their dose. However; if there is an abrupt change in liver function they may require dose adjustment. The development of jaundice is also a sign that the liver may not be able to metabolise methadone or Buprenorphine/Naloxone at the normal rate.

Where there is significant impairment it is suggested that the methadone serum level is checked every 2 to 3 months to ensure that it is not rising due to impaired metabolism of methadone. Seek the advice of BOPAS or a specialist gastroenterologist if there are concerns.

## Respiratory disorders

Methadone or Buprenorphine/Naloxone is a respiratory depressant and care should be taken in prescribing methadone or Buprenorphine/Naloxone to patients with these disorders.

## Epilepsy

Note that carbamazepine, phenytoin and phenobarbitone interact with methadone (see Methadone or Buprenorphine/Naloxone interactions section).

## Mental health disorders

Note that antidepressant and antipsychotic medications may interact with Methadone or Buprenorphine/Naloxone (see Methadone or Buprenorphine/Naloxone interactions).

# Pain management

### Acute pain:

Mild to moderate acute pain can usually be effectively managed with simple analgesics (including mild opioid medications) and/or other appropriate medications.

**Opioid maintenance patients with acute severe pain usually require higher doses of opioid agonists than non-opioid tolerant patients in order to achieve adequate pain relief. (Many receive inadequate analgesia for acute severe pain.)**

In the event an OST patient is hospitalised their GP prescriber will need to liaise with the hospital staff to ensure continuation of methadone or Buprenorphine/Naloxone in hospital, cancellation of the prescription at the community pharmacy and the resumption of prescribing at the community pharmacy on discharge. BOPAS can assist as required.

### Chronic pain:

Chronic pain in Opioid maintenance patients should be managed in the same way as it is for other patients.

Methadone or Buprenorphine/Naloxone as prescribed for maintenance treatment may provide partial relief for some chronic pain.

BOPAS advises consultation with a specialist pain management service or BOPAS medical officer before considering the regular prescribing of opioid medication for the management of chronic pain.

**Note: Long term methadone treatment can saturate and dull opioid receptors leading to increased patient pain levels as the body tries to compensate for inhibited pain recognition (hyper-analgesia; increased sensitivity to pain secondary to long-term blockade of opiate bases pain receptors)**

# Transfers between pharmacies

The Case Manager and or Addiction Liaison Clinician may assist you with this. Otherwise:

* establish with the patient which dispensing pharmacy in the area is suitable and confirm with the pharmacy that they are able to dispense to the patient
* cancel the script at their existing pharmacy
* write a new script for the new pharmacy and fax it to them if necessary
* contact the Addiction Liaison Clinician to request that an ‘Introduction to Pharmacy’ letter with a photo ID is sent to the new pharmacy
* the patient will be required to provide photo-ID at the new pharmacy.

# Transfers to another Opioid Substitution Treatment (OST) programme

Contact the BOPAS OST service with details about the proposed new location of the patient and request assistance with the transfer.

***Note: Waiting times for transfer to other OST programmes vary considerably throughout the country.***

Where a patient is stable the programme at the new location may agree to the transfer of the patient directly to a GP authorised by that programme and the transfer may be achieved more quickly. Alternatively out of area prescribing may be arranged until such time as the local OST programme is able to take them onto their programme. However; during this interim period the patient should return to be seen at least 3 monthly by their prescribing doctor.

# Prescribing when GP is on leave/absent

GPs are urged to appoint a locum or practice partner to prescribe mMethadone or Buprenorphine/Naloxone to their authorised patients in their absence and **to ensure that BOPAS OST, locum/practice partner and other practice staff are informed of this.**

The BOPAS Addiction Liaison Clinician is also available to support the locum/practice partner.

Should the GP plan to be away for longer than three months he/she needs to contact the Addiction Liaison Clinician so that BOPAS can arrange authorisation(s) for the locum or a practice partner (as required by MedSafe) and provide training and extra support.

# Prescribing for holidays/travel

### Public holidays: (Please contact BOPAS for support as required.)

The GP is responsible for identifying when a patient’s dispensing day/s fall on a public holiday and should annotate the prescription accordingly, i.e. write instructions for any change in dispensing required due to closure of the pharmacy. If space is limited use an additional sheet and attach it to the prescription. The Addiction Liaison Clinician can assist with a generic holiday schedule that can be adjusted to suit individual needs.

