

Guidelines on Methadone Therapy in Myanmar

for Prescribers and Dispensers



**Department of Health, Ministry of Health
Union of Myanmar
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Methadone Guidelines for Prescribers



About these guidelines

These guidelines are divided into two separate parts: one for prescribers and one for dispensers. They are bound in one volume to enable ready access to the guidelines provided to your professional colleagues, enhancing coordination and cooperation between the practices of both professional groups. The book should be wire-bound for easy access to the information relevant to your practice – simply turn your section to the front.

The guidelines have been prepared by practitioners with expertise in the use of methadone to treat opioid dependence. They are intended to assist medical practitioners and dispensers to treat opioid-dependent patients in a safe and effective manner. The guidelines are general recommendations and are provided for information purposes only. The guidelines cannot provide detailed direction in respect to the management of every patient in every clinical situation, and do not constitute specific treatment advice. Individual medical practitioners and dispensers are responsible for decisions about the safety and effectiveness of treatment used for each patient. The guidelines are not intended to replace professional judgment in individual cases.

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Summary

Section 1: Introduction

Heroin problems and the effectiveness of methadone treatment. The risks inherent in use of methadone. Methadone use for withdrawal or long-term maintenance, and as an effective component of a harm reduction strategy for heroin use.

Section 2: Clinical Pharmacology and Toxicology of Methadone

Safe and effective use of methadone. Its distinctive pharmacology. Metabolism and drug interactions. A description of adverse effects and toxicity.

Section 3: Becoming a Methadone Prescriber

Training for medical practitioners intending to seek approval to prescribe methadone. Arrangements for dispensing to patients, and covering prescriber's absence.

Section 4: Intake Procedures

Establishing the identity of the patient, assessing their suitability for treatment with methadone, and undertaking the clinical assessment necessary for effective treatment. Registration requirements.

Section 5: Prescribing Guidelines - Maintenance

Induction into treatment, the prescription, maintenance dose, counselling, review, co-operation with allied health professionals, and dispensing arrangements. Managing patients with special needs. Take-Away doses. Transfer between prescribers and dispensers. Termination of treatment. Prevention of methadone-related deaths

Section 6: Prescribing Guidelines - Withdrawal

Using methadone for withdrawal. Initial dose and rate of withdrawal.

Section 7: General Information

Prescription drug abuse, legal responsibilities, confidentiality, driving and methadone. Forms use in methadone treatment.

Appendices

List of clinical support services, features of a methadone prescription, and guidelines for deputizing colleagues.

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Section 1

Prescribers

Essentials of Methadone Prescribing

1. Familiarize yourself with the unique benefits (Section 1), toxicity and pharmacology of methadone in the treatment of opioid dependence (Section 2).
2. Establish (Section 4):
 - ◆ The identity of the patient
 - ◆ That the patient is opioid dependent
 - ◆ The degree of neuroadaptation
 - ◆ Goals of treatment on which you and the patient both agree.
3. Establish an appropriate starting dose (Section 5.1). This dose should usually be 20 - 30 milligrams per day. It is unusual for patients to require higher doses. Patients rarely require doses of more than 40 - 50 milligrams at the end of the first week of treatment.
4. Register the patient as a drug user participating in the methadone program before prescribing methadone, to enable coordination of the patient's treatment and to avoid the risk of multiple dosing with methadone (and / or other opioids) by other practitioners.
5. Ensure the prescription gives clear, unequivocal directions to the dispensing point, including (Section 5.3):
 - ◆ The precise dose in words and figures
 - ◆ The date of the last dose on this prescription before review
 - ◆ The name of the dispensing point at which it is to be dispensed.
6. Review the patient's condition before the third or fourth dose, to determine the need for dose revision and to manage the high risk of methadone or combined drug toxicity during induction into treatment (Section 5.1).
7. When transferring a patient between dispensing points, or Drug Treatment Centres, avoid the risk of duplicated dosing by providing clear instructions in writing to both sites about their respective finishing and starting dates (Section 5.10).
8. Before authorizing take-away doses:
 - ◆ Contact the dosing dispensing site to check the regularity of dosing and the patient's progress, and
 - ◆ Ensure the patient is stable and meets all the criteria specified in the guidelines (Section 5.9).
9. Send notification to the Department of Health as soon as you terminate treatment.
10. Do not increase the methadone dose by more than 10 milligrams at a time, and not by more than 30 milligrams over any seven-day period.
11. Remember: "Start Low, Go Slow, Aim High"

Introduction

These guidelines have been developed to assist practitioner and patient decisions about the safe and effective use of methadone to treat opioid dependence.

1.1 Methadone - An Effective Treatment for Opioid Addiction

Methadone has become established in many parts of the world as an effective treatment for opioid dependence. Some long-term heroin users can be successfully treated with detoxification and abstinence-based treatments, but studies have shown that more than 70 per cent will relapse to illicit opiate use within one to two years. Methadone can prove valuable in assisting these people to successfully manage physical dependence, drug craving and compulsive drug use.

Methadone has been used to treat opioid dependence, both in detoxification from opioids and maintenance treatment for more than 40 years. It is useful for these purposes because:

It has cross-tolerance with other opioids, enabling it to be substituted for abused drugs such as heroin, morphine and opium.

It can be taken orally, so drug-dependent patients can avoid the reinforcing effects of injecting.

It is long acting, enabling once-daily dosing.

Drug dependence is a complex condition involving social, psychological and biological components. Dependence on illicit opiates is a serious condition currently associated with severe morbidity, risk of Blood Borne Viruses transmission and death. These risks arise from both drug overdose and the morbidity and injury that result from chronic illicit drug use, injecting or misuse of licit opioids. Methadone can be compared to other drugs that are effective in treating serious chronic relapsing conditions such as hypertension and diabetes; these conditions, like opiate dependence, are chronic, require daily treatment, and have a high risk of adverse effects if treatment compliance is poor.

Methadone is effective in reducing dependence on heroin. Supervised daily supply of an adequate dose of methadone in a structured program has been demonstrated to:

Reduce or limit illicit heroin use.

Decrease criminal activity.

Stabilise the patient's life.

Reduce chaotic drug taking.

Make it possible for heroin and opium users to lead productive lives.

Decrease high-risk needle use such as sharing.

As a result there are substantial benefits for the individual, their family and society.

Benefits of Methadone Treatment

Decreases illicit opiate drug use.

Reduces illness and death from illicit drug use.

Reduces criminal activity.

Reduces high-risk needle sharing.

Enhances social productivity.

Methadone maintenance treatment may be delivered in a variety of different settings including:

- substance use treatment centres/clinics (outpatient/inpatient);
- community-based health centres/clinics;
- hospital-based health clinics;
- mental health hospitals
- correctional facilities.

Practitioners from many different disciplines and backgrounds - including medicine, substance use treatment, nursing, social work and mental health, among others - may be involved in delivering methadone maintenance treatment programs. Their roles will vary, depending on factors such as qualifications, program setting, available resources and geographic location.

The Myanmar methadone program will initially be based on delivering services through specialist drug treatment centres and selected hospitals. It will make methadone more readily available, and will enable integration of the treatment of opioid addiction with general medical care. This is important, because many opioid-dependent patients have experienced serious illness, HIV infection or injury as a result of their years of injecting drug use and dependence. In the future under the coordination of the referral DTC, methadone may be dispensed in community-based programs so treatment of drug addiction will be normalized and de-stigmatized, and the congregation of large numbers of patients around drug treatment centres will be avoided. It will then be easier for patients to retain their anonymity. With a wider spread of medical and dispensing services, accessibility and choice will be improved. It is also expected that co-location of treatment services for opioid dependence, tuberculosis and HIV will provide efficiencies for patient access and improve adherence with treatment for these common comorbid conditions.

Despite the proven success of methadone programs, there are some risks. Methadone is a potentially toxic drug with a low therapeutic index (The therapeutic dose is close to the toxic dose). It is often used to treat patients who may have a history of compulsive and reckless drug use. Some patients have psychiatric and social problems. Using a potentially toxic drug to treat a patient whose behavioural history may put them at special risk warrants a cautious approach.

The Myanmar methadone program is structured through careful initiation processes and dose increases with supervised dosing to minimize the risks involved and maximize the benefits through long term treatment, counselling and support. It is for these reasons that the Myanmar methadone programme's motto is **"Start Low, Go Slow, Aim High"** meaning a progressive carefully monitored beginning and progress in dosification aiming to reach effective therapeutic levels of methadone expected to be between the range of 60 to 120 mg per day for most of the patients.

1.2 The Problem of Heroin Use

Heroin and opium are short acting opiates with a marked tendency to develop a dependence syndrome, when used in a recreational manner for their euphoric or analgesic properties. The mode of administration of these drugs may in addition generate a risk of drug overdose or blood born virus transmission. The illicit and often expensive nature of heroin and opium contribute to the criminal behaviours associated with their use; primarily acquisitive crime and drug trafficking. There are often substantial behavioural changes associated with the dependence syndrome which have their own social cost as individuals diminish interest in other activities, relationships and their own health.

1.3 Risks Associated with the Methadone Program

Methadone is an opioid drug, and as such is prone to misuse and toxicity. The methadone program provides treatment to a high-risk population amongst whom misuse of prescription drugs and alcohol is highly prevalent. Under these circumstances, considerable care is necessary. The planned Myanmar program is designed to minimize the risks and enhance the effectiveness of methadone maintenance treatment. The risks of methadone treatment and the countermeasures to minimize them are described in the following table.

Table A: Risks of methadone treatment

Risk	Countermeasure
Complicated pharmacokinetics, prescriber/dispenser unfamiliarity	Prescriber/dispenser training; an registration system
Dosing by multiple prescribers and dispensers	A registration system
Poor compliance and diversion of syrup to illicit use and trafficking	A supervised dosing program; limit on the number of take-away doses
Trafficking and consequent overdosing of non-tolerant people not on the methadone program	Tight control of take-away doses; discretion in judging patient suitability for take-away doses
Illicit injection of take-away doses	Dilution of take-away doses to at least 200 millilitres; discretion in judging patient suitability for take-away doses
Child poisoning with methadone	Tight control of take-away doses; child-resistant packaging and dilution of doses
Multiple dosing at time of transfer	Meticulous arrangements for transfer of registration
A high risk of drug overdose in the first 10 days of treatment	Meticulous care and frequent patient review in the first 10 days; dispenser alertness to signs of toxicity
A high risk of combined drug toxicity deaths	Dispenser alertness to signs of toxicity; comprehensive assessment of patients and the management of polydrug abuse provision of warning to patient about risk, and education of patient and family/friends about signs of overdose and coma (unrousable, 'snoring', respiratory depression, cyanosis)
Injury	Provision of warning to patient about risks of driving / using machinery during dose stabilization or while the dose is increasing
Psychiatric co-morbidity, including suicide risk	Assessment of suicide risk; assessment of patient psychiatric status; maintenance of a high index of suspicion, and timely response to suicide risk; referral to specialist methadone service if appropriate for management of dual disability
Discontinuation of treatment	Set-up of supervised dosing to be as convenient as possible; discrete use of take-away doses

1.4 Types of Methadone Treatment

Withdrawal. Methadone can be used to medicate withdrawal for opioid-dependent patients, however relapse is no less common than other withdrawal regimens. A dosage schedule reducing the dose of methadone over 10 - 30 days can assist in significantly reducing withdrawal symptoms (Section 6).

Maintenance. A high proportion of patients who have withdrawn from opioid dependence will relapse. A program of maintenance on methadone for many months to several years can help these patients (Section 5).

In Myanmar the methadone program is initially to be delivered by drug treatment specialists and hospital dispensaries. Specialist methadone services at Drug Treatment Centres provide support for the assessment and management of complicated cases. Training is expected to be provided in the future for community practitioners who wish to become involved in the program.

1.5 Harm Reduction

A harm reduction philosophy involves accepting that despite all efforts to control supply and reduce demand, many people will continue to have access to licit and illicit drugs, and to use them in a way that puts them and society at risk of serious harm. Cigarettes, alcohol, prescription drugs and illicit drugs such as heroin and stimulants are readily accessible, and they are used in quantities and manners that can cause harm. Harm reduction aims to reduce the adverse health, social and economic consequences of drug use.

Harm Reduction activities include:

Improving access to sterile needles and syringes to reduce the need to reuse and share this injecting equipment, which exposes injecting drug users to the risk of transmission of blood-borne viruses such as hepatitis B and C and HIV.

Providing information about safe injecting practices.

Providing information about the prevention and management of heroin-related overdose.

Methadone treatment provides an opportunity for patients to avoid the need to obtain and inject heroin. This is useful for individuals for whom abstinence-based methods of dealing with their heroin addiction have failed because they continue to relapse. Effective doses of methadone have been demonstrated to reduce the quantity and frequency of illicit heroin use, along with the consequent criminal activity and the risk of transmission of blood-borne viruses.

The goals of methadone treatment include normalizing the patient's life, integrating them back into their family and the community, and keeping them in treatment when necessary. Methadone patients should be treated as far as possible in the same way as other patients.

Section 2

Prescribers

Clinical Pharmacology and Toxicology of Methadone

2.1 Methadone Pharmacology

Familiarity with three characteristics of methadone pharmacology is necessary for the safe and effective use of this drug. Most prescribers are unfamiliar with the use of a drug with a slow onset of peak blood levels (four hours), long half-life (25 hours) and low therapeutic index (overlap of toxic and therapeutic blood levels). Methadone has a complex range of effects that can vary widely among individuals. It is used as a long-acting analgesic, and as a substitute treatment for opioid (mostly heroin) addiction. Methadone action results from binding to the opioid receptors in the brain. Oral methadone is well absorbed from the gastrointestinal tract, and it is fat soluble. It undergoes extensive first-pass metabolism in the liver. It binds to albumin and other proteins in the lung, kidney, liver and spleen, and there is gradual equilibration between these tissues and blood over the first few days of dosing. Repeated dosing leads to accumulation.

An understanding of methadone pharmacology is necessary to enable its safe use by patients with compulsive drug use problems, often complicated by co-abuse of other CNS-depressant drugs. The highest risk of overdose occurs in the first few days of treatment as ingested methadone equilibrates with tissue stores, and the patient's drug taking stabilises.

- **Half-life.** After a single first dose, the apparent half-life is shorter than in extended use, because much of the initial dose is distributed into the tissue stores described. Following ingestion, blood levels rise for about four hours, then begin to fall. The apparent half-life of a single first dose is 12-18 hours, with a mean average of 15 hours (See figure C).

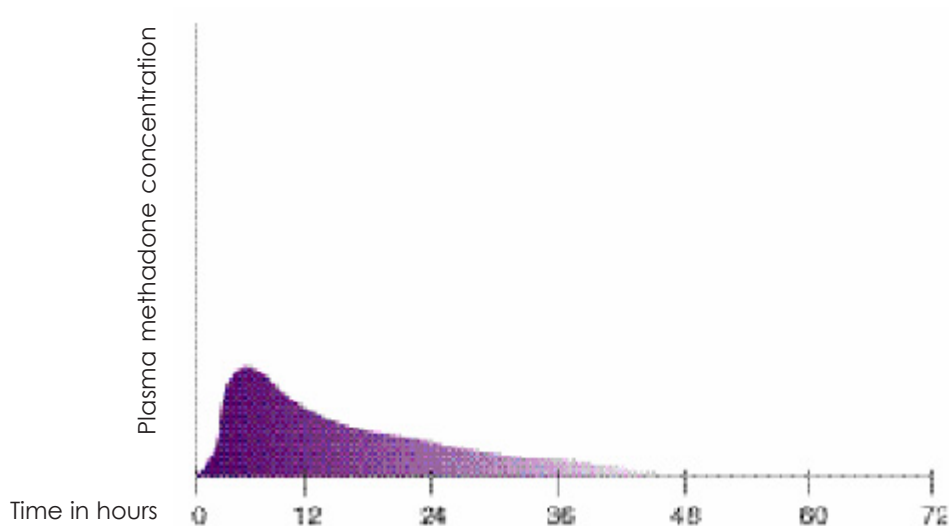


Figure C: Blood Levels after Single First Dose of Oral Methadone¹

Methadone Pharmacology

Slow build to peak blood levels (4 hrs)
Long half-life (25 hrs)

Low therapeutic index
Accumulation from repeated dosing

¹ Source: Victorian Methadone Guidelines, Department of Human Services, Victoria, Australia

- Commencement of treatment.** Over the first few days of treatment, methadone binds to plasma proteins and tissues (lung, kidneys, liver, spleen), and blood levels equilibrate with these tissue stores. The half-life reflects clearance from the system, and therefore extends to 13-47 hours, with a mean average of 25 hours (See figure D).