It is preferred that no more than three consecutive takeaway doses are approved at any one time, except in the case of public holidays where pharmacies are not providing a service or in exceptional circumstances. In such cases 1 (one) additional takeaway dose (i.e. a total of four takeaway doses) may be prescribed for a patient providing the Patient, the Addiction Liaison Clinician and the GP are confident that it is a safe arrangement

### Patient holidays (within New Zealand)

The GP, with Addiction Liaison Clinician support, is responsible for organising alternative dispensing arrangements for patients on holiday. See transfers between pharmacies.

Patients should provide the GP with adequate notice of holidays.

### Travel overseas

GPs are advised to contact the Addiction Liaison Clinician for information and assistance with arranging overseas travel as soon as they receive a request from a patient. It is preferred that arrangements be made for the patient to be dispensed Methadone or Buprenorphine/Naloxone via a programme in the country of destination.

***Note: If the patient needs to travel with methadone or Buprenorphine/Naloxone doses require an exportation letter (explains dose and form (usually tablets) prescribed and the dates the medication is prescribed for).***

Adequate notice (usually several weeks) is required to make these arrangements. More time may be required when a patient is travelling to more than one destination or where other complexities exist. There are a number of countries where OST is not available and/or where importation of Methadone or Buprenorphine/Naloxone is illegal. In an emergency situation overseas travel may be arranged more quickly but this does not apply to all countries of destination.

### Hospitalisation

The hospital may phone to confirm a patient’s prescription. BOPAS will need to file an authority to prescribe form to the hospital’s medical staff while the patient is in hospital. If patients are not dispensed by their usual pharmacy for more than seven days they will require a new prescription on discharge from hospital.

### Imprisonment/detention in Police custody

If a patient is detained in police custody or prison, the GP is to contact the Addiction Liaison Clinician who will organise for Methadone or Buprenorphine/Naloxone to be prescribed by BOPAS medical officer while the patient is detained.

If OST patients are sentenced to a prison term, Methadone or Buprenorphine/Naloxone treatment will continue in the prison environment. Upon release from police custody or prison and once stabilised patients may return to the care of the GP.

# Treatment completion

“Entering and staying in treatment, coming off opioid substitution treatment and exiting structured treatment are all important indicators of an individual’s recovery progress, but they do not in themselves constitute recovery. Coming off OST or exiting treatment prematurely can harm individuals, especially if it leads to relapse, which is also harmful to society. Recovery is broader and more complex journey that incorporates overcoming dependence, reducing risk-taking behaviour and offending, improving health, functioning as a productive member of society and becoming personally fulfilled. These recovery outcomes are often mutually reinforcing.”

The National Treatment Agency for Substance Misuse (2012) in the NZ Practice Guidelines for Opioid Substitution Treatment (2014) p26.

Where a patient expresses an intention or desire to withdraw from methadone or Buprenorphine/Naloxone please contact the Addiction Liaison Clinician for support with this. **Consider**:

* **motivation** for withdrawal
* giving information to the patient e.g. the orange *“Coming off Methadone”* booklet
* discuss withdrawal options (see dose reductions see next page and p14, discuss Buprenorphine/Naloxone p10) and develop a plan with the patient
* patients may also stop reduction for a period or have small dose increases before recommencing reductions. As with the opening quote; Recovery is broader and more complex journey
* review the withdrawal process each time the patient is seen or at the patient’s request
* offer and negotiate a ‘window period’ of between 0 and 12 weeks with the patient during and prior to the completion of the withdrawal from Methadone or Buprenorphine/Naloxone. The window period is the time after the last Methadone or Buprenorphine/Naloxone dose is consumed within which the patient can choose to immediately restabilise on Methadone or Buprenorphine/Naloxone. (Note: The restabilisation on Methadone or Buprenorphine/Naloxone will be carried out by BOPAS, and the patient transferred back to the GP programme as appropriate)
* notify the Addiction Liaison Clinician of the date on which the patient last consumed Methadone or Buprenorphine/Naloxone and of the negotiated window period
* if the patient makes contact wishing to re-stabilise on Methadone or Buprenorphine/Naloxone within the window period contact the Addiction Liaison Clinician about making an appointment at BOPAS for assessment regards restabilisation
* if the patient makes contact wishing to recommence on Methadone or Buprenorphine/Naloxone after the window period is completed then refer them to BOPAS for reassessment.

If you believe that positive treatment outcomes will be compromised by withdrawal contact the Addiction Liaison Clinician to arrange a joint appointment with the patient to discuss and decide on an appropriate course of action, or contact the BOPAS, medical officer for advice/support.

# Method of withdrawal

There is no ideal method of withdrawal from Methadone or Buprenorphine/Naloxone. It is important that any reduction plan is done in consultation with the client, GP and Addiction Liaison Clinician.

Possible approaches to withdrawal are:

**Fixed**

The rate of reduction of Methadone or Buprenorphine/Naloxone is set by the GP in consultation with the patient and can only be altered by the GP. Recommended methadone reduction rate is 2.5mgs per script cycle. Some patients tolerate larger and faster initial reductions. Statistically the faster the reductions, the higher the rate of relapse as smaller reductions are better tolerated and momentum maintained.

**Flexible**

The rate of reduction of Methadone or Buprenorphine/Naloxone is entirely within the control of the client.  The client and GP agree on a rate that is then added to the prescription, for example “1mg per week or 2mg per fortnight AT REQUEST”.  It then allows the client to access a reduction from the pharmacy whenever they feel ready. These patient initiated dose changes may only be   reductions, any increase in dose must be renegotiated with the GP and a new prescription written.  The script must then be annotated with "adjust dose for reduction" to allow pharmacist to adjust the dose accordingly.

**Blind**

The patient has the option of requesting a blind reduction, to be arranged by the GP in consultation with the Addiction Liaison Clinician and Pharmacist and the script to be appropriately annotated by the GP. The details of the dose reductions and administration are arranged by the GP with the pharmacist.

Decisions must be made after assessment of the patient's needs and preferences, and in consultation with the patient.

### Rate of withdrawal:

The following guidelines are recommended:

|  |  |
| --- | --- |
| **Current methadone or buprenorphine/naloxone dose/day** | **Weekly or fortnightly or monthly reduction** |
| Above 50mg | 5mg or less |
| 30-50mg | 2.5mg or less |
| Less than 30mg | 1-2mg or less |

The rate of withdrawal should be reviewed each time a patient is seen. If there is evidence that a patient's treatment outcomes are compromised by the rate of withdrawal, a slowing or cessation of the dose reduction, or even a temporary increase in the dose is recommended, rather than introducing ancillary medication.

Note:  Once down to 20mg per day or less, consider changing to the Biodone 2mg/ml substance to enable small reductions to be made more easily. The pharmacy will need to be notified in advance so that they can order this in.

If clients struggle with the reduction off lower doses of methadone, they could be offered a transfer to Buprenorphine/Naloxone, as this might be better tolerated.

# Patient complaints

Wherever possible changes to a patient’s treatment should be made with patient participation and the reasons for any decision clearly conveyed to the patient.

When a patient is unhappy about such changes the following process can occur:

* encourage the patient to discuss the issue further with you
* if they are unwilling, or still unhappy, the patient can contact the Addiction Liaison Clinician to review the decision and attempt to find a resolution
* if still unhappy, the patient can request that the Addiction Liaison Clinician or BOPAS Coordinator set up a case conference between the patient, a support person and/or a Health Advocate, the GP and relevant BOPAS staff. Minutes of this meeting will be made by a BOPAS staff member and placed in the patient’s file, and a copy made available to all participants.

Patients should be informed that they may make a formal written or verbal complaint to the BOPAS manager (see contact details) or the Health & Disability Commissioner but advised that the above process may be a speedier way of addressing clinical issues. The process outlined above does not compromise in any way the patient’s treatment by the service or prevent the patient from choosing to follow the formal complaints process via the manager of the service.

# Contact details

Bay of Plenty Addiction Service (BOPAS)

Kowhai House, Tauranga Hospital, Cameron Road

Private Bag 12024, Tauranga 3143

*Opening Hours: Mon-Fri 8.30am-5.00pm*

Email: bopas@bopdhb.govt.nz

|  |  |  |
| --- | --- | --- |
| **Area** | **Phone** | **Fax** |
| BOPAS, reception | (07) 579 8391 | (07) 5718095 |
| BOPAS, Team leader (*Sally Whitelaw*) | (07) 579 8391027 836 1959 | (07) 5718095 |
| GP Liaison Nurse*(Sue Coleman)* | (07) 579 8391027 287 9727 | (07) 5718095 |
| BOPAS Lead Clinician*(Dr……* | (07) 579 8391 | (07) 5718095 |
| BOPAS, Clinical Lead*(Nick White)* | (07) 579 8391021 867 747 | (07) 5718095 |
| BOPAS, Consumer Advisor (position vacant) | (07) 579 8391 | (07) 5718095 |
| MHAS Crisis team (after hours) | (07) 579 83290800 800 508 | (07) 571 8647 |

**Note: Please do not provide individual staff phone numbers to patients.**

**References**

Bazire, S. 2000. Psychotropic Drug Directory. Wiltshire, Mark Allen Publishing. British National Formulary 2001. Wallingford, Pharmaceutical Press.