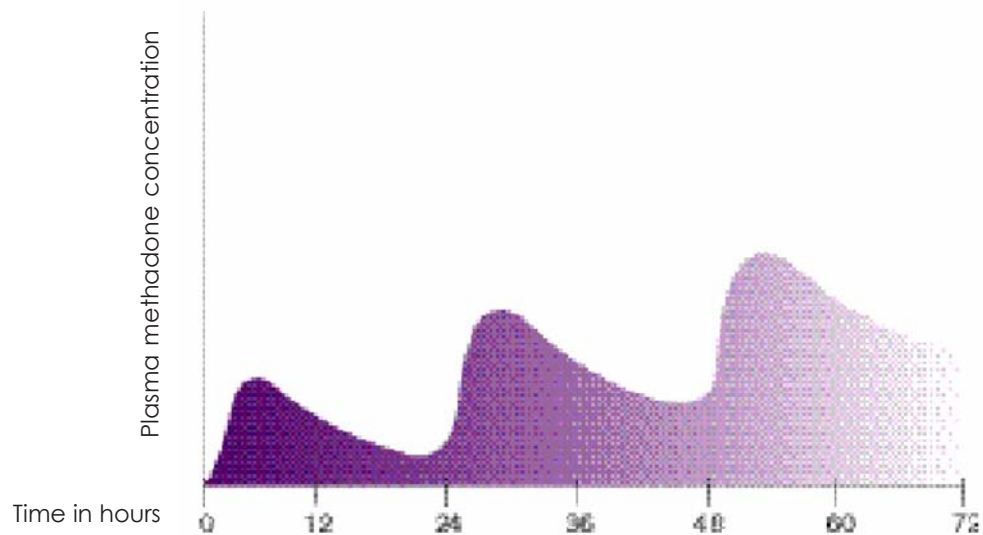


Figure D: Blood Levels after First Three Days of Oral Once-Daily Dosing²

- Regular dosing.** Once tissue and blood levels have equilibrated, variations in blood concentration are relatively small. Once-daily dosing is adequate to control craving and achieve the objectives of treatment for opioid dependence (See figure E).

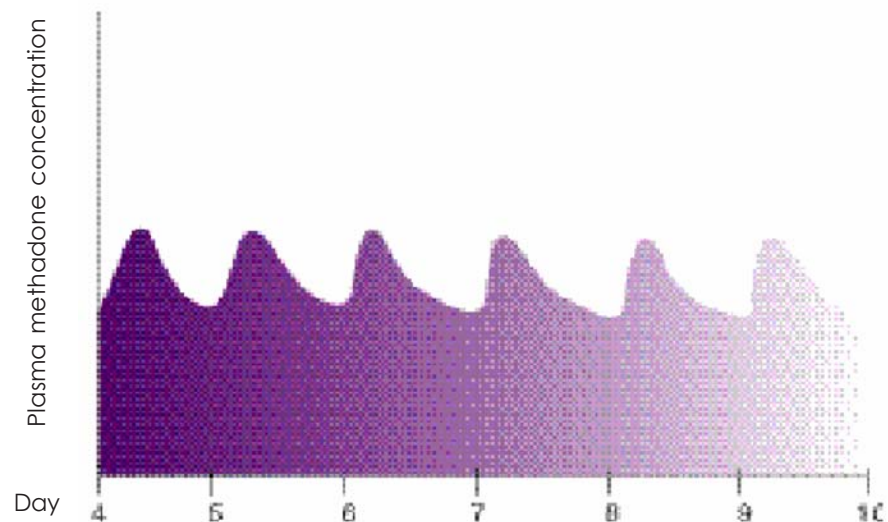


Figure E: Blood Levels during Established Once-Daily Dosing with Oral Methadone (Steady State)²

- Missed dose.** If one day's dose is omitted from a regular daily dosing regime, the blood concentrations fall gradually over 24-48 hours. Twenty-four hours after the last dose, levels fall to about 50 per cent of the peak level at four hours after dosing; after another 24 hours, they fall to about 25 per cent of the peak level (See figure F).

¹ Source: Victorian Methadone Guidelines, Department of Human Services, Victoria, Australia

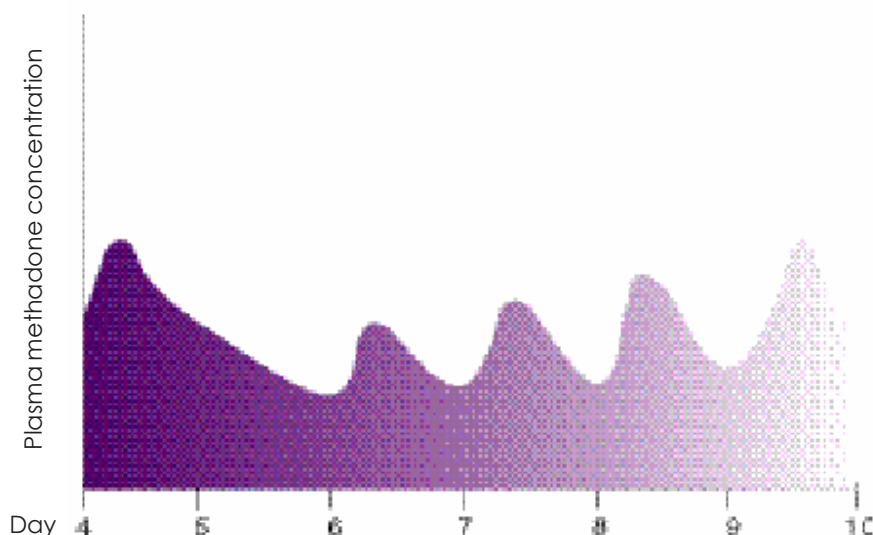


Figure F: Blood Level Recovery over Three Days after a Single Missed Daily Dose³

- Tolerance. Tolerance to the effects of opioids (including methadone) is the result of brain changes that occur when opioids are constantly present for several days. The brain's natural opiates are suppressed, receptor sites increase and the rate at which opiates are metabolized increases. Change at the nerve endings is called neuroadaptation.

2.2 Metabolism and Drug Interactions

Methadone is largely metabolized by the P450 enzyme CYP3A4, which is found in the liver primarily and in small quantities in the gastrointestinal mucosa.

- Renal clearance. Renal clearance contributes a small proportion of total clearance at a urine pH of 7. If urine is acid (pH below 6), then renal clearance increases up to about 30 per cent of total body clearance; if urine is alkaline (pH above 7.8), then renal clearance is reduced to zero. Advise patients about the use of urinary alkalinisers or acidifiers, including aspirin.
- Pregnancy. Methadone clearance increases during pregnancy, resulting in a corresponding decrease in trough plasma concentrations. This may lead to a greater risk of treatment failure, self-medication and toxicity. Pregnant women may benefit from split dosing. Given the variability of methadone clearance by pregnant women, they are regarded as a high-risk group.

2.2.1 Pharmacokinetic Drug Interactions

There is potential for pharmacokinetic interaction between methadone and drugs that inhibit or induce methadone metabolism by P450 enzymes, predominantly CYP3A4.

Potential Inhibitors Methadone Metabolism

- SSRIs (sertraline, fluvoxamine, etc.)
- SNRIs (venlafaxine, nefazodone)

- Broad-spectrum antifungals and antibacterials (clotrimazole, etc.)
- HIV drugs (zidovudine, ritonavir, etc.) See Appendix 4
- Hormones (progesterone, ethinylestradiol, dexamethasone)
- Calcium channel antagonists (nifedipine, verapamil, diltiazem)
- Antibiotics (erythromycin, ciprofloxacin, chloramphenicol, etc.)
- Miscellaneous (quinidine, midazolam, cyclosporin, vinblastine, bromocriptine, cimetidine)

Potential Inducers Methadone Metabolism

Some antiepileptics (phenobarbitone, phenytoin, primidone, carbamazepine, but not valproate or

benzodiazepines,)

HIV drugs (Nevarapine, Efavirenz) See Appendix 4

Glucocorticoids

Antituberculosis drugs (rifampin, rifabutin)

Avoid commencing any drug that inhibits or induces the activity of CYP3A4 during induction into treatment with methadone. When commencing methadone in patients who use medications that inhibit CYP3A4, prescribe conservative methadone doses, review the patient carefully for signs of toxicity during induction, and advise the patient of the potential for drug interaction.

Other drugs induce or inhibit enzymes that affect methadone metabolism. Alcohol and tobacco smoke are common inducers, and common inhibitors include allopurinol, dextropropoxyphene, disulfuram, isoniazid and enoxacin.

2.2.2 Pharmacodynamic Drug Interactions

Almost all methadone-related deaths occur in the presence of other CNS depressants, and patients who abuse or depend on other drugs may be at greater risk of methadone toxicity.

- Opioids are CNS depressants and may increase the risk of respiratory depression when used with methadone.
- Benzodiazepines do not usually cause respiratory depression on their own, but may increase the risk of respiratory depression when methadone is present.
- Alcohol is a CNS depressant capable of causing respiratory depression and death. The combination of non-fatal doses of alcohol and methadone may cause fatal toxicity, particularly in males.
- Tricyclic antidepressants (TCAs) can cause respiratory depression and pulmonary oedema at high doses, and may interact with methadone to increase the risk of toxicity. Assess patients on TCAs for suicide risk, and review them carefully for signs of toxicity during induction into treatment

2.3 Adverse Effects and Precautions

The adverse effects of methadone are similar to those for other opioid analgesics (dependence, nausea, vomiting, constipation, respiratory depression, coma). Patients develop tolerance to most of these effects after long-term use. However, methadone is unique: its pharmacology differs from that of most other opioids. It has a long interval between ingestion and peak blood levels; a long half-life, with marked variation among individuals; considerable tissue distribution; and accumulation after successive doses. For full product information, consult the manufacturer's product monograph.

2.3.1 Pharmacokinetic Factors

These are relevant to the consideration of side effects and safe prescribing.

- ◆ Peak plasma concentration occurs one to five hours after oral dosing.
- ◆ Metabolism to inactive metabolites occurs in the liver, so consider impaired liver function when prescribing.
- ◆ The elimination half-life varies considerably (with a range of 15-60 hours).
- ◆ Large differences in plasma concentration occur among patients, and wide fluctuations occur in individual patients. Adjust the dose carefully when administering repeatedly.

2.3.2 Contraindications

- ◆ Hypersensitivity to methadone.
- ◆ A history of respiratory depression, especially with cyanosis, excessive bronchial secretions during acute asthma attack (as with other opioids).
- ◆ Acute asthma or chest infection
- ◆ Acute alcoholism, head injury, raised intracranial pressure.
- ◆ Treatment with MAO inhibitors.
- ◆ Active ulcerative colitis or Crohn's disease.
- ◆ Severe hepatic impairment.
- ◆ Biliary and renal tract spasm.

2.3.3 Precautions

- ◆ Elderly patients
- ◆ Hepatic impairment.

2.3.4 Adverse Effects

- ◆ Dependence.
- ◆ Nausea and vomiting, dizziness, drowsiness, light headedness, a dry mouth, sweating (especially at night) and confusion (as with other opioids).
- ◆ Respiratory depression, particularly when combined with the use of other CNS depressants.
- ◆ Occasional reports of hypotension, collapse and oedema.
- ◆ Spasm of biliary and renal tracts.

- ◆ Loss of appetite, nausea and vomiting (although usually settles down quickly).
- ◆ Change in menstruation. Irregular menstruation is common in individuals using heroin or other opiates. Some women return to a normal cycle during methadone treatment, but others continue to have irregular menstruation. Consider the need for contraception when commencing a female patient on methadone.

Table B: Common Adverse Effects

Side Effect	Common Causes	Response
Drowsiness after dose	Excessive dose Use of other CNS depressants (alcohol, benzodiazepines)	Review and maybe reduce dose Reduce patient's use of other drugs.
Craving for heroin (hanging out)	Insufficient dose	Review and maybe increase dose.
Constipation	Methadone Dysfunctional diet Other lifestyle behaviours	Advise a high-fibre diet, adequate fluid intake, stool softeners and exercise. Bowel stimulants if necessary
Dental problems (decayed teeth, periodontal disease)	Drug-induced reduced saliva volume (xerostomia) Poor dental hygiene High sugar diet	Advise enhanced dental hygiene (frequent brushing, flossing, avoiding sugary foods/drinks, chewing non-sugar gum).
Weight gain	Fluid retention. Improved appetite. Decreased activity. Hypothalamic hormone suppression	Review dose and reduce patient's salt intake. Review and change patient's diet. Advise patient to increase exercise carefully.
Insomnia	Excessive or insufficient dose. Timing of dose. Stimulation by other drugs (coffee, tobacco, drugs such as amphetamines and pseudoephedrine).	Review dose. Review timing of dose. Identify stimulant drugs and advise patient to avoid them. Review patient's general sleep hygiene.
Lowered libido	Higher doses. Psychological or social / situational problems.	Review dose. Check patient's history and consider counseling.
Sweating	Methadone Increased with SSRIs Weight gain / decreased fitness	Antiperspirants Weight loss Gradual increase exercise
Infertility	Methadone Cachexia Hypothalamic suppression Hypereprolactinaemia	Check hormone levels Consider hormone replacement Counsel patience

2.3.5 Dental Health

Drug-dependent individuals are vulnerable to dental health problems. Methadone users have a high prevalence of decayed teeth and periodontal disease. Methadone and other opioids may reduce the volume of saliva (xerostomia), which may contribute to dental decay. A history of poor dental hygiene during periods of drug dependence may also contribute to the problem.

A few simple countermeasures may assist the management of the dental health of methadone patients.

- ◆ The mouth and gums should be examined in the initial and subsequent physical examinations, and a management plan agreed for any problems identified.
- ◆ If xerostomia is identified as a problem, sugar-free gum can be recommended to stimulate saliva production.
- ◆ Recommend avoidance of cariogenic drinks for supervised dosing, or a water mouth rinse to follow dosing.

- ◆ Provide information about diet and oral hygiene when appropriate.
- ◆ Recommend treatment at community dental clinics for concession cardholders, or by private dentists in other cases.

2.4 Methadone Toxicity

The toxicity of methadone resembles that of other opioids: sedation; coma; respiratory depression; and miosis (pinpoint pupils) following an overdose. But its pharmacokinetics are unique, particularly the long interval between ingestion and maximum effect, and its long half-life (which results in tissue accumulation). Interaction with other CNS depressants can exacerbate the sedative effects of methadone. The highest risk of overdose and death occurs in the first 10 days of treatment. During this time the patient may engage in unsanctioned misuse of other CNS depressants (including alcohol and benzodiazepines) or continue with illicit drug use in an effort to minimise withdrawal symptoms before becoming stabilised in treatment (Section 5).

Methadone Toxicity: Symptoms and Signs

Mixed poisoning is usual. The usual opioid poisoning triad (coma, pinpoint pupils, respiratory depression) may be preceded by:

- Slurred speech
- Unsteady gait
- Poor balance
- Drowsiness
- Retarded movement
- Stupor.

This is a serious medical emergency. Urgent review by the prescriber is necessary:

Poisoning may proceed to:

- Coma (The patient is unrousable, snoring, flaccid, cyanosed.)
- Respiratory depression and hypoxia
- Death.

Patients suitable for a methadone program usually present because they have difficulty in controlling their drug use; compulsive drug use is characteristic of drug addiction. Polydrug abuse is highly prevalent in this group. This involves the non-medical use of quantities of illicit drugs (such as heroin, marijuana or and amphetamines), prescription psychoactive drugs (such as opioids and benzodiazepines) and licit substances (such as alcohol and nicotine). Many of these drugs are CNS depressants. Users frequently obtain prescription drugs by drug shopping, and take the drugs in doses that far exceed usual therapeutic doses.

These patient and methadone pharmacological characteristics create a complex combination requiring careful evaluation and clinical management, particularly during the first two weeks of treatment. Warn the patient of the risk of CNS depression as a result of interaction between prescription drugs and methadone if they are prescribed benzodiazepines or other CNS depressants.

Section 3

Prescribers

Preparing to Become a Methadone Prescriber

3.1 Training

Familiarity with methadone pharmacology and the management of drug addiction is necessary before prescribers can begin to treat opioid addiction successfully and safely.

3.2 Approval

Approval by Department of Health as a methadone prescriber follows training and assessment. Approval is granted subject to initial conditions such as limits on the number of patients treated at any one time.

3.3 Arrangements for Dispensing

Dispensing sites approved to dispense methadone solution will provide supervised dosing. It is important to become familiar with all the options for supervised dosing. The local Drug Treatment Centre will be able to provide information on local dispensing sites. Good communication with the dispensing site will avoid misunderstandings and enhance the safety of treatment.

3.4 Dosing Fees

In the future, open approval by the Department of Health, some dispensing sites may be entitled to charge a fee for dispensing methadone in a cost sharing process.

3.5 Arrangements to Cover Prescriber Absence

There will be times when prescriber is unavailable to supervise the treatment of patients—for example, anticipated absences (leave or sessions at other locations) or sudden and unexpected absences (leave for sickness, injury or family reasons). The risks this situation presents are due to unsupervised treatment, interruption of treatment, or treatment by a colleague who has little experience with the issues of methadone treatment, or who is unfamiliar with the patients being treated. Methadone prescribers are responsible for the management of each patient whom they have registered, and they should remain the main person treating these patients. To minimize the risks of a prescriber's absence, they may prepare by making the arrangements in the following box.

Preparation for Anticipated or Unexpected Absence of Methadone Prescriber

Document and maintain up-to-date individual patient management plans in your patient records, so as to enhance communication between you and your colleagues.

Make arrangements for a colleague (preferably an approved methadone prescriber) to deputise for you by continuing the documented management plan for each patient.

Request that any colleague deputising for you record treatment changes in the patient notes.

A deputising practitioner may or may not be already approved to prescribe methadone.

3.5.1 Deputising by Approved Methadone Prescribers

For stable patients requiring only the continuation of an expired prescription without an increase of dose or take-away frequency, take a history and examine the patient.

Check with the dispensary that the patient has attended regularly for daily dosing.

- Contact the Officer in Charge of a major Drug Treatment Centre if:
 - ◆ If there are any management problems or concerns about the safety of the patient.

Document any advice given and the name of the DTC consultant in the patient's notes.

- Follow the relevant recommendations on 'Essentials of Methadone Prescribing' (at the start of these guidelines).

3.5.2 Deputising by a Practitioners Who is Not an Approved Methadone Prescriber

Being unfamiliar with the risks of methadone treatment, these prescribers must adopt a cautious approach to treating patients (Appendix 3). Only approved methadone prescribers can commence patients on methadone treatment.

- For stable patients requiring only the continuation of an expired prescription without an increase of dose or take-away frequency, take a history and examine the patient.

Check with the dispensary that the patient has attended regularly for daily dosing.

- Contact the Officer in Charge of a major Drug Treatment Centre if:
 - ◆ If the prescriber has management problems or concerns about the safety of the patient.
 - ◆ If a dose increase or take-away dose appears necessary. Do not provide an increased dose or take-away dose unless advised to do so by DTC consultant. Document the advice given and the name of the DTC consultant in the patient's notes.
- Follow the relevant recommendations on 'Essentials of Methadone Prescribing' (at the start of these guidelines).

All deputising practitioners should manage the patient as described in the following box.

Management by Deputizing Prescribers

Continue the usual prescriber's management plan and dosage regimen as documented in the clinical record. (It is acceptable to reduce the dose if the patient is experiencing toxicity.)

Note on the prescription the temporarily deputizing for the patient's usual prescriber.

Limit the duration of the prescription to the expected period of absence of the usual prescriber, indicating precise starting and finishing dates.

Arrange for the usual prescriber to review the patient as soon as possible thereafter.

Document details of consultations and methadone prescriptions in the patient's notes.

3.6 Maximum Number of Patients

Once approved to prescribe methadone, prescribers may be limited for some months to prescribing for twenty methadone patients (unless under the close supervision of an established methadone prescriber). The methadone program in Myanmar initially aims to incorporate methadone treatment into drug treatment services. In the future it may be possible to integrate methadone prescribing into community services to limit the congregation of large numbers of injecting drug users at the one centre or dispensing site, and to meet all of the patient's needs for medical and drug addiction treatment in the framework of a normal general practice.

Section 4

Prescribers

Intake Procedures

4.1 Establishing the Identity of the Patient

Establish the identity of the patient to avoid dual dosing of the same person. The patient must be requested to provide a form of identification (for example national registration card). The patient will also need to provide four current photographs - one to be attached to the medical record, one to be attached to the drug user registration card, one to be attached to the prescription card at the dosing point, and one to be kept in reserve for possible future transfers.

4.2 Assessing the Patient

4.2.1 Current Level of Drug Use

For each patient, assess:

- All the drugs they use
- The frequency of drug use
- The quantity they use on a daily or weekly basis
- The length of the current period of use
- The date and time of their most recent drug use.

4.2.2 Degree of Neuroadaptation and Dependence on Opioids

Evaluate the patient's neuroadaptation to and dependence on opioids to determine appropriate treatment. Neuroadaptation can be assessed by:

- Using evidence from the patient's history (for example, descriptions of withdrawal, and features of tolerance). The patient may exaggerate the amount of opioids used, so do not base the starting dose on history alone.
- Conducting a physical examination, looking for signs of withdrawal and chronic use.
- Conducting a urine drug screen. A positive screen is a sign of recent opioid use, not neuroadaptation. A negative screen without objective features of withdrawal suggests a low degree of neuroadaptation.
- Naloxone testing, although this is of limited value and can be distressing for the patient. It is not recommended.

4.2.3 History of Drug Use

Assess the patient's past use of alcohol, illicit drugs and prescribed drugs.

4.2.4 Previous Treatment for Substance Use

The patient's account of previous treatment and relapse can provide valuable information to help determine appropriate treatment and prevent relapse in the future. It can also provide insight into the patient's reasons for requesting treatment, and the action required for success.

Request information on the patient's:

- Types of treatment (detoxification, methadone, unsupervised withdrawal) and reasons for failure and relapse.

- Number of attempts at methadone programs.
- Length of time on treatment.
- Perceived benefits from treatment.
- Maximum dose.
- End of treatment, and reasons for terminating treatment.

It is advisable to seek verification of these from the Drug Treatment Centre.

4.2.5 Psychiatric and Medical Co-Morbidity

Many patients seeking methadone maintenance to resolve substance abuse problems have pre-existing psychiatric conditions (including psychoses) or mood disorders such as depression and anxiety disorders. A history of injecting drug use and polydrug abuse may contribute to circumstances that cause or exacerbate mood disorders. Substance abuse is a risk factor for suicide. Patients with complicated psychiatric conditions should be referred to a specialist DTC methadone service (Appendix 1) for assessment and treatment, or for initiation of methadone treatment that a general practitioner may continue later. Injecting drug use may adversely affect the patient's social relationship with family and friends, jeopardising social supports. Unemployment and a criminal history may compound such problems experienced by the patient.

Many injecting drug users experience adverse medical consequences of their substance abuse, including infectious complications such as hepatitis and endocarditis. Many also experience physical injury. Offer hepatitis B vaccination if the patient is not immune, and advise hepatitis C carriers about the risks of blood-to-blood transmission and its prevention.

A full assessment of the patient's medical and psychiatric needs is recommended early in the treatment of their substance abuse to assist with the preparation of a treatment plan.

4.2.6 Social and Personal History

Assess the patient's living circumstances and social supports.

4.2.7 Legal History and Current Legal Status

Inquire about any current and previous charges, custodial history and juvenile justice experience.

4.2.8 Physical and Mental State

A physical examination should be conducted to obtain evidence of injecting drug use and diseases, injuries and infections associated with injecting drug use and alcohol misuse.

4.2.9 Risk Behaviour

Assess whether the patient has injecting behaviour (for example, needle sharing and reuse) associated with the transmission of blood-borne viruses (Hepatitis B, C and HIV).

4.2.10 Risk of Methadone Toxicity

Some patients are at greater risk of methadone toxicity, particularly during induction into treatment. The following circumstances suggest high risk:

- This is the patient's first presentation to as a drug user, and their medical and drug use history is unclear.
- The patient has a high risk of polydrug abuse and dependence.
- The degree of neuroadaptation is unclear.
- The patient has a risk of overdosing on methadone or any other drug.
- The patient has a clinically significant respiratory disease.
- The patient has a clinically significant liver disease.
- The patient uses drugs that inhibit CYP3A4 enzyme (Section 2.2.1).

Methadone-related drug deaths due to methadone toxicity alone are rare: most (about 90 percent) involve prescription drugs and alcohol. Prescription drug abuse is common, and these drugs contribute to potentially dangerous toxicity, cognitive impairment and anterograde amnesia.

Corroborating evidence should be sought (for example, a urine drug screen and physical examination to confirm injecting drug use) if there is a possibility that the patient has an increased risk of methadone toxicity. Allow sufficient time in the first consultation to establish rapport, avoid increasing the patient's dose during the first two to four days, and review the patient on the third day. Methadone plasma levels peak about four hours after ingestion—a suitable time to assess for Methadone or combined drug toxicity.

4.2.11 Investigations

Urinalysis

Urinalysis can be used to screen for opioids, benzodiazepines, psychostimulants, antidepressants, etc. If the patient's history and examination lead to a diagnosis of heroin dependence, then urinalysis can provide additional evidence. However, this is often unnecessary if the diagnosis is clear.

As with any diagnostic procedure, only use urinalysis if it is anticipated that it will influence treatment. It can be useful if there are grounds for doubt about heroin use or dependence, if the patient is previously unknown, or if the features of heroin dependence are equivocal. Urinalysis is subject to a number of limitations; for example, a result may not be available for hours or days, and the usual EMIT analysis only screens for opiates (not for other opioids such as pethidine, methadone, buprenorphine and oxycodone).

Pathology tests

The following investigations may be decided to be appropriate: FBE, LFTs, hepatitis B and C, and HIV serology where indicated. Serology should be voluntary, conducted with the patient's informed consent and with appropriate counseling before and following screening. Maintain stringent confidentiality precautions, in accordance with the DoH guidelines for VCCT. Do not set these tests as a precondition for receiving methadone treatment.

4.3 Establishing Suitability for Treatment

Methadone treatment is usually appropriate for people who are opioid dependent, possessing (in the previous 12 months) three or more of the World Health Organization criteria for dependence.

World Health Organization Dependence Criteria

- Withdrawal syndrome
- Tolerance
- Use of opiates to avoid/relieve withdrawal
- Subjective compulsion to use
- Narrowing repertoire of behaviour
- Placement of increasing importance on the use of opiates at the expense of other behaviours
- Early relapse into opiate use following cessation

Neuroadaptation (physical dependence) is demonstrated by the occurrence of withdrawal symptoms and tolerance. It is not a prerequisite for diagnosis of drug dependence, and commencement methadone treatment may be chosen if it is considered that its potential benefit to the individual's health and social functioning outweighs the potential disadvantage of methadone treatment.

Consider the patient's goals for treatment to ensure that methadone is a suitable form of treatment that is consistent with these goals. In some cases methadone treatment may be suitable even if the individual is not currently opioid dependent, but is at high risk of relapse into opioid dependence (for example, on release from prison or hospital). Generally, individuals should be older than 16 years of age or have the written permission of a parent or legal guardian.

Alternatives to methadone treatment may be preferred for the following groups:

- ◆ Very young drug users
- ◆ Acutely psychotic drug users
- ◆ Polydrug (including alcohol) users for whom opioids are not the prime drug of dependence
- ◆ Heavy alcohol users
- ◆ Patients with a short history of opiate use
- ◆ Patients at high risk of overdosing
- ◆ Patients with clinically significant liver disease.

If there are any doubts about the suitability of the patient for methadone treatment, a second opinion may be sought from a major Drug Treatment Centre. It is appropriate to give priority to HIV-positive patients, pregnant women and individuals with substantial medical problems (e.g. TB, opportunistic infections).

4.4 Discussing Treatment Options

Discuss treatment options with the patient, including detoxification, withdrawal using methadone, and methadone maintenance program. The prescriber and the patient can decide in consultation whether a methadone program will help them to achieve their treatment goals. Patients vary in the level of support and treatment they require—from patients requiring a high level of medical, casework and other services, to those who can be treated satisfactorily without extensive additional services. Total abstinence from unsanctioned use of opioids is only one of a range of treatment objectives, although the patient may achieve this stage during the course of treatment.

4.5 Providing Patient Information

The prescriber should provide the following information to the patient:

- The delay of two to four hours before methadone has a peak effect.
- The accumulation of methadone over time, which results in a greater effect over five days or more, even on a fixed dose.
- The possibility that it may take one or two weeks to establish a maintenance dose that will satisfactorily substitute for the opioid on which the patient is dependent (because the equilibration of tissue and blood levels takes time).
- The high risk of drug overdose in the first ten days of treatment, and the risks from
- combining methadone with the unsupervised use of other CNS depressant drugs (particularly benzodiazepines and alcohol). Binge drinking carries a special risk.
- The fact that some medications can induce or inhibit CYP3A4 enzyme activity on methadone concentrations (Section 2.2).
- Effects and side effects of methadone use.
- Guidelines for, and conditions on, participation in the methadone program.
- Methadone's impairing effects on driving ability (until the patient is stabilized on a constant dose).
- The addictive nature of methadone.
- Expected behaviour on the program.
- The likely duration of treatment. The benefits are maximized if the patient remains in treatment for at least 12 months.
- The costs of treatment (medical and pharmaceutical).
- The length of time required to withdraw from methadone. The patient may experience slight discomfort at this time.
- The causes of drug overdoses, the high-risk situations associated with overdose, the symptoms and signs of overdose, and action to take when overdose is suspected. The patient needs to inform family, friends and/or associates about the symptoms and signs of overdose, and of the urgency of response required when they suspect an overdose.
- The complaints process (Section 7.5).
- Support and information services (Appendix 1).
- Information about harm reduction (covering how to prevent the transmission of blood-borne viruses and how to inject safely).

You may provide the patient with some written information or booklet about *Methadone Treatment in Myanmar*

Information to Give Patients

- The dynamics of stabilization
- The hazards of polydrug use, particularly in the first week of treatment
- The effects and side effects of methadone use
- Program guidelines and conditions
- The risks of driving while stabilizing
- Expected behaviour
- Risks and symptoms of an overdose.

4.6 Dealing with Patients Aged 16 years or Younger

After consultation with consultant at a DTC possible to confirm suitability for methadone, obtain written permission from a parent or legal guardian before commencing treatment of a young person.

4.7 Registering a Patient to Prescribe Methadone

A Notification of Registration of a Drug User must be sent to Department of Health Drug Treatment Centre. Treatment should not be commenced until the prescriber has registered the user and confirmed that they are not already on methadone treatment from another DTC. The commencement of methadone treatment should also be notified to Department of Health Drug Treatment Centre at the time and on the monthly summary report of new patients commenced on treatment.

Section 5

Prescribers

Prescribing Guidelines-Maintenance

5.1 Induction into Treatment

Having established that the patient is suitable for methadone treatment and Registered them as a Drug User, an initial dose should be decided by the prescriber that will be comfortable and safe for the patient. An initial dose should usually be 20-30 milligrams per day. It is unusual for patients to require doses higher than 30 milligrams, though patient review may show evidence of opioid withdrawal during the first few days of methadone treatment. Initial doses higher than 30 milligrams should only be used if there is confidence that the patient has a high degree of neuroadaptation to opioids; is at low risk of abusing other substances; and has good liver function. Commence patients with a low level of neuroadaptation on a dose of less than 20 milligrams.

If the patient has a low level of physical dependence or the prescriber is unsure of the degree of neuroadaptation, treatment should commence with a low dose (10 to 20 milligrams) and the dose adjusted after reviewing the patient soon after commencement. At review before the third dose, the dose should be titrated according to the patient's symptoms (either opioid withdrawal or methadone toxicity) and their continued use of opioids and other CNS depressants.

A cautious approach to dosing should be adopted (with careful review during the first week of treatment) for patients who are identified as being at high risk of methadone toxicity (Section 4.2.10) including those on medication that inhibits CYP3A4 enzyme activity (Section 2.2).

Factors determining the Initial Dose

- The degree of neuroadaptation to opioids
- Concurrent medical conditions, including impaired hepatic function
- The time since the patient's last drug use
- The patient's state of withdrawal or intoxication
- Interactions with other prescribed medications
- The perceived likelihood of the patient's misuse of alcohol, prescription or illicit drugs
- The patient's weight.

Dose	Condition
15 to 20 mg	Severe medical conditions Low or Uncertain levels neuroadaptation High risk polydrug use
20 to 25 mg	Moderate level neuroadaptation or some risks
25 to 30 mg	High level neuroadaptation Patient well known to doctor/no risk factors Prior methadone treatment with frequent review

5.1.1 Timing of the First Dose

If methadone is commenced in the morning, it may facilitate review for evidence of methadone or combined drug toxicity when peak blood levels occur two to four hours after dosing, before the third or fourth dose.

The first dose of methadone should not be delayed because of a patient's use of heroin the same day. It is important to start treatment and begin the behaviour change when the opportunity presents itself. If a patient is intoxicated with heroin, their first (or any) dose of methadone should be delayed some hours and a dose chosen to reflect their higher risk.

Because of methadone's slow onset of action most patients will have recovered from any recent heroin effect by the time of peak methadone effect. Substantial risk of overdose only exists when heroin (or other drugs) are used at the peak of the methadone effect (4-6 hours after dosing).

5.1.2 The Prescription

- Indicate the initial dose, not a dose range, on the prescription. Do not increase the dose without personally reviewing the patient.
- Limit the prescription duration to less than one week, to encourage the patient to return frequently for review during the first week (the highest risk period of treatment).

Do not prescribe commencement doses of above 30 milligrams for patients seeking treatment for dependence on prescription opioids (morphine, codeine, oxycodone or pethidine). Dose equivalents published in pharmacology textbooks usually refer to the dose that produces a similar analgesic effect, not the equivalence of other effects (including toxicity and respiratory depression); further, they are only approximations. Do not rely on them to determine the initial dose of methadone.

5.1.3 Review during the First Week

Review the patient's condition before the third or fourth dose. A review two to four hours after the last dose, when peak blood levels occur, will enhance the prescriber's assessment of methadone toxicity. The review enables the most effective dose to be determined and an opportunity for the prescriber to manage the high risk of methadone or combined drug toxicity during induction. If there is evidence of opioid withdrawal, it may be decided to increase the dose carefully; however, patients rarely require doses of more than 40 - 50 milligrams at the end of the first week of treatment.

It is recommended to increase the dose only after 3 to 5 days (steady state) because more rapid dose increases can result in accumulation & toxicity. Dose increases of 2.5 to 5 mg at a time are usually adequate when taking less than 60 mg methadone, though increases of 5 to 10 mg may be safe if still significantly underdosed. Dose increases of greater than 10 mg are not safe. The dose should only be increased after reviewing the patient and where clinically indicated.

It will be common for patients to be admitted to the Drug Treatment centre for up to two weeks for close observation during the induction onto the methadone program.

5.1.4 Split Dosing

Split dosing may be used if there is uncertainty about the appropriate starting dose. The patient may be given an initial low dose (10 - 20 milligrams) and reviewed after four hours when peak blood levels are reached. The patient can then be given a further 10 or 20 milligrams if they are experiencing opioid withdrawal symptoms. A combined dose can be given the following day.

WARNING

During the first few days of treatment there is a high risk of potentially fatal drug overdose involving methadone and other CNS depressant drugs. The patient must be reviewed before the fourth dose, and the prescriber must be available for the patient to see or the dispenser to consult if there is suggestion that the patient may be experiencing methadone toxic.

A prescription for only three days supply will ensure the patient returns for review.