Bezchlibnyk-Butler, K & Jeffries, J. 2000. Clinical Handbook of Psychotropic Drugs, 10th Ed. CMPMedica (NZ) Ltd. (2010). *Mims New Ethicals* (Jan-Jun 2010, Issue 12). Auckland: CMPMedica Ltd.

Donaher, P. A., & Welsh, C. (2006). Managing Opioid Addiction with Buprenorphine [Electronic version].

*American Family Physician, 73, 1573-78.*

Hayes, B. D., Klein-Schwartz, W., & Doyon, S. (2008). Toxicity of Buprenorphine Overdoses in Children [Electronic version]. *Pediatrics, 121, 782-86.*

Matua Raki. (2011). *Substance Withdrawal Management: Guidelines for medical and nursing practitioners in primary health, specialist addiction, custodial and general hospital settings.* Wellington: Matua Raki.

Minstry of Health. (2010) *New Zealand Clinical Guidelines for the Use of Buprenorphine (with or without Naloxone) in the Treatment of Opioid Dependence.* ISBN 978-0-478-35932-9 (online) HP 5067

Minstry of Health, (2014) New Zealand practice Guidelines for Opioid Substitution Treatment.

ISBN 078-0-478-42786-8 (online) HP 5816

Stockley, Ivan H., 2001. Drug Interactions Fifth Edition. London, Pharmaceutical Press.

[www.torsades.org](http://www.torsades.org/)

Buprenorphine/Naloxone Data Sheet. (2006). Retrieved on 10th October, 2013, from [http://www.medsafe.govt.nz/profs/datasheet/s/Buprenorphine/Naloxonetab.pdf](http://www.medsafe.govt.nz/profs/datasheet/s/Suboxonetab.pdf)

Toronto, Hogrefe & Huber. Dept. of Health UK, Scottish & Welsh Offices Dept. of Health, Dept. of Health & Social Services, Northern Ireland. 1999. Drug Misuse & Dependence -- Guidelines on Clinical Management. Norwich, Her Majesty’s Stationary Office.

Turning Point. (2005). *Buprenorphine/Naloxone: A Guide to Treatment.* Australia: Turning Point.

Waitemata District Health Board. (2012). *Buprenorphine (with naloxone) treatment with CADS.* Auckland: Waitemata District Health Board.

Wiegand, T. J. (2013). *Buprenorphine/ Naloxone Toxicity*. Retrieved October 10th, 2013, from <http://emedicine.medscape.com/article/1641147-overview>.

# Appendix (a)







# Appendix (b)



# Appendix (c)

**Authority for a general practitioner to prescribe controlled drugs for the treatment of addiction**

**(section 24(2)(d) MODA)**

#### This form should be used by a lead clinician when authorising a general practitioner (GP) to prescribe controlled drugs for dependence under Section 24(2)(d) Misuse of Drugs Act 1975.

I, [name of medical practitioner], [specialist service], authorise:

|  |  |  |
| --- | --- | --- |
| GP name |  | GP practice |

#### to prescribe controlled drugs for the treatment of addiction to:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Consumer name |  | NHI |  | Consumer address |

The conditions of this authority are set out below.

|  |  |
| --- | --- |
| [Specify general or particular conditions of authority including, where relevant:* the particular controlled drug
* consume of premises
* takeaway dose(s)
 | [insert drug and dose] [insert days and pharmacy] [insert days] |

This authority expires on [date].

|  |  |  |
| --- | --- | --- |
| Signature |  | Date |

**[Medical practitioner]**

[Specialist service]

#### cc. [GP]

[Dispensing Pharmacy]

Consumer file

Medicines Control, Ministry of Health, PO Box 5013, Wellington

(medicinescontrol@moh.govt.nz)

Example

|  |  |
| --- | --- |
| Specify general or particular conditions of authority including, where relevant:* the particular controlled drug
* consume of premises
* takeaway dose(s)
 | Methadone 70 mg dailyMonday/Wednesday/Friday at Radius Care Pharmacy Tuesday/Thursday/Saturday and Sunday |