5.2 Maintenance Dose

As with the drug treatment of other medical conditions, dose is an important determinant of effectiveness. Prescribing should not focus on reducing the dosage to a level to minimize the risk of adverse effects or decrease dependence, but rather on effectively controlling the patient's craving for and continued use of illicit opioids.

- The maintenance dose should be individualized to the patient's needs.
- Evidence indicates that a maintenance dose of at least 60 milligrams per day is more effective than lower doses in achieving treatment outcomes such as decreased illicit drug use.

An Effective Dose

In general a daily maintenance dose of at least 60 milligrams has been found to be more effective than lower doses in achieving the goals of treatment, with most patients being controlled within the range 60 to 120mg.

5.3 The Methadone Prescription

As for any other Controlled Drug, a dispenser or pharmacist cannot dispense methadone without holding a valid prescription. The prescription for methadone must be written indelibly in ink, with the usual requirement that the quantity to be dispensed be written in words and figures.

In the first two months of treatment while the patient is being stabilized and the risk of toxicity is high, prescribe a precise dose. Any adjustment to dose requires review of the patient. To avoid misunderstanding, it is essential that the following information is speci-

fied on the prescription (Appendix 2):

- ◆ The date when the first dose is to be dispensed.
- ◆ The date when the authorization to dispense will end (to encourage the methadone patient to attend for review at an appropriate interval).
- ◆ The name of the dispensing site at which the methadone is to be dispensed.

5.4 Review of Patient Progress

Regular contact with patients is recommended throughout their treatment with methadone. To ensure attendance for review, the life of the prescription should be limited to the period between reviews.

In general, the patient should be seen at least twice during the first week, and at least weekly during the initial one-month period of stabilization. The patient should then be seen at least fortnightly during the second and third months, then regular contact maintained at least every three months (preferably monthly) while the patient is on the methadone program.

A review every three months is usually sufficient if the patient wants a low-intensity program without take-away privileges. If take-away doses are required, more frequent review (monthly) and urinalysis may be required.

Review individual treatment program progress (in relation to the objectives of treatment and agreed treatment goals) at 12-month intervals. For this review, consider the factors described in the following box.

Factors for Annual Review of Individual Treatment Program

- The effect on illicit opioid use
- The patient's use of other drugs
- Change in the patient's lifestyle, social functioning and situation
- The patient's physical health and wellbeing
- Achievement of mutually agreed goals
- Change in the patient's legal status
- The regularity of attendance and dosing
- A psychological assessment
- Other considerations (HIV, hepatitis B and C status, etc.).

5.5 Counselling

Counselling may help the patient address their drug addiction problem. The prescriber choose to counsel the patient himself or refer them to another counsellor. The patient's dispenser may also provide limited counselling. Patients with special counselling needs may need to attend a specialist Drug Treatment Centre or psychiatric service.

Counselling should also be provided about risk behaviours and the prevention of transmission of blood-borne viruses (HIV and hepatitis B and C) and testing for these diseases (Appendix 1).

5.6 Allied Health Professionals

A diverse range of organizations fund professionals to support methadone patients and others with their substance use and harm arising from it. When patient management involves these workers, it is important to ensure their roles and responsibilities are clearly documented and understood. In any situation, decisions about the appropriate and safe prescribing of methadone remains the responsibility of the trained prescriber; as with the prescribing of any drug, such decisions should be based on an adequate clinical assessment. Both the prescriber and the dispenser should be satisfied that changes to doses and clinical management are appropriate.

5.7 Dispensing Arrangements

5.7.1 Supervised dosing at Drug Treatment Centres

- Written dosing instructions will be documented on a patients dosing card held at the dispensary. DTCs may vary in the format of the dosing card which will have details of the patient and a photograph attached.
- The dosing card will be used at the DTC to review the attendance of the patient and changed doses will be written directly on the card by the prescriber.

5.7.2 Supervised dosing arrangements through outside dispensing sites and hospital pharmacies.

- Contact the dispensing site that has been agreed for the patient to attend to arrange for daily supervised dosing.
- Record at the DTC of the dispensing site at which dosing is to be done.
- Forward to the dispensing site
 - ◆ The prescription for methadone.
 - ◆ A recent photograph of the patient endorsed by the prescribing doctor.
 - ◆ Written commencement / transfer form specifying the date of administration of first dose, the name of the dispensing site at which the patient is to be dosed and the duration of the transfer (if relevant).
- In an emergency when it is not possible to provide an original written prescription to the dispensing site before dosing, verbal instructions may be provided, then a fax to the dispensary of a copy of the prescription, endorsed with the name of the dispensary to which it is being sent. This fax must be confirmed in writing by forwarding the original prescription to the dispensary as soon as practicable (Section 5.3).
- Alternatively, place the documentation and prescription in a sealed envelope marked 'Confidential', and signed across the seal for the patient to give the dispensing site with the prescription endorsed with the name of dispensary. Contact the dispenser by telephone before sending the documentation; or fax the prescription to the dispensary and send the documents with the patient.
- Inform the dispenser of any dose change using a prescription, which should reach the pharmacist before the change in dose is to be effected.
- The Drug Treatment Centre should be visited of any change in methadone dispensing location.

5.7.3 Communication between the Prescriber, Patient and the Dispensing Site.

It is important that there is good communication with the patient and among the treatment team involved with the patient. Each party has particular information that is useful to the other.

- The prescriber, having taken a history, examined the patient and run laboratory tests, should also be aware of the patient's medical condition and social circumstances.
- The dispenser sees the patient daily; may establish good rapport and even provide counselling. The dispenser may notice irregular presentation for dosing, unsanctioned drug use, medication abuse, and evidence of drug toxicity. They may refer the patient back to the prescriber for review of management.
- The patient may have the benefit of previous experience with methadone.

It is desirable that dispensers be able to contact the prescriber at all times, so it is recommended that they be provided with full contact details, including after-hours contact numbers. It is vital to communicate all information about dosing in writing, and to record telephone conversations in the patient's notes. Dispensers are not permitted to provide a dose to a patient in the absence of a valid order from the prescriber.

5.7.4 Split Dosing

Once treatment is established, a very small proportion of patients may benefit from split dosing. The prescriber may seek approval for daily split dosing with the second daily dose as a take-away dose when:

- A specialist methadone service has assessed the patient and provided a letter supporting this method of dosing.

5.7.5 Provision of Methadone in Prison or Police Custody

Patients who are held in remand may be entitled to continue methadone treatment until release or sentencing. Those sentenced may be able to continue methadone treatment in prison or alternatively undergo planned withdrawal.

If a patient on MMT is being held in remand or sentenced to a short prison term, a place should be maintained if possible for that patient to return to the program if they wish after release. Custody arrangements should not interrupt the treatment of patients if possible.

- The patient's usual prescriber may be possible to continue methadone treatment in police custody.
- Police can arrange to have a special prescription collected from the doctor, which is placed in the patient's prisoner file and moves through the prison system with them.
- Police may arrange for the delivery of the prescription to an appropriate dispensing site, where the dispenser verifies the prescription, checks the timing of the last dose with the previous dispensary, provides a methadone dose for police to administer and return the original prescription to the prisoner file.

5.8 Managing Patients with Special Needs

5.8.1 HIV-Positive or TB Patients

Patients with positive HIV status or TB should be given priority access to methadone treatment where it is appropriate. If illness or behavioural problems complicate the patient's management, they may be referred to a specialist DTC, respiratory or infectious disease unit or advice sought from these specialists. Information about specific AIDS/HIV clinical and support services are provided in Appendix 1. Infection control precautions should be exercised with all patients regardless of their HIV status (details of recommended procedures are included in the Department of Health infection control guidelines).

Advantages of methadone treatment in HIV and TB positive patients

Improved compliance with ARV or TB treatment
Decreased frequency and urgency of injecting
Decreased opportunities for sharing contaminated using equipment
Improved nutrition
Reengagement with wider society for support and counselling
Improved motivation to seek treatment for HIV, TB and opportunistic infections

Unfortunately all first-line HIV and TB treatment regimens in Myanmar include anti retroviral/antituberculous medications which interfere with methadone metabolism (Appendix 4). Referral to a specialist Drug Treatment Centre is advised if there is any doubt about the dose adjustment (increase) required when ARV or TB treatment is initiated in a patient on methadone.

5.8.2 Pregnant Opioid-Dependent Women

Pregnant women seeking methadone treatment of their opioid dependence should be given priority if possible. Methadone provides a stable drug milieu for the unborn child, in contrast to the fluctuating levels of opioids experienced in the case of injectors of heroin. The foetus in utero also experiences opioid withdrawal in the mother. The advantages and disadvantages of methadone treatment of opioid dependence in pregnant women are described in the following box.

The advantages gained in the antenatal period should be weighed against the disadvantages encountered in the neonatal period. However, evidence suggests that substituting methadone for illicit opiates during pregnancy provides the best outcome for mother and child.

Some patients prefer to be drug free at the time of delivery, but there is a risk of relapse to injecting drug use once patients have withdrawn from opioids. Opioid detoxification is not usually recommended.

In general, methadone treatment should consist of:

- Stabilization of the patient on an appropriate dose sufficient to cease illicit drug use.
- Maintenance at a level that keeps the woman comfortable, and avoids drug withdrawal during pregnancy. Do not encourage dose reduction.
- Reassessment of dose in the days immediately following delivery to avoid oversedation.

- Keeping the patient on the maintenance dose for a minimum of two to three months postpartum before any dose reduction.
- A consideration of the need to address other substance abuse problems (smoking, alcohol, benzodiazepines) that have adverse effects on pregnancy outcomes.

Advantages of Methadone Treatment of Pregnant Women

Avoids contaminants that may harm the unborn child.

No known foetal abnormalities are associated with pure heroin or methadone.

Involves a known, regular dose.

Avoids periods of drug withdrawal that may be associated with miscarriage early in the pregnancy, or foetal growth retardation and stillbirth late in pregnancy.

Reduces the incidence of prematurity.

Reduces the incidence of intra-uterine growth retardation.

Increases attendance for antenatal care.

Disadvantages

Increases the severity and duration of neonatal withdrawal compared with that of infants of untreated opioid-dependent mothers.

Involves longer hospitalization and treatment of newborn children.

Leads to greater neonatal weight loss.

Reduces feeding.

Methadone dose requirements often increase during pregnancy because the increase in plasma volume and metabolism of the drug may result in withdrawal symptoms. These withdrawal symptoms may cause patients to withdraw from treatment or self-medicate, increasing the risk of polydrug abuse. Pregnant women may benefit from split dosing, receiving half the dose twice a day.

See Appendix 1 for services for pregnant women and Appendix 5 for guidelines on treatment of neonatal withdrawal syndrome.

5.8.3 Patients with Co-existing Mental Health Problems

Take particular care to evaluate the patient's psychiatric state early in treatment (Section 4.2.5). Substance abuse is associated with a high prevalence of psychiatric disorder, including mood disorders (particularly depression), personality disorder and psychosis. There is a risk of suicide during methadone treatment, and the prescriber should evaluate patients for suicidal ideation. Patients whose treatment is complicated by psychiatric problems should be referred to a specialist drug treatment centre and / or psychiatrist.

Depression is a very common co-existent complaint at the time of initiation of methadone treatment. It is recommended that treatment of it should be delayed for some weeks and follow reassessment at the time of stabilisation of the methadone dose. If concerns exist regarding suicidality then inpatient methadone induction is appropriate. Depression may also reappear and require treatment at any time during the course of methadone maintenance or reduction.

Methadone has few significant interactions with antidepressants or anti-psychotics though Fluvoxamine is a particular exception. The anti-convulsants are more problematic, often causing methadone withdrawal, with lithium carbonate generally a better choice for mood stabilisation. Methadone, because of its low grade mood mellowing effect and stabilisation of behaviour, can be a useful adjunct in the treatment of comorbid schizophrenia and personality disorder, in the presence of opiate dependence. Note that co-existent mental illness will be readily exacerbated by over-rapid methadone dose reduction.

5.8.4 Chronic Pain and Methadone

Methadone is a strong opioid with proven analgesic efficacy. Its role in the treatment of chronic pain, including cancer pain, is well established. Because it has substantial success in treating opioid addiction, it is a logical choice for people with chronic pain whose management is complicated by concurrent opioid dependence. For these patients, methadone is used in a way similar to the treatment of heroin addicts (including supervised daily dosing). Analgesic effectiveness in certain situations may be better with 8 to 12 hourly dosing, so there may be need to consider split dosing, taking appropriate caution (Section 5.7.3).

Patients stabilised on methadone who experience acute severe pain and need opioids may require higher-than-normal opioid doses to overcome tolerance. In some cases they may also require a temporary increase in their methadone dose. It may be worthwhile discussing such cases with an experienced Drug Treatment Specialist at a major DTC, because these treatment situations are frequently difficult.

Referral to a DTC is recommended. They offer diagnostic and therapeutic services which include medication management, referral for appropriate specialist medical consultation, review of prior medical records and diagnostic tests, physical examination, psychological assessment and treatment, physical therapy, vocational assessment, counselling and other facilities as appropriate. They are generally best able to assess and treat both the physical and the psychosocial aspects of a patient's complaints. Assessment at one of these clinics by a pain management drug treatment specialist, a psychiatrist or psychologist and others, may provide the optimal treatment.

They will seek validation of the patient's claimed treatment history from previous general practitioners and specialists, and the Drug Treatment Centre.

A patient pain management plan can be prepared that includes not only prescription of methadone, but also other medications where appropriate and adjunctive treatment modalities such as physiotherapy, counselling and crisis management.

5.9 Take-Away (TAKE HOME) Doses

Methadone is used to treat drug dependence. It is a Controlled Drug (drug of dependence), subject to misuse and trafficking. People with a history of substance abuse may misuse it to achieve a 'high'(sedation), sometimes by mixing it with other psychoactive drugs such as the benzodiazepines and / or alcohol. Another characteristic of substance misuse is the phenomenon of sharing with associates. Methadone is no exception, and patients may share it with non-tolerant associates, with serious adverse consequences. Methadone related deaths occur each year as a result of patients sharing their take-away doses of methadone with friends or partners. Deaths have also occurred where drug dependent friends or partners have stolen a patient's take-away dose. Methadone is toxic in overdose. There is little margin between therapeutic and toxic doses. Blood

levels achieved in treatment and those detected in drug overdose overlap. Doses of 30 - 40 milligrams tolerated by opioid-tolerant people in treatment may be lethal in non-tolerant individuals. Children are particularly vulnerable to overdose.

Risks of Take-Away Doses

- Hoarding and deliberate overdose of self or others
- Use in dangerous combination with other drugs
- Self-administration by injection, with the potential for sorbitol toxicity, bacterial infection and blood-borne virus transmission
- Diversion of methadone for illicit use
- Trafficking to provide funds for heroin purchase
- Accidental overdose (by children or other non-tolerant substance misusers)
- Poor compliance with treatment plan
- Sharing of dose with partner or associates

Nevertheless, take-away doses can lessen the constraints on stable patients who are attempting to normalize their lives, integrate into the community, and meet work and family commitments with minimal disruption from the demands of daily supervised dosing. Take-away doses are important for those who need them for unusual situations such as court appearances, visiting distant sick relatives, holidays or conferences. Most importantly, take-away doses contribute to the acceptability of prolonged methadone maintenance and patient retention in treatment.

Arrangements for take-away doses should balance the need to minimize the risk to the patient and their associates (or others not involved in the methadone program) with the stable patient's need to normalize their lives. Take-away treatment should depend on the following conditions:

Requirements for Take-Away Doses

- The prescriber must authorize any take-away doses.
- The dispenser should be contacted to confirm that recent behaviour and dose collection have been stable.
- Take-away doses should be available to only clients who are stabilized on the methadone program.
- They are usually not available to clients in their first two months of treatment.
- They should be the same dose as that normally consumed.
- They should not be available if there is concern they may be misused.

Contraindications to Take-Away Doses

- Unstable and/or unsanctioned patterns of substance use, including significant use of alcohol, illicit drugs, benzodiazepines or other sedating medication.
- Significant unstable psychiatric conditions, including active psychosis, significant suicidal ideation and depression.
- The possibility of diversion or inappropriate use of the methadone. This requires an assessment of the stability of the patient's home environment (for example, whether they are living with another substance abuser), their means of securing the methadone doses away from children and other potential misusers, and their past performance with take-away doses.

Subject to the above considerations, take-away doses may be authorized for patients stable for three months with approval from the Drug Treatment Specialist at the DTC. Supervised dosing is the preferred method of methadone administration, but discretion may be exercised in selected cases:

Schedule of Prescriber-Authorized Take-Away Doses

After three months, the prescriber may authorize in writing, with permission from the Drug Treatment Centre, one take-away at the normal dose for special circumstances.

Under exceptional special circumstances (for example, illness restricting mobility, travel, employment responsibilities), the prescriber may authorize take-away doses for up to three consecutive days no more than once per month, subject to the client satisfying the above requirements.

Approval by the specialist at the Drug Treatment Centre is needed to authorize a take-away dose.

Even when approved by the Drug Treatment Specialist, usually no more than three take-away doses (up to total 300mg) should be provided at one time. When a patient requests more than two consecutive take away doses, first ensure no other arrangements can be made for supervised dosing, to avoid the extended use of take-away doses. Patients should consume at least four doses per week under direct supervision.

Approval may very rarely be given for daily split dosing with the second daily dose as a take-away dose, by a specialist at the drug treatment centre who has assessed the patient and provided a letter supporting this method of dosing.

5.10 Transfer of Methadone Treatment

Patients may transfer to other dispensing locations (township) temporarily for work, holiday or other reasons. Consider the patient's suitability for transfer before making these arrangements. The usual requirements and contraindications for providing take-away doses apply to patients seeking transfer (Section 5.9).

Patients may also require permanent transfer to another prescriber or another dispensing site. There is a risk of confusion about when the last dose was administered at the transferring dispenser, creating the possibility of dual dosing on the same day, with resultant methadone toxicity. Good communication between transferring and receiving prescribers and dispensing sites is vital. Transfer may be intrastate, interstate or international.

The transferring doctor makes the arrangements about the transfer of dosing points. For safety reasons, ensure that clear, written instruction is provided to both dispensaries about the timing of the last dose at the transferring dispensary and the first dose at the receiving dispensary. These arrangements are made to avoid the risk of double dosing. The local Drug Treatment Centre can provide details of local dispensing sites.

The intended receiving prescriber should be provided with details of the patient's name, date of birth, methadone dose, dates to be dosed, the patient's address at the new location (if known) and the reason for transfer. This can be done by forwarding a copy of the completed Notification of Transfer form to the receiving prescriber.

The receiving methadone prescriber should be trained in methadone maintenance treatment before prescribing.

5.10.1 Procedures for Arranging International Transfers

- Find details about the International Coordination and Information Service for Methadone Patients Seeking to Travel Abroad at <http://home.muenster.net/~indro/travel.htm>

The intended receiving prescriber should be provided with details of the patient's name, date of birth, methadone dose, dates to be dosed, the patient's address at the new location (if known) and the reason for transfer.

5.10.2 Receiving Transfers

If a prescriber has accepted a transferred patient, sufficient information should be obtained from the transferring prescriber to ensure safety of treatment and continuity of care, and to facilitate decisions about take-away doses. It may be necessary to contact the transferring prescriber and request appropriate documentation. The documentation should include:

- o Patient's full name, date of birth, old and new address in Myanmar
- o Current methadone dose in milligrams
- o Date and strength of the last methadone dose provided under the transferring prescriber's care (including the number of take-away doses provided, if relevant).

5.11 Termination of Treatment

Given the risk of relapse to illicit opiate use following cessation, methadone treatment is usually quite long term; patients should be encouraged to remain in treatment for as long as they benefit from the program and preferably more than 3 years. The continued use of heroin, while it should be discussed, is not a reason to terminate treatment. The patient will still benefit from reduced drug use, decreased risky behaviours and decreased risk of opioid overdose. The program offers the patient relief from the need to obtain drugs, and an opportunity to stabilize their lives and withdraw from the drug-taking culture. Evidence suggests the benefits increase when the patient remains in treatment for more than 12 months.

Voluntary Withdrawal from Methadone

Patients may wish to cease treatment for a variety of reasons. Premature withdrawal should be discouraged and the patient warned of the high risk of relapse, particularly if there is rapid reduction of the methadone dose.

The decision to withdraw and the rate of withdrawal may be determined by agreement between the patient, the prescriber, and others in the treatment team (including the dispenser and counsellor). Closely monitor the patient, and if they experience difficulties, cease the dose reduction until they stabilize. (See Section 6 for more information about withdrawal.)

The minority of patients tolerate these maximum rates of withdrawal:

Methadone Dose Maximum Rate of Withdrawal (Per Week or fortnight)
Over 50 milligrams : 5 milligrams
30 - 50 milligrams 2.5 milligrams
Less than 30 milligrams 1-2 milligrams

The rate of withdrawal should be reduced if the reduction jeopardizes successful withdrawal. The withdrawal can recommence after a period of stabilization. The patient may benefit from antidepressant treatment and intensive counselling during and after the withdrawal process. General guidance is that reduction of the daily dose by 1mg per fortnight or 25mg per year is usually achievable when all social factors are favourable.

5.11.1 Involuntary Withdrawal from Methadone

It may be decided to discontinue treatment because the patient is making unsatisfactory progress or behaving unacceptably. Sometimes the potential dangers to the patient, treatment staff and other patients outweigh the benefits of continued treatment. (The patient may be referred to a specialist Drug Treatment Centre for management and supervision.)

Some reasons for involuntary withdrawal are described in the following box:

Reasons for Involuntary Withdrawal

Violence, threats or abuse to staff or other clients
 Diversion of methadone from the dosing point
 Confirmed drug dealing or other illegal activities around dosing points
 Continued use of dangerous quantities of other CNS depressant drugs
 Failure repeatedly to attend for treatment (see below)
 Trafficking of take-away doses.

Involuntary withdrawal should occur over a reasonable period, depending on the patient's dose and the circumstances. Four weeks are usually sufficient for patients on doses below 50 milligrams; however, up to eight weeks may be required for patients on higher doses. Explore alternative treatment options with the patient.

Abrupt termination of treatment or dramatic reductions in dosage is rarely warranted and associated with marked deterioration in behaviour, drug use and emotional stability. Drug induced psychosis may present in the context. However, immediate termination may be appropriate if the safety of staff and other patients cannot be assured.

Whatever the reason for termination of treatment a 'Notification of Termination of Methadone Treatment' form should be sent to the Drug Treatment Centre and DoH within two weeks of the patient's withdrawal.

5.12 Failure to Attend for Dosing

For patients who miss up to three doses there is no need to reduce the recommencement dose. Given the risk of loss of tolerance and potential toxicity, patients who fail to attend for dosing on three consecutive days should not receive methadone without the prescriber being consulted.

Dispensers are advised to notify the prescriber in these circumstances who should consider:

- ◆ The reasons for failure to attend
- ◆ Drug use during this period
- ◆ The patient's report of opiate withdrawal
- ◆ Physical evidence of withdrawal or intoxication.

5.12.1 The Recommencing Dose

The decision about the recommencing dose should account for the number of consecutive missed doses; opioid use during this period; possible current misuse of other CNS depressants; and the likelihood of a loss of opioid tolerance.

- ◆ For patients on a dose of greater than 40 milligrams, generally reduce the dose by half if they miss more than three days (or 5mg / missed day if their narcotic tolerance is high). If they miss more than five days, reduce the dose to 40 milligrams or less and increase as per commencement guidelines.
- ◆ For patients previously on a dose of 40 milligrams or less, reduce the recommencing dose by approximately 5 to 10 milligrams. Review the patient the following day and adjust the dose accordingly.

This situation has inherent risks, so if there are any doubts about the recommencing dose, advice should be sought from the specialist at the Drug Treatment Centre.

5.13 Vomited Doses

Patients may vomit after ingesting their methadone dose, creating uncertainty about whether they have absorbed it. Consider the interval between ingestion and vomiting. Methadone is almost fully absorbed within 20 - 30 minutes of ingestion. Vomiting early after ingestion may prevent full absorption of the dose, although the patient may not vomit all the stomach contents. If vomiting occurs more than 20 minutes after ingestion, an adequate dose is likely to have been absorbed.

If vomiting is witnessed within 20 minutes of ingestion of the dose, review the patient. (If the patient is reviewed within four to six hours after consumption of their dose, plasma levels will be at their peak). If there is good evidence of opioid withdrawal, administration of a supplementary dose may be recommended (half the usual dose). If there are doubts about the amount of methadone absorbed despite vomiting, it is better to be cautious and not recommend administration of additional methadone but to review the patient the next day.

Patients sensitive to the emetic effects of opiates may require anti-emetic treatment (eg pre dose domperidone, prochlorperazine or metoclopramide) for a few days of initial treatment. Additional care should be exercised with pregnant patients because opioid withdrawal can cause fetal distress.

5.14 Prevention of Methadone-Related Deaths

Most prescribers and dispensers will initially be unfamiliar with the unusual pharmacokinetics of methadone: slow onset of action and a long half-life requiring about 10 days for tissue and plasma levels to equilibrate. Given methadone's unique pharmacokinetics and potential to cause prolonged coma and respiratory depression in patients who may continue to misuse other substances such as alcohol and prescription CNS depressants, special care is needed particularly during initiation and stabilization in the first ten days.

The injecting drug user's risk of drug overdose death is considerably reduced once they are stabilized on methadone maintenance treatment. Nevertheless, a history of illicit and polydrug abuse or alcohol misuse places the methadone patient at greater risk of drug overdose than that of the general community. Some methadone patients suffer from psychiatric conditions that expose them to the risk of suicide. Injecting drug use is hazardous, and may co-exist with psychiatric illness or risk-taking behaviour, exposing patients to the risk of injury or violent death such as suicide, homicide or trauma.

Several categories of methadone-related drug deaths provide opportunities for prevention:

- Deaths during commencement of treatment while the patient is being stabilized.
- Combined drug toxicity deaths involving the misuse of other drugs (alcohol, illicit drugs and benzodiazepines).
- Deaths preceded by a long period of coma during which the high risk of death is not recognized by others.
- Deaths involving psychiatric complications such as suicide and psychosis.

5.14.1 Commencement of Treatment

The highest risk of drug overdose occurs during commencement of treatment, when ingested methadone is equilibrating with tissue reservoirs and accumulating in the body. During this time the patient's lifestyle and drug taking may still be chaotic.

Blood levels during this period may not be sufficient to prevent craving, or may reach toxic levels if the clinical judgment about neuroadaptation is incorrect. The patient may continue using illicit opioids or high doses of prescription drugs to self-manage symptoms.

Countermeasures

- Give a high priority to assessing the patient's risk of unsanctioned drug and alcohol use during initiation of treatment. If there is a high risk, arrange to review the patient frequently in the first few days before further dosing, and communicate any concerns to the dosing dispenser.
- Provide advice about the risks of unsupervised drug and/or alcohol use, particularly while establishing an effective dose of methadone.
- Undertake close supervision if it is judged that the patient is at high risk of misusing other CNS depressant drugs, or of experiencing methadone toxicity.
- Frequently review the patient during the first 10 days of treatment, particularly during the first week.
- Maintain good communication with the patient's dispenser, particularly about the recognition and management of methadone toxicity while the patient is being stabilized.

Methadone Toxicity: Symptoms and Signs

Mixed poisoning is usual. The usual opioid poisoning triad (coma, pinpoint pupils, and respiratory depression) may be preceded by:

- ◆ Slurred speech
- ◆ Unsteady gait
- ◆ Poor balance
- ◆ Drowsiness
- ◆ Retarded movement
- ◆ Stupor.
- ◆ Snoring

This is a serious medical emergency. You need to review the patient urgently. Poisoning may proceed to:

- ◆ Coma (unrousable, atypical snoring, flaccid, cyanosed)
- ◆ Respiratory depression and hypoxia
- ◆ Death.

5.14.2 Combined Drug Toxicity

Deaths due to methadone alone are rare; deaths almost always involve other CNS depressant drugs, particularly psychoactive prescription drugs such as the benzodiazepines, and alcohol. The benzodiazepines flunitrazepam, clonazepam and diazepam appear to be overrepresented in methadone-related drug deaths. Methadone tablets prescribed for pain, or diverted from licit prescribing for misuse contribute to methadone-related deaths

Countermeasures

- Advise the patient of the considerable risks of misuse of psychoactive drugs (such as the benzodiazepines) and alcohol while on methadone.
- Conduct a drug screen of supervised urine collections, or discuss drug use with the patient. Inform them of the risks of using CNS-depressant prescription drugs and alcohol while in treatment with methadone.

5.14.3 Recognition of Coma

Deaths from combined drug toxicity involving methadone may involve a long period of coma, during which the deceased has been left to 'sleep it off' and subsequently dies. A methadone patient who is unrousable and making noises suggestive of a blocked upper airway and depressed reflexes (snoring, gurgling, spluttering) is at very high risk of dying from drug overdose.

Countermeasures

- Advise the patient, family, friends and associates about the signs of coma, and the need to take urgent action if it is suspected. A patient who is unrousable and snoring (or making other sounds that suggest airway obstruction) is a medical emergency.
- The comatose patient should be positioned on their side with their head extended (left lateral position) and taken to hospital immediately.
- A methadone induced coma may require prolonged respiratory support and /or repeated administration of the opioid antagonist naloxone -often in an IV infusion over 24 to 36 hours. This can best be provided in an intensive care or high dependency inpatient environment.
- Apart from respiratory suppression, methadone, like other opioids, is not otherwise organ toxic in overdose.

5.14.4 Other Deaths Associated with Methadone Maintenance

Risk-taking behaviour exposes many methadone patients to a high risk of death from injury, particularly due to road trauma and homicide. Lifestyle factors such as poor nutrition and the high prevalence of smoking increase the risk of death from chronic non-communicable disease such as ischaemic heart disease and stroke. Illicit drug use is also associated with many infectious complications such as sub-acute bacterial endocarditis, septicaemia and blood-borne viruses (HIV and hepatitis B and C).

Suicide is the second most common cause of death of methadone patients (after drug overdose). Some methadone patients will have a history of psychiatric illness such as depression or psychosis, which may predispose them to the risk of suicide. They may have suppressed harmful emotions and symptoms during the period of injecting drug use, which may become evident once the patient is stabilized in methadone maintenance.

Countermeasures

- Undertake a psychiatric assessment as part of the initial patient assessment.
- Maintain a high index of suspicion for signs of suicidal intent, depression and other psychiatric complaints throughout treatment.
- Refer dual-disability patients (patients with addiction and a psychiatric illness) to a specialist methadone service for assessment and management, if appropriate.

Section 6

Prescribers

Prescribing Guidelines - Methadone for Heroin Withdrawal

6.1 Opioid Withdrawal Using Methadone

The goal of methadone-assisted withdrawal is to provide symptomatic relief during withdrawal from opioids. A 5 -14 day course of reducing doses of methadone can be expected to diminish but not completely relieve withdrawal symptoms. Some withdrawal symptoms may continue after methadone cessation, so it is often necessary to provide a limited and controlled supply of additional medication for symptomatic relief.

There should be close supervision of the supply of methadone and other medications subject to abuse. Methadone may be supplied as an outpatient supervised daily dose, and because the patient will be attending a dispensary each day, the dispensing site will be the most convenient method of supplying any withdrawal-assisting drugs likely to be abused (such as the benzodiazepines). It is not appropriate to supply prescriptions for large quantities (25 to 50) of benzodiazepine tablets to assist opioid withdrawal.

Detoxification can occur in a residential setting (home or community detoxification unit) or hospital, or via close supervision as an outpatient. Methadone assisted detoxification may be appropriate if:

- ◆ The patient has a history of previous unsuccessful withdrawal efforts without methadone.
- ◆ There is an urgent need to stabilize a patient with medical or psychiatric conditions.
- ◆ The patient expresses a preference for this withdrawal treatment.

Additionally, a positive treatment experience with methadone, even short term, may help a patient eventually decide to opt for the longer-term benefits of methadone maintenance. Advise patients that this is a possible outcome of commencing short-term withdrawal using methadone.

Registration is still required to provide methadone treatment before writing any prescription, including methadone-assisted opioid withdrawal.

Opioid withdrawal treatment without methadone or other treatment options may obviate the need for methadone for patients with a short history of opioid use. Short-term use of methadone to assist withdrawal may then be successful if there is:

- ◆ Strong patient motivation to become drug free
- ◆ Good social support for the patient
- ◆ A short history of opiate use
- ◆ No use of any other drug
- ◆ A patient request for this treatment option.

Provide a supportive and encouraging approach to the patient during withdrawal. Discuss treatment options so the patient's decision to undergo withdrawal is well informed. Counselling should also be provided, together with advice about relapse prevention. It is important to warn the patient to expect a loss of opioid tolerance and to watch for the

danger of heroin overdose when reducing the dose of methadone is reduced and when abstinence is achieved.

6.2 Initial Methadone Dose and Rate of Dose Reduction

Base the initial dose and rate of withdrawal on the patient's:

- ❖ Previous experience of opioid withdrawal
- ❖ Current level of opioid use
- ❖ Social circumstances and support.

After discussing treatment options, and the benefits, risks and degree of discomfort to expect, make a joint decision with the patient about a withdrawal plan. Commence withdrawal over 10 to 14 days with an initial dose of 20 to 30 milligrams, then reduce the dose each day by 2.5 to 5 milligrams. Hold the dose at the same level one or two days if the patient experiences discomfort or circumstances make it difficult to manage the discomfort of withdrawal on that day.

A limited extension of the planned schedule of dose reduction may be allowed at the patient's request; however, if withdrawal appears likely to extend beyond 10 - 14 days, review the intent of withdrawal with the patient so they fully understand the implications of extending the withdrawal period. Discuss the patient's ability to accept the level of discomfort and to control the opioid use they are attempting to cease. Extending the withdrawal period or needing to increase the dose of methadone to control heroin use raises the need to strongly consider maintenance.

Patients undergoing opioid detoxification may experience withdrawal symptoms that may be unpleasant enough to contribute to relapse to heroin use. Other symptomatic treatment may limit the level of discomfort. Prepare the patient for some withdrawal discomfort, particularly as the dose of methadone is reduced and in the two to four days after the last methadone dose.

Arrange to review the patient after they complete the methadone treatment, to assess their progress and discuss relapse prevention.

Section 7

Prescribers

General Information

7.1 Prescription Drug Abuse

Prescription drug abuse is widespread among injecting drug users. The psychoactive drugs preferred include the benzodiazepines and prescription opiates such as morphine, codeine and pentazocine. Drugs are often taken in doses far exceeding normal therapeutic use. In the case of the benzodiazepines, this can contribute to anterograde amnesia, cognitive impairment, sleep disorders, benzodiazepine dependence, and a severe withdrawal syndrome (including seizure if the patient stops taking the drugs suddenly). All CNS depressants can contribute to respiratory depression, coma and death due to combined drug toxicity.

Patients on methadone treatment may continue to seek and misuse benzodiazepines, and their benzodiazepine dependence must be managed.

7.2 Management of Benzodiazepine Abuse

- ❖ Urine drug screening allows the prescriber to monitor the patient's unsanctioned use of other substances, including benzodiazepines.
- ❖ Counsel the patient about the adverse effects and risks of polydrug abuse, including information about the interaction of CNS depressants (benzodiazepines, opioids and alcohol) and about the half-lives of benzodiazepines. This is particularly necessary while the patient is initiating or being stabilized on methadone maintenance treatment.
- ❖ If the provision of benzodiazepines is necessary for either maintenance or gradual withdrawal, there should be a single prescriber and daily dispenser. After arranging daily dispensing, prescriptions should be endorsed with a statement indicating that it is to be dispensed only at a particular dispensary on a daily basis.
- ❖ Advice about the management of benzodiazepine dependence should be sought from the specialist at the Drug Treatment Centre.

7.3 Legal Responsibilities

The legal framework for the methadone program in Myanmar is the Narcotic Drugs and Psychotropic Substances Law 1993.

Prescription and Supply of Controlled Drugs

- The prescribing doctor should take all reasonable steps to ensure a therapeutic need exists, and then prescribe/supply Controlled Drugs only for the medical treatment of a patient under their care.
- For Controlled Drugs, the prescribing doctor should ascertain the identity of the patient.
- The prescribing doctor must not prescribe a Controlled Drug merely to support drug dependence.
- Medical practitioners are prohibited from self-prescribing and self-administering Controlled Drugs.
- A prescription for a Controlled Drug must contain full details of the prescriber, the patient, the drug, the quantity and the maximum number of repeats (in words and figures). It must also include precise directions (except where complex directions are provided separately), and must be signed by the prescriber. Prescriptions may be

handwritten or computer generated (provided there handwritten drug name, dose and signature).

- In an emergency, a doctor may contact doctors at the local Drug Treatment Centre for supply of Controlled Drugs.
- When a doctor supplies a Controlled Drug (including samples), they must label the pack with specified details.

Drug-Dependent Patients

- If there is reason to believe that the patient is drug dependent, they must be registered for their dependency with DoH.
- Their dependency must have been registered with DOH before they are treated with a Controlled Drug.

Prescriptions

- A pharmacist / dispenser must possess a valid prescription before supplying a Controlled Drug to a person (except in an emergency - see above).

Other Matters to be Notified

- Lost Controlled drugs or a lost Drug Dependent Patient Register must be reported to the police and the DoH.
- If there is suspicion that a person has obtained a Controlled Drug (or a prescription for them) by false pretences, the police and DoH must be notified.
- The police and DoH must be notified if prescription pads are lost or stolen. (Stationery should always be kept out of sight in a secure place.)

Storage and Record Keeping

- Controlled Drugs must be stored in a facility providing no less security than that provided by a locked steel drug cabinet.
- Details of the administration or supply of Controlled Drugs must be recorded, and these records must be readily retrievable for up to three years. In addition, Controlled Drug transaction records must be able to be readily sorted by drug, and they must show a true and accurate balance of each drug.

7.4 Confidentiality

As with many other forms of medical treatment, patients are entitled to protection of their privacy. Doctors have an ethical responsibility to only provide information to others with the patient's consent. Take special care to prevent access to clinical or other records that may reveal that the patient is being treated with methadone.

7.5 Driving and Methadone

While being inducted into treatment or having their dose changed, patients may experience impairment of their ability to perform complex tasks such as driving a motor vehicle or operating machinery. Similarly, methadone patients taking other CNS depressants such as alcohol or benzodiazepines may experience impairment.

In both these circumstances patients should be advised not to operate machinery, or drive a motor vehicle if they feel the drug is adversely affecting their ability to do so. Once a patient is stabilized on treatment, their ability to perform complex tasks such as driving is unlikely to be impaired (provided their dose has not recently increased).

For those who are prescribed methadone and who are well controlled, it is recommended that they may drive if they are under regular review and stable. However, such patients need to be warned about the effects of dosage changes.

In the case of narcotic, methadone or analgesic abuse, individuals should not drive if there is clear evidence of abuse or dependence.

7.6 Forms

The Drug Treatment Service uses a number of forms to enable coordination of the registration and take-away dose system.

Forms for Treatment of Opiate-Dependent Patients with Methadone Solution

- Registration of a Drug User card is completed and endorsed "Methadone Treatment" for the patient to carry, with summary details recorded at the DTC.
- The 'Notification of Commencement of Methadone Treatment' form in addition to the Drug User Registration form is used to notify the Yangon DTC that treatment with methadone has commenced.
- The 'Notification of Termination of Methadone Treatment' form is used to notify the Yangon DTC that treatment with methadone has ceased.
- The 'Methadone Treatment Program Report' form is used to provide a contemporary record (at the end of each month) to the Yangon DTC (and DoH) of the number of patients actively engaged in treatment and their doses.

Appendix

Prescribers

Appendix 1: Clinical and Support Services

(needs update and contact details)

Drug Treatment Centres are a valuable resource particularly for health and welfare professionals, the service provides advice and information on the clinical management of patients with drug and or alcohol problems, including:

- Advice on recognizing and managing withdrawal syndromes
- Information about drug use complications
- Drug information
- Prescribing information
- Assistance with cases of acute intoxication.

Hepatitis B & C Information

Hepatological department at Yangon General Hospital

HIV/AIDS Information

HIV Team OPD Service, Yangon General Hospital

TB Information

TB Clinic - Respiratory Unit, Yangon General Hospital

Appendix 2: Features of a Methadone Prescription

To be written on paper for sealed envelope and in patient held outpatient book.



Patient Prescription Book

Drug Treatment Centre

Name of the Patient

Date of Birth

National Registration No.

Narcotic Registration No.

Address

Clinical Remarks

..... Drug Treatment Centre

DATE

Name of the Patient

Methadone Solution5mg/ml.....

Dispensemg(in words)


From start date

To end date

At Dispensary

.....

Prescriber's signature

Dr ABC Prescriber	_____	your name, address, contact details
Drug Treatment Centre		
Helpful Hospital		
Phone 01 222 3333		
	29 / 10 / 2010	date
<hr/>		
Maung AB Patient	_____	patients name and address
123A Home Street		
Friendly Township		
Rx Methadone Solution 5 mg/ml	_____	script written indelibly in ink
Dispense 60mg (sixty)	_____	dose in words and figures
from: 30 October 2010	_____	date of first dose on this script
until: 29 November 2010 inclusive	_____	date of last dose on this script
	_____	for computer- generated script, particulars of script also hand written
	_____	signature
To be dispensed at:	_____	pharmacy at which methadone is to be dispensed
DTC Dispensary		
Helpful Hospital		

Appendix 3: Safe Prescribing Recommendations for Deputizing Colleagues Who Are Not Yet Approved to Prescribe Methadone

Given the risks of toxicity associated with methadone treatment, if the prescriber is unfamiliar with the risks of methadone treatment then they must be extremely cautious when prescribing for patients.

o For stable patients requiring only the continuation of an expired prescription without an increase of dose or take-away frequency, take a history and examine the patient. Check with the dispensary that the patient has attended regularly for daily dosing.

o Contact the specialist at the Drug Treatment Centre:

If there are any management problems or concern about the safety of the patient

- If a dose increase or take-away dose appears necessary. Do not provide an increased dose or take-away dose unless advised to do so by the specialist. Document the advice given and the name of the consultant in the patient's notes.

All deputizing practitioners should manage the patient as described in the following box:

Management by Deputizing Prescribers

Continue the usual prescriber's management plan and dosage regimen as documented in the clinical record. (It is acceptable to reduce the dose if the patient is experiencing toxicity.)

Note on the prescription that you are temporarily deputizing for the patient's usual prescriber.

Limit the duration of the prescription to the expected period of absence of the usual prescriber, indicating precise starting and finishing dates.

Arrange for the usual prescriber to review the patient as soon as possible thereafter.

Document details of consultations and methadone prescriptions in the patient's notes.

In addition, ensure the prescription gives clear, unequivocal directions to the dispenser, including (Section 5.3):

- The precise dose in words and figures
- The precise starting date
- The date of the last dose on this prescription
- The name of the dispensing site at which it is to be dispensed.

Treatment should not be initiated or transfer of patients arranged between dispensing sites without discussion with a consultant at a major DTC.

Before authorizing take-away doses:

- Contact the dispensing site to confirm the regularity of dosing and the patient's progress.
- Ensure the patient is stable and meets all the criteria specified in the guidelines (Section 5.10).

Appendix 4: ARV Methadone Interactions

MODULE 5 - SPECIAL PATIENTS GROUPS

Table of interactions between methadone and HIV related medications

Not all interactions have now been studied. Many of the studies that have been done are short term with relatively few patients. Pharmacological changes such as AUC (are under curve – indication for how much medication the patient has absorbed) do not always correlate with the need clinically to make dosage adjustments.

Note that withdrawal effects caused by commencement of ARV or other medications may be delayed in their onset by the slow induction of liver enzymes over several days. Patients on methadone who are commenced on ARV should be reviewed by the Drug Treatment Specialist observing for signs of withdrawal or intoxication several times over the first two weeks from relevant ARV commencement or cessation.

Medication Names in bold are the common brand names	Effect on methadone	Effect of methadone on medication
AZT Zidovudine	None	Increase AZT AUC by 40%, dose change usually not necessary.
DDI Didanosine	None	Decrease DDI AUC by 60%, may need to increase DDI.
D4T Stavudine	None	Decrease D4T AUC by 18%, no dose change necessary.
3TC Lamivudine	None	Not studied, use usual dose.
Abacavir	Increase methadone clearance. May need to increase methadone dose.	Delay to peak concentrations, no dose change necessary.
Nevarapine	Withdrawal symptoms, need to increase methadone dose by 25% - 50%.	No change in Nevarapine.
Efavirenz	Withdrawal symptoms (decreases methadone levels 48%), increase methadone 40% - 50%.	No change in Efavirenz.
Protease Inhibitor Class	All medications below have complex effects on hepatic metabolism and protein binding. Give usual doses, observe the patient for symptoms and signs of withdrawal and adjust methadone accordingly.	
Nelfinivir	Decreased methadone levels, but no withdrawal symptoms, adjust dose only if necessary.	No change in Nelfinivir.
Ritonivir	Decreased methadone levels, but but unclear withdrawal symptoms, adjust dose only if necessary.	No change in Ritonivir.
Ritonivir/Saquinivir	Complex changes involving racemic types of methadone and protein binding, adjust dose only if necessary.	No change in Ritonivir/Saquinivir.
Amprenivir	Decreased methadone levels, but no withdrawal symptoms, adjust dose only if necessary.	Decrease Amprenivir AUC – may need to increase Amprenivir
Lopinivir	Decreased levels reported, adjust only if necessary.	No change in Lopinivir.
Indinivir	Not formally studied, adjust if symptoms occur.	No change in Indinivir.

Source: The International Centre for the Advancement of Addiction Treatment, 2002

Appendix 5: Neonatal Opiate Abstinence Syndrome

Neonatal Abstinence (withdrawal) Syndrome occurs in 60% of all fetuses exposed to drugs. Heroin, cocaine, and amphetamine withdrawal usually occurs within the first 48 hours of life. Methadone withdrawal can occur up to 2 weeks after birth, but most likely occurs within the first 96 hours after birth. The syndrome is typically an autonomic multisystemic reaction, the symptoms of which are mostly neurological and may be prolonged.

All babies born to drug dependent mothers should undergo normal postnatal monitoring. In addition, specific use of the assessment tools (eg. Modified Finnegan NASS) should commence 2 hours after birth and subsequently every 4 hours. The assessment tool is usually scored every 4 hours (half to one hour after feeds) with pharmacological treatment initiated when 3 consecutive scores average greater than or equal to 8; or with two consecutive scores greater than or equal to 12.

Babies of mothers on higher dose methadone (> 80mg/day) should be observed for up to a week after birth to monitor for late development of a neonatal withdrawal syndrome.

Neonatal Abstinence (withdrawal) Scoring Chart for term infants (Modified Finnegan NASS)

System	Signs	Score	Date and Time
Central nervous system disturbances	High pitched cry	2	
	Continuous high pitched cry	3	
	Sleeps <1 hour after feeding	3	
	Sleeps <2 hours after feeding	2	
	Sleeps <3 hours after feeding	1	
	Mild tremors, disturbed	1	
	Mod-severe tremors, disturbed	2	
	Mild tremors, undisturbed	3	
	Mod-severe tremors, undisturbed	4	
	Increased muscle tone	2	
	Excoriation (specify area)	1	
	Myoclonic jerks	3	
	Generalised convulsions	5	
Metabolic / vasomotor/respiratory disturbances	Fever (37.3-38.3°C)	1	
	Fever (38.4°C and higher)	2	
	Frequent yawning (3-4 times)	1	
	Nasal stuffiness	1	
	Sneezing (>3-4 times)	1	
	Nasal flaring	2	
	Respiratory rate >60/min	1	
	Respiratory rate >60/min with retractions	2	
Gastrointestinal disturbances	Excessive sucking	1	
	Poor feeding	2	
	Regurgitation	2	
	Projectile vomiting	3	
	Loose stools	2	
	Watery stools	3	
	TOTAL SCORE		
	Scorers Initials		

Treatment:

Supportive care:

Pacifier, swaddling, close wrapping, small frequent feeds, close skin contact with mother.

Opiates:

Opium Tincture: Use a 1:25 dilution. When ordering such a medication, be sure to emphasize that a dilute solution of the tincture is needed in a 1:25 ratio. Without this emphasis, the pharmacy may deliver undiluted tincture of opium (used for adults).

Starting dose: 0.05-0.1 mL/kg PO q4-6h

Maintenance dose: 0.05 mL/kg q4-6h; increase by 0.05 mL/kg at the end of every 4-h period until desired response is achieved; then, maintain dose for 3-5 d; then begin taper of 10% (of peak dose) every 2-3 d; rare to exceed 0.7 mL/dose; not to exceed 1-2 mL/kg/24h

Morphine elixir, 1 mg/mL – If available may be used as an alternative to diluted tincture of opium.

Starting dose: 0.02 mg/kg PO q4-6h

Maintenance dose: 0.02 mg/kg PO q4-6h; increase by 0.02 mg/kg at the end of every 4-h period until the desired response is achieved; then maintain dose for 3-5 d; then, begin taper of 10% (of peak dose) q2-3d

Sedatives:

Phenobarbitone, diazepam and chlorpromazine have all been used in this context but the control of symptoms, convulsions and return to normal feeding is not as satisfactory as with opiates.

Until weaning of the dose has begun, constantly monitor patient's vital signs and oxygen saturation.

Adverse effects include sedation and constipation; overdosing may cause narcosis, manifested by decreased reflexes and poor Moro reflex, sucking, grasping, and response to pain; more profound narcosis includes hypotonia, obtundation, coma, irregular shallow respirations, apnea, bradycardia, and hypothermia

If signs of opioid toxicity are observed, do not give naloxone; withdrawal seizures can occur, but provide general including respiratory support.

The neonatal withdrawal syndrome and its treatment may require a two to four week post natal admission period. Particular attention is required over this time to establish satisfactory breast feeding and normal maternal bonding processes.

Appendix 6: Methadone Client Transfer Facsimile

To: (Prescriber / Drug Treatment Centre)

Fax:

From: (Name of Prescriber)

Subject: transfer of methadone patient

PATIENT AND PRESCRIBER DETAILS

Hospital registration Number

Patient Names:

Date of Birth:

National Registration Number

Narcotic Treatment Board Number

Father's Name

Prescriber: Dr

Telephone:

This dispensary has been asked to provide methadone doses (including take-away doses)* to this patient for treatment up to and including:

Date


Final dose: milligrams

Prescriber's Signature:

Place prescriber / DTC site label or stamp here with prescriber and dispensary names, addresses, telephone numbers and fax numbers.

* Strike out if inapplicable.

Methadone Guidelines for Dispensers



About these guidelines

These guidelines are divided into two separate parts: one for prescribers and one for dispensers. They are bound in one volume to enable ready access to the guidelines provided to your professional colleagues, enhancing coordination and cooperation between the practices of both professional groups. The book should be wire-bound for easy access to the information relevant to your practice - simply turn your section to the front.

The guidelines have been prepared by practitioners with expertise in the use of methadone to treat opioid dependence. They are intended to assist medical practitioners and dispensers to treat opioid-dependent patients in a safe and effective manner. The guidelines are general recommendations and are provided for information purposes only. The guidelines cannot provide detailed direction in respect to the management of every patient in every clinical situation, and do not constitute specific treatment advice.

Individual medical practitioners and dispensers are responsible for decisions about the safety and effectiveness of treatment used for each patient. The guidelines are not intended to replace professional judgment in individual cases.

Each guideline should be used only for the purposes stated.

Treating professionals may be subject to various statutory, common law and contractual obligations.

Acknowledgments

See page 1

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Essentials of Methadone Administration

These guidelines provide advice relating to the supply and administration of methadone to patients of the Myanmar methadone program. This is conducted in accordance with the Myanmar Narcotic Drugs and Psychotropic Substances Law 1993

In circumstances not specifically covered by the guidelines, you should:

- Contact the prescriber or the local Drug Treatment Centre.
 - Address the situation in accordance with the following principles:
1. **Ensure positive identification of the patient before administering a dose.** Refer to the patient's photograph, which the prescriber has certified.
 2. **Ensure the dose is prepared as authorized by the prescriber.** Examine the prescription to verify the dose and ensure the prescription is current.
 3. **Determine that it is safe to administer a dose.** Determine precisely when the previous dose was administered, contacting the previous dosing point when necessary; do not dose but contact the prescriber if three or more consecutive doses have been missed. Also, assess the patient for signs of intoxication.
 4. **Ensure the dose is consumed with no possibility of diversion.** Observe that the patient takes the dose, and have the patient speak to demonstrate that they swallowed the dose.
 5. **Ensure the prescriber is advised of irregularities in a patient's attendance,** behaviour or condition. Contact the prescriber and record details of the communication. Take a pro-active role in interaction with the methadone prescriber.
 6. **Ensure the necessary information is readily available to all dispensers.** Ensure patient records, records of administration and details of communications with the prescriber are clearly and consistently maintained. Also, ensure methadone program guidelines are readily available for reference.

Section 1

Dispensers

Introduction

These guidelines have been developed to assist practitioner and patient decisions about the safe and effective use of methadone to treat opioid dependence.

1.1 Methadone - An Effective Treatment for Opioid Addiction

Methadone has become established in many parts of the world as an effective treatment for opioid dependence. Some long-term heroin users can be successfully treated with detoxification and abstinence-based treatments, but studies have shown that more than 70 per cent will relapse to illicit opiate use within one to two years. Methadone can prove valuable in assisting these people to successfully manage physical dependence, drug craving and compulsive drug use.

Methadone has been used to treat opioid dependence, both in detoxification from opioids and maintenance treatment for more than 40 years. It is useful for these purposes because: It has cross-tolerance with other opioids, enabling it to be substituted for abused drugs such as heroin, morphine and opium.

It can be taken orally, so drug-dependent patients can avoid the reinforcing effects of injecting.

It is long acting, enabling once-daily dosing.

Drug dependence is a complex condition involving social, psychological and biological components. Dependence on illicit opiates is a serious condition currently associated with severe morbidity, risk of BBV transmission and death. These risks arise from both drug overdose and the morbidity and injury that result from chronic illicit drug use, injecting or misuse of licit opioids. Methadone can be compared to other drugs that are effective in treating serious chronic relapsing conditions such as hypertension and diabetes; these conditions, like opiate dependence, are chronic, require daily treatment, and have a high risk of adverse effects if treatment compliance is poor.

Methadone is effective in reducing dependence on heroin. Supervised daily supply of an adequate dose of methadone in a structured program has been demonstrated to:

Reduce or limit illicit heroin use.

Decrease criminal activity.

Stabilize the patient's life.

Reduce chaotic drug taking.

Make it possible for heroin and opium users to lead productive lives.

Decrease high-risk needle use such as sharing.

As a result there are substantial benefits for the individual, their family and society.

Benefits of Methadone Treatment

Decreases illicit opiate drug use.

Reduces illness and death from illicit drug use.

Reduces criminal activity.

Reduces high-risk needle sharing.

Enhances social productivity.

The Myanmar methadone program will initially be based on delivering services through specialist drug treatment centres and hospital dispensers. It will make methadone more readily available, and will enable integration of the treatment of opioid addiction with general medical care. This is important, because many opioid-dependent patients have experienced serious illness, HIV infection or injury as a result of their years of injecting drug use and dependence. In the future in a community-based program, treatment of drug addiction will be normalized and de-stigmatized, and the congregation of large numbers of patients around drug treatment centres will be avoided. It will then be easier for patients to retain their anonymity. With a wider spread of medical and dispensing services, accessibility and choice will be improved. It is also expected that co-location of treatment services for opioid dependence, tuberculosis and HIV will provide efficiencies for patient access and improve adherence with treatment for these common co-morbid conditions.

Despite the proven success of methadone programs, there are some risks. Methadone is a potentially toxic drug with a low therapeutic index (the therapeutic dose is close to the toxic dose). It is often used to treat patients who may have a history of compulsive and reckless drug use. Some patients have psychiatric and social problems. Using a potentially toxic drug to treat a patient whose behavioural history may put them at special risk warrants a cautious approach.

The Myanmar methadone program is structured through careful initiation processes and dose increases with supervised dosing to minimize the risks involved and maximize the benefits through long term treatment, counselling and support. These guidelines are consistent with the national drug abuse prevention and control program prepared by the Department of Health.

1.2 The Problem of Heroin Use

Heroin and opium are short acting opiates with a marked tendency to develop a dependence syndrome, when used in a recreational manner for their euphoric or analgesic properties. The mode of administration of these drugs may in addition generate a risk of drug overdose or blood born virus transmission. The illicit and often expensive nature of heroin and opium contribute to the criminal behaviours associated with their use; primarily acquisitive crime and drug trafficking. There are often substantial behavioural changes associated with the dependence syndrome which have their own social cost as individuals diminish interest in other activities, relationships and their own health.

1.3 Risks Associated with the Methadone Program

Methadone is an opioid drug, and as such is prone to misuse and toxicity. The methadone program provides treatment to a high-risk population amongst whom misuse of prescription drugs and alcohol is highly prevalent. Under these circumstances, considerable care is necessary. The planned Myanmar program is designed to minimize the risks and enhance the effectiveness of methadone maintenance treatment. The risks of methadone treatment and the countermeasures to minimize them are described in the following table.

Table A: Risks of methadone treatment

Risk	Countermeasure
Complicated pharmacokinetics, prescriber/dispenser unfamiliarity	Prescriber/dispenser training; an registration system
Dosing by multiple prescribers and dispensers	A registration system
Poor compliance and diversion of syrup to illicit use and trafficking	A supervised dosing program; a limit on the number of take-away doses
Trafficking and consequent overdosing of non-tolerant people not on the methadone program Illicit injection of take-away doses	Tight control of take-away doses; discretion in judging patient suitability for take-away doses Dilution of take-away doses to at least 200 millilitres; discretion in judging patient suitability for take-away doses
Child poisoning with methadone	Tight control of take-away doses; child-resistant packaging and dilution of doses
Multiple dosing at time of transfer	Meticulous arrangements for transfer of registration
A high risk of drug overdose in the first 10 days of treatment	Meticulous care and frequent patient review in the first 10 days; dispenser alertness to signs of toxicity
A high risk of combined drug toxicity deaths	Dispenser alertness to signs of toxicity; comprehensive assessment of patients and the management of polydrug abuse provision of warning to patient about risk, and education of patient and family/friends about signs of overdose and coma (unroutable, 'snoring', respiratory depression, cyanosis)
Overdose risk increased with respiratory problems	Careful assessment, lower starting doses, smaller and slower dose increases, inpatient treatment and appropriate medications for all respiratory problems such as asthma, bronchitis, tuberculosis
Injury	Provision of warning to patient about risks of driving / using machinery before dose stabilisation and while the dose is being adjusted
Psychiatric co-morbidity, including suicide risk	Assessment of suicide risk; assessment of patient psychiatric status; maintenance of a high index of suspicion, and timely response to suicide risk; referral to specialist methadone service if appropriate for management of dual disability
Discontinuation of treatment	Set-up of supervised dosing to be as convenient as possible; discrete use of take-away doses

1.4 Types of Methadone Treatment

Withdrawal. Methadone can be used to medicate withdrawal for opioid-dependent patients, however relapse is no less common than other withdrawal regimens. A dosage schedule reducing the dose of methadone over 10 - 30 days can assist in significantly reducing withdrawal symptoms (Section 6).

Maintenance. A high proportion of patients who have withdrawn from opioid dependence will relapse. A program of maintenance on methadone for many months to several years can help these patients (Section 5).

In Myanmar the methadone program is initially to be delivered by township medical officers, drug treatment specialists and hospital dispensers. Specialist methadone services at Drug Treatment Centres provide support for the assessment and management of complicated cases. Training is expected to be provided in the future for community practitioners who wish to become involved in the program.

1.5 Harm Reduction

A harm reduction philosophy involves accepting that despite all efforts to control supply and reduce demand, many people will continue to have access to licit and illicit drugs, and to use them in a way that puts them and society at risk of serious harm. Cigarettes, alcohol, prescription drugs and illicit drugs such as heroin and stimulants are readily accessible, and they are used in quantities and manners that can cause harm. Harm reduction aims to reduce the adverse health, social and economic consequences of drug use.

Harm Reduction Activities include:

1. Improving access to sterile needles and syringes to reduce the need to reuse and share this injecting equipment, which exposes injecting drug users to the risk of transmission of blood-borne viruses such as hepatitis B and C and HIV.

Providing information about safe injecting practices.

Providing information about the prevention and management of heroin-related overdose.

2. Methadone treatment provides an opportunity for patients to avoid the need to obtain and inject heroin. This is useful for individuals for whom abstinence-based methods of dealing with their heroin addiction have failed because they continue to relapse. Effective doses of methadone have been demonstrated to reduce the quantity and frequency of illicit heroin use, along with the consequent criminal activity and the risk of transmission of blood-borne viruses.

The goals of methadone treatment include normalizing the patient's life, integrating them back into their family and the community, and keeping them in treatment when necessary. Methadone patients should be treated as far as possible in the same way as other patients.

Section 2

Dispensers

Clinical Pharmacology and Toxicology of Methadone

2.1 Clinical Pharmacology

- Methadone is an opioid with a full range of opioid effects, including sedation, analgesia, pupillary constriction and respiratory depression.
- It is cross-tolerant with other opioids, including heroin, and can be used to substitute for them.
- It is well absorbed orally, and is metabolized in the liver.
- It has a slow onset of peak blood levels of about four hours. This slow onset of action blunts its euphoric effect, making it unattractive as a principal drug of abuse.
- Peak activity occurs from four to eight hours after dosing.
- The duration of action for substitute therapy is about 25 hours, making it suitable for once-daily dosing.
- After the first dose, methadone is distributed into and binds with tissues such as the lung, kidney and liver. The half-life is shorter (about 15 hours) than when the patient is stabilized.
- Dosing over subsequent days results in equilibration with tissues, and the half-life increases to about 25 hours.

Methadone Pharmacology

Slow onset of action (4+ hours)
Minimal euphoric effect
Long half-life (25 hours)
Equilibration of tissue levels over five to seven days
Accumulation from repeated dosing
Low therapeutic index.

2.2 Toxicology

- Methadone has a low therapeutic index. Plasma levels found in cases of methadone-related deaths overlap those found during treatment.
- A therapeutic dose of 50 milligrams of methadone may be fatal for a non-tolerant adult. A lower dose may be fatal if combined with other CNS depressants such as alcohol or benzodiazepines.
- Deaths due to methadone toxicity alone are rare. They are usually due to combined drug toxicity, with alcohol, illicit drugs and prescription drugs (mostly benzodiazepines) contributing to CNS depression.
- The highest risk of overdose occurs in the first 10 days of treatment, when the patient is being inducted into treatment and may be engaged in unsanctioned drug use (heroin and benzodiazepines) and hazardous alcohol use.
- Prescribers and dispensers should be familiar with the symptoms, signs and management of methadone toxicity.

2.3 Methadone Toxicity: Symptoms and Signs

Mixed poisoning is usual. The usual opioid poisoning triad (coma, pinpoint pupils, respiratory depression) may be preceded by:

Slurred speech

Drowsiness

Unsteady gait

Retarded movement

Poor balance

Stupor.

This is a serious medical emergency. Urgent review by the prescriber is necessary. Poisoning may proceed to:

Coma (unroutable, snoring, flaccid, cyanosed)

Respiratory depression and hypoxia

Death.

Section 3

Dispensers

Setting up for the Methadone Program

3.1 Approval

Education and training are recommended for participating nurses, medical staff and dispensers. Approval as a methadone dispenser may be granted by the consultant at the Drug Treatment Centre after approved training.

If the dispensing site is not open seven days per week, it may accept only stable patients for whom the prescriber has authorized take-away doses (unless special arrangements can be made for dosing on the closed days).

3.2 Development of Procedures

The methadone program may be conducted in a number of ways, and all dispensers employed in the dispensary should have access to accurate information about the program. These guidelines should be readily available for reference by all dispensers.

Certification by Dispensers

It is strongly recommended that all dispensers employed in the clinic, dispensary or pharmacy be required to complete training and certification to confirm that they are familiar with the methadone program guidelines and the principles of methadone administration (Appendix A).

Retain signed certification documents in a designated file, with a copy readily available for reference by all dispensers.

Training of Dispensers

It is also strongly recommended that all dispensers employed in the dispensary be encouraged to complete the education and training course outlined above.

3.3 Storage

Methadone is a Controlled Drug and must be stored, according to the regulations, in a locked metal cabinet (or safe). Keep the bottle in use in a secure location and return it to the locked cabinet when it is no longer in use.

Methadone Solution has a shelf life of twelve months and does not require refrigeration.

3.4 Patient Records

It is recommended that a separate record be maintained for each patient so all necessary information is readily available to the administering dispenser when the patient attends (for example, separate school exercise books for each patient). Separate records also help ensure that information relating to one patient is not available to another. Large, bold lettering of patient's names on the covers of books should be avoided so that they will not be visible to other customers (and if possible these documents should be kept out of sight).

The records should clearly record the date and time of each dose, and provide for signatures by the patient and dispenser to confirm that a dose has been administered

(see example Appendix B). Details of payments and prescription expiry dates may also be included. The current prescription and patient photograph should be readily available to all dispensers. It is recommended that these be prominently located in the patient records (for example, the photograph firmly attached inside the front cover of the patient record book, with the current prescription firmly attached inside the rear cover). Each dispenser should have access to all relevant patient details, including details of communications with the prescriber, variations in dosage and details of take-away dose authorisation. It is recommended that such details be recorded in a permanent, readily retrievable and consistent manner where they are not readily accessible to patients (for example, in chronological order on a separate page of the patient book) (Appendix C).

3.5 Records of Administration

In addition to the patient records, a dispensary must retain an accurate record of each dose administered to each patient. These records may be computerized or manually prepared (Appendixes D and E).

The volume of methadone solution (expressed in millilitres) is commonly recorded, but these records should also clearly identify the dose of methadone (expressed in milligrams) so there is no possibility of misinterpretation.

For methadone dispenser, it is necessary to record the remaining balance on at least a daily basis. The records of administration may be in a form that enables the daily reconciliation to be carried out therein or within the Daily Attendance Register (Appendix F). Records must show the actual balance, not merely a calculated balance, and these should be reconciled on a regular basis.

Section 4

Dispensers

Dispensing Guidelines

4.1 Accepting New Patients

In accepting a new patient, contact should be made with the prescriber to ascertain whether the patient is new to the methadone program or merely transferring from another dosing point. Special management issues apply in each case (Section 4.7.2).

To ensure potential patients are fully aware of the structure and requirements of the methadone program, they may be interviewed before accepting them as methadone patients. A written agreement or contract may be considered as the basis for accepting new patients (Appendix G).

The prescriber must provide a photograph (certified on the back with signature of the prescriber) and the original written authorization (for example, the prescription) before the initial dose can be administered. A new patient should also be carrying their drug user registration card endorsed "Methadone Program" and an outpatient book.

Prescriptions are valid for the duration specified by the prescriber (which should not exceed six months), and dosing must not continue in the absence of a current prescription.

4.2 Prescriptions

Generally, a patient may not be dosed until the prescriber has provided the original written authorization (for example, a prescription). However, in an emergency the prescriber may verbally communicate instructions to the dispenser. The prescriber should fax a copy of the prescription (endorsed with the name of the dispensing site to which it is being sent) for the dispenser to use to confirm the details of emergency verbal instructions and/or a prescription delivered by the patient. In all cases, the prescriber should forward the original prescription to the dispenser as soon as practicable. Similarly, any increased dose should not be administered unless the prescriber has provided an original written authorization (prescription). In an emergency the prescriber's verbal communication of instructions is sufficient for increasing a dose, again followed by a faxed confirmation and then the original as soon as practicable.

A dispensing site should have a consistent method for clearly identifying the impending expiry of prescriptions. The aim is to give patients and/or prescribers ample warning. Clearly record the expiry date on the cover and/or corresponding page of the patient book, for example, or provide reminder notes to patients to alert them to impending expiry dates.

Expired prescriptions should be retained for three years, and should be filed in a secure manner that will preclude the possibility of confusing such prescriptions with the current prescription (for example, in a separate file or a pocket in the patient's book).

4.3 Preparation of Doses

Each dose of methadone syrup should be diluted with fruit juice or cordial. Conical measures may not be sufficiently accurate for measuring methadone liquid, so a syringe or displacement pump is recommended.

It is recommended that methadone doses be prepared at the time of a patient's attendance.

Some dispensaries transfer the methadone syrup to another container (for example, a bottle with a displacement pump) and some dispensaries dilute the methadone syrup to create a consistent strength working solution (for example, 5 milligram per 1 milliliter). In such instances, clearly label the container to indicate the concentration of the methadone syrup which is being used, so as to prevent administration of an incorrect (under or over) dose.

4.4 Administration of Doses

A discreet location for the administration of methadone is desirable for patient confidentiality, but patients should not be granted access to the dispensary. To prevent possible diversion of the methadone, directly supervise the patient as they take the dose, and engage them in conversation to ensure they have consumed the dose.

It is recommended that methadone doses be administered in disposable containers, or that the dispensary has some appropriate means of sterilizing glass or similar dosage vessels. The aim is to ensure a satisfactory standard of hygiene.

The patient should be observed for signs of methadone or other drug toxicity (Section 2), and dosing delayed if they appear intoxicated (Section 4.7.6).

4.5 Take-Away (TAKE HOME) Doses

Only the prescriber may authorize take-away (take home) doses. The prescriber should authorize take-away doses in writing, and details of that authorization should be prominently located (for example, in the patient book).

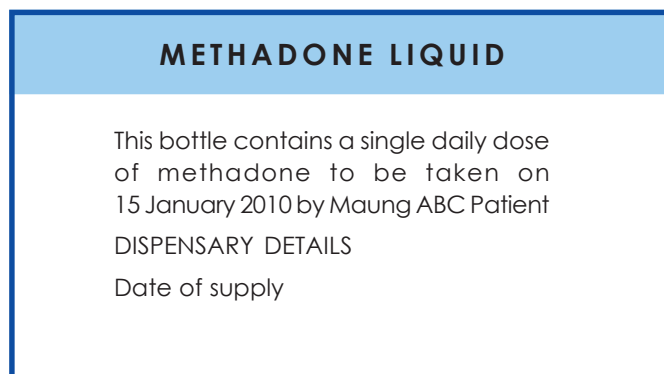
The methadone program is a supervised dosing program, and take-away doses should only be authorized for consistently attending patients, stable for three months. If a patient is observed to be missing doses, the prescriber should be notified so that they can review if it is appropriate to continue take-away doses.

The Guidelines for Prescribers contain the number and frequency of take-away doses that may be authorized with approval from the consultant at DTC. Under special circumstances (for example, illness or court appearances) prescribers may authorize take-away doses for up to three consecutive days no more than once a month, subject to the patient satisfying certain requirements for take-away doses. The prescriber should contact the dispenser to confirm that recent behaviour and dose collection have been stable, and that there is no concern that the dose may be misused. Contraindications to take-away doses include unstable patterns of substance use; unstable psychiatric conditions; and/or concerns that the methadone may be diverted or used inappropriately.

Schedule of Prescriber-Authorized Take-Away Doses

- After three months, the prescriber may authorize with permission from the DTC one take-away dose at the normal dose for special circumstances.
- Under exceptional special circumstances (for example, illness restricting mobility, travel, employment responsibilities), the prescriber may authorize take-away doses for up to three consecutive days no more than once per month, subject to the client satisfying the above requirements.
- Approval by the specialist at the Drug Treatment Centre is needed to authorize a take-away doses.

To deter injection or consumption by another person (especially a child), dilute each take-away dose with fruit juice or other particulate matter (for example, cordial) to a volume of 200 milliliters, and supply it in a container with a child-resistant closure. Adequately label take-away dose containers with the patient's name, the name of the drug and the date on which the dose is to be consumed.



Also attach the following warnings to the container:

- ***'This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery.'***
- ***'Keep out of reach of children.'***
- ***'May cause death or serious injury if taken by another person.'***

Details of take-away doses should be clearly recorded in the patient book and the administration records. Patients should be advised to store their take-away doses in a secure place out of the reach of children and other drug users. Take-away doses that are claimed to have been lost or stolen cannot be replaced without the prescriber's written authorization.

4.6 Termination of Treatment

Patients request most treatment terminations. Involuntary termination may also occur as a result of unacceptable behaviour. Attempt to avoid abrupt withdrawal if termination of treatment is necessary. A decision about termination is the responsibility of the prescriber. Patients terminating treatment should be advised of other treatment options, the likely loss of tolerance and the risk of overdose.

The dispenser may wish to cease dosing a particular patient because they have failed to comply with the agreement made at the start of treatment. This may include problems with compliance or with agreed payment schedules. In most circumstances, an attempt should be made to resolve the problem with the patient and notification made to the prescriber. Finally, the patient should be told of the failed negotiation and intention to cease dosing, preferably with a period sufficient to enable transfer to an alternative dosing point. The patient can either be referred to another methadone dispensing site or the prescriber requested to do so.

4.7 Periodic Management Issues

4.7.1 Patients Who Are New to the Methadone Program

During the initial stabilization period, the blood levels of methadone take some days to plateau as the drug is distributed to the body tissues. There is a significantly greater risk of toxicity due to lack of recognition of the long half-life of methadone and the possibility of concurrent polydrug use. Therefore the maximum daily dose for new patients should not exceed 40 milligrams. Further, it should be increased only gradually. The prescriber should have advised the patient about the risks of polydrug use and other related risks (for example, impairment of their ability to drive). However, when interviewing a prospective patient, endeavor to ensure the patient has been suitably informed of these risks.

4.7.2 Transfers

When accepting a patient who has been previously dosed at another location, confirm the date and amount of the final dose at the transferring dispensary (including any take-away doses). This is necessary to reduce errors in dosing. Transfer between dispensing sites may create risks for the patient.

- Dual dosing on the same day by different dispensing sites may cause severe methadone toxicity.
- The patient may not have been dosed for more than three days, and will have reduced tolerance for opioids, causing a risk of potentially dangerous opioid toxicity.

The prescriber may not be fully aware of all details, so confirm relevant information with the previous dosing point.

Before Administering a Dose to a Transferred Patient

Contact the previous dosing point to confirm the dose and verify precisely when the last dose was given. It is recommended that you ask for written confirmation of this information (for example, Attachment H).

Ensure you hold a current prescription and certified photograph of the patient. Contact the client's prescriber to confirm the dose and determine whether the client is to be reviewed before a dose of methadone is administered. You may also require a new prescription or other written confirmation.

A single missed dose may not be significant but you must advise the prescriber when a client attends irregularly for methadone doses.

4.7.3 Temporary Absences

Some patients will be admitted to hospital, taken into police custody, or temporarily transferred to another dosing point. On these occasions there may be a dispenser to whom the patient has been transferred - they should contact the usual dosing point to confirm the details (including the amount of the last dose and when it was consumed).

When patients are discharged from hospital, are released from custody, or wish to return to their usual dispensing site, there may have been a change in prescriber, a change in the patient's medication regimen, or a period in which methadone was not administered. The prescriber may not be fully aware of all details, so it is appropriate to confirm the relevant information with the previous dosing point and pass any extra information on to the prescriber. Inaccurate or incomplete information could result in a patient receiving an excessive, possibly toxic, dose.

4.7.4 Irregular Attendance

Regular attendance leads to less fluctuation in methadone levels and greater patient stability. Irregular attendance may be indicative of ongoing illicit drug use or a patient's need for counselling or review.

A single missed dose may not be significant but the prescriber must be advised when a client attends irregularly for methadone doses.

Take-away doses should only be authorized for, consistently attending patients stable for three months. If a patient is observed to be missing doses, notify the prescriber so they can review the appropriateness of continuing take-away doses.

4.7.5 Three Missed Doses

If a patient attends after missing two consecutive doses, decrease the dose by 5mg per missed day and contact the prescriber for advice. The prescriber may wish to review the patient. The patient's possible loss of tolerance to methadone means the prescriber may wish to further reduce the patient's methadone dose with a new prescription required.

4.7.6 Possible Intoxication

Given the risk of overdose or drug interaction, the dose must not be administered if a client appears to be intoxicated. The apparent intoxication may be due to the use of alcohol, prescription drugs or illicit drugs, or to methadone toxicity.

Common signs of intoxication or toxicity are:

- Slurred speech
- Unsteady gait
- Drowsiness or drooping eyelids
- Pupil constriction
- Shallow breathing.

In such circumstances, the prescriber should be contacted for instructions. If the prescriber cannot be contacted, advice may need to be sought from the Drug Treatment Centre.

It may be necessary to:

- Instruct the patient to return later in the day (mild intoxication).
- Instruct the patient to consult the prescriber (moderate intoxication).
- Instruct the patient to attend a hospital (severe intoxication).
- Administer a reduced or placebo dose (when the patient refuses to accept advice).

It must be remembered, that a prescription represents authorization to administer, but professional judgment must still be exercised about the appropriateness of dosing. In situations where safety is uncertain or there appears to be a risk of overdose caution should be exercised. The dispenser has the final word and must administer an authorized dose only if it is safe to do so.

Appendix

Dispensers

Appendix A: Methadone Program-Dispenser Certification

All dispensers involved in the administration of methadone should review the information on the reverse of this page and the following principles for administering methadone to patients on the methadone program.

Principles of Methadone Administration

- 1. Ensure positive identification of the patient before administering a dose.** Refer to the patient's photograph, which the prescriber has certified.
- 2. Ensure the dose is prepared as authorized by the prescriber.** Examine the prescription to verify the dose and ensure the prescription is current.
- 3. Determine that it is safe to administer a dose.** Determine precisely when the previous dose was administered, contacting the previous dosing point when necessary; do not dose if three or more consecutive doses have been missed without seeking advice from the prescriber. Also, assess the patient for signs of possible intoxication.
- 4. Ensure the dose is consumed with no possibility of diversion.** Observe that the patient takes the dose, and have the patient speak to demonstrate that they swallowed the dose.
- 5. Ensure the prescriber is advised of irregularities in a patient's attendance,** behaviour or condition. Contact the prescriber and record details of the communication. Take a pro-active role in your interaction with methadone prescribers
- 6. Ensure the necessary information is readily available to all dispensers.** Ensure patient records, records of administration and details of communications with the prescriber are clearly and consistently maintained. Also, ensure methadone program guidelines are readily available for reference. Refer to the guidelines for dispensers for more information and specific examples relating to the supply and administration of methadone to patients on methadone treatment in Myanmar.

In circumstances not specifically covered by the guidelines:

- Contact the prescriber or the local Drug Treatment Centre for instructions or clinical advice.
- Address the situation in accordance with the above principles.

Declaration

I certify that I have familiarized myself with the principles of methadone administration and the methadone treatment guidelines. I understand the requirements and undertake to act in accordance with these principles and guidelines.

Name:

Signature: Date:

Information Relating to Methadone Treatment

About the Methadone Program - for patients

Drug addiction is a chronic relapsing condition. More than one program/treatment may be necessary before a patient's circumstances and condition may be considered stable. Abstinence from illicit drug use is a major goal, but it is accepted that some patients will continue to inject heroin and use other drugs. However, concurrent use of methadone with such drugs may represent a risk to the patient, and dispensers need to be alert to symptoms of intoxication or toxicity.

The methadone program represents a relatively long-term commitment (usually expressed in years) for patients attempting to break with the routines and habits associated with the acquisition and use of illicit drugs.

It is a common misapprehension of prescribers and pharmacists that lower doses of methadone are better for the patient, as with other drugs. But evidence indicates that longer treatment programs and higher maintenance doses (60 milligrams or more daily) are generally more effective in achieving treatment outcomes such as decreased illicit drug use. It is therefore important that the dispenser does not encourage a patient to seek a lower maintenance dose or reduce their methadone dose prematurely without consulting the prescriber. It is important that the patient receives consistent advice from all health care providers.

When a methadone program is to be discontinued, the dose should be reduced gradually over a lengthy period.

About Methadone

Following ingestion, blood levels rise for about four hours and then begin to fall. After a single initial dose, the methadone is distributed into the body tissues and the apparent half-life (approximately 15 hours) is shorter than that which applies during a period of extended treatment.

After successive daily doses, methadone blood levels equilibrate with the levels in body tissues, and the half-life progressively increases until it reaches a mean average of 25 hours. Once-daily dosing should then be sufficient to maintain a stable patient. Methadone has a low therapeutic index (overlap of toxic and therapeutic blood levels), so a double dose can be fatal.

New Patients

The highest risk of overdose/toxicity occurs during the first few days of treatment when the life of the drug is shorter and there is a greater risk of concurrent polydrug use.

Missed Doses

If one day's dose is missed from a regular daily dosing regime, the blood level will fall gradually. After 24 hours from the last dose, the blood level will fall to about half of the peak level (at four hours after dosing); after another 24 hours, it will fall to about a quarter of the peak level.

Methadone Dispensing Record Book for Patient



Methadone Dispensing Record Book

Drug Treatment Centre/ Dispensary.....

Patient Name

Registration No.

Date	Time	Dose (mg)	Dose (mls)	Patient Signature	Dispensers Signature	Comment

Appendix C: Suggested Format for Notes about History and Dosing

This is a suggested format for recording relevant information and contemporaneous notes in the back of each patient record book (exercise book or other record) showing patient history and dosing. All entries that are made should be initialed and dated. It is suggested that entries should be made in a section of the record book that is not readily visible to the patient. Comments should be treated as confidential.

Date	Time	Comments	Dispenser
21/07/03	9.30am	Patient appeared intoxicated or under influence of drugs. Withheld dose.	DF
21/07/03	9.35am	Dr Dr Puy to inform him of above. He gave instructions not to dose, and to refer the patient back to him.	DF
23/08/03	6.00pm	Rang Dr Puy about patient frequently missing doses but still having take – aways. Dr Puy unavailable.	JM
23.08.03	6.30pm	Dr Puy rang back. Gave instructions not to supply take – away doses and to direct patient to make an appointment to see him.	FB
01/10/03	10.00am	Received phone call from hospital pharmacy department (Pharmacist Mr Razak). Patient has been discharged and has received today's dose. Requested confirmation by fax – received. Instructed all other dispensers not to dose today (see front of book).	FB
01/12/03	11.00am	Dr Puy phoned to authorize three take – away doses; confirmed by fax.	RB

Appendix D: Suggested Format for Single-Day Preparation Sheet for Multiple Patients



Methadone Utilization Record Book

Drug Treatment Centre/ Dispensary.....

Date	Patient	Dose of Methadone (mg)	Dose of Methadone (mls)	Doctor	Dispenser to sign

Suggested Alternative Format for Daily Dosing Book for Multiple Patients

An accounting ledger / two-column cash book is ideal.

Doctor	Admin. 1/6/04 (mg)	Dose of Methadone (5mg/ml)	Disp. to sign	Admin. 2/6/04 (mg)	Dose of Methadone (5mg/ml)	Disp. to sign	Admin. 3/6/04 (mg)	Dose of Syrup (5mg/ml)	Disp. to sign
Black	8mg	1.6ml	jd	8mg	1.6ml	ch	8mg	1.6ml	ch
Grey	60mg	12.0ml	jd	60mg	12.0ml	cp	60mg	12.0ml	cp
Green	15mg	3.0ml	jd	15mg	3.0ml	sk	missed	-	sk
Red	30mg	6.0ml	jd	30mg	6.0ml	jd	28mg	5.6ml	jd
	113mg	22.6ml	jd	113mg	22.6ml	jd	96mg	19.2ml	jd

Note: the daily total of methadone syrup should be transferred to the Methadone Syrup Register on a daily basis. Alternatively this book may serve as a methadone register (for example a bound book with consecutive numbered pages), in which case the remaining balance should be recorded daily.

Appendix E: Suggested Format for Methadone Syrup Register

Use the normal controlled drug register.

Date	Name and Address of Supplier; Name of Patient	In (ml)	Out (ml)	Balance (ml)	Dispensers Signature	Name of Doctor; Invoice No.
31/05/04	Ex supplier	1000ml		200ml	JD	23106
1/06/04	Doses as per daily dose sheet		62ml	138ml;	JD	
2/06/04	Doses as per daily dose sheet		30ml	108ml	JD	
3/06/04	Doses as per daily dose sheet		46ml	62ml	JD	

Note : Methadone syrup is usually 5mg/ml

Appendix F: Sample Terms and Conditions for Methadone Administration

Welcome to the methadone program. We hope that our association will be a positive experience for all involved and that you will achieve a successful outcome. While receiving methadone you are reminded that taking other drugs (including alcohol) can be extremely dangerous and in some cases fatal. Methadone is a depressant and can interact with other depressants such as alcohol or tranquilizers.

Where possible this dispensary should dispense all medication prescribed by a doctor for you, to allow us to check your medication history. It is also preferable that your methadone doctor prescribes all your medication. It is important that your methadone prescriber is aware of other drugs prescribed for you by other doctors so they can safely manage all your medication and decrease the risk of overdose.

You should be aware of the following program conditions:

Conduct

Methadone patients can expect to be treated in the same manner as any other customer. Our agreement to administer methadone may be terminated if your conduct causes offence to our staff or other customers.

Attendance

Regular attendance is required for a successful outcome to the program. The methadone program is a supervised dosing program, so you should consume your dose within the dispensary and in clear view of the dispenser/ pharmacist.

- You need a current prescription and a certified photograph from your methadone prescriber before a dose may be administered.
- No methadone will be administered to any patient who appears to be adversely affected by alcohol or drugs.
- If you miss three consecutive doses, then a further dose may not be administered without the express authorization of your methadone prescriber.

Payment

Dispensers take time to prepare, document and administer your dose, and donation may be offered this. Donation between 20 and 200 Kyats per day is adequate.

Take-Away Doses

Prescribers may authorize take-away doses only for those patients who receive their supervised doses consistently on a daily basis for more than three months.

- Take-away doses should be stored in a secure place that is inaccessible to children.
- Take-away doses will be cancelled if you fail to attend regularly for supervised doses.

I have read this agreement and understand its contents. I agree to comply with these conditions at all times.

Patient's name: Patient's signature:
 Address:
 Dispens / Pharm signature:
 Phone: Date:

Appendix G: Methadone Client Transfer Facsimile

To: (Pharmacy/dispensing site)

Fax:

From: (Name of dispenser)

Subject: transfer of methadone patient

PATIENT AND PRESCRIBER DETAILS

Patient Names:

Given Names:

Date of Birth:

National Registration Numbes:

Prescriber: Dr.....

Telephone:

This dispensary has provided methadone doses (including take-away doses)* to this patient for treatment up to and including:

Date

Final dose: milligrams

Dispenser's Signature:

Place pharmacy / dispensing site label or stamp here with dispenser name, address, telephone number and fax number.

* Strike out if inapplicable.

