Methadone is established in many parts of the world as an effective treatment for opioid dependence. The administration of methadone as an opioid substitution therapy is an evidence-based intervention, highly recommended by WHO and other United Nations agencies, to prevent the transmission of HIV among people who inject drugs and to treat drug dependence. As the HIV epidemic among people who inject drugs enters its third decade in Myanmar, expanding the use of opioid substitution therapy is of increasing importance. The Myanmar methadone programme commenced in 2006 and has been based on the delivery of services through specialist drug treatment centres and selected hospitals.

The revised Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar give some new directions to the programme and add updated information considered relevant to strengthen service delivery. The use of these guidelines will assist in the scale-up of methadone therapy and ensure that more patients receive treatment in Myanmar.

These practical 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 in providing safe and effective treatment to opioid-dependent patients.
Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar

Department of Health, Ministry of Health
The Republic of the Union of Myanmar
2012
About these guidelines ..............................................................................................................vi
Acknowledgements ...................................................................................................................vii
Acronyms and abbreviations......................................................................................................ix
Glossary......................................................................................................................................xi

Section-1: Essentials of prescribing methadone .................................................................1
  1.1 Introduction ................................................................................................................2
  1.2 The problem of drug dependence and heroin use ....................................................2
  1.3 Methadone—an effective treatment for opioid addiction ........................................2
  1.4 Risks associated with the methadone programme ...................................................4
  1.5 Types of methadone treatment ..............................................................................5
  1.6 Opioid dependence and harm reduction .................................................................6

Section-2: Clinical pharmacology and toxicology of methadone .........................................11
  2.1 Methadone pharmacology ....................................................................................11
  2.2 Metabolism and drug interactions ........................................................................11
  2.3 Side-effects and precautions ...............................................................................13

Section-3: Preparing to become a methadone prescriber ....................................................17
  3.1 Training ..................................................................................................................17
  3.2 Approval ................................................................................................................17
  3.3 Arrangements for dispensing ..............................................................................17
  3.4 Dosing fees ..........................................................................................................17
  3.5 Arrangements to cover prescriber’s absence ..........................................................17

Section-4: Intake procedures and assessing suitability for treatment ....................................23
  4.1 Establishing the patient’s identity ........................................................................23
  4.2 Assessing suitability for treatment .......................................................................23
  4.3 Brief interventions during assessment ..................................................................25
  4.4 Establishing suitability for treatment by diagnosing opioid dependence ..............26
  4.5 Considering treatment options ............................................................................28
  4.6 Obtaining consent for treatment .........................................................................30
  4.7 Registering a patient for prescribing methadone ..................................................30

Section-5: Opioid substitution therapy ..................................................................................33
  5.1 Induction into treatment: careful induction and review during the first week ..........33
  5.2 Establish an effective maintenance dose ..............................................................34
  5.3 The methadone prescription .................................................................................35
  5.4 Reviewing the patient’s progress regularly ............................................................35
5.5 Side-effects of methadone .................................................................36
5.6 Counselling .........................................................................................39
5.7 Dispensing arrangements .......................................................................39
5.8 Dispensing of methadone in closed settings: prison or police custody .........41
5.9 Take-away (take-home) doses ..............................................................41
5.10 Transfer to another methadone treatment centre ....................................43
5.11 Termination of treatment .......................................................................44
5.12 Dealing with specific clinical situations ................................................46
5.13 Combined drug toxicity ........................................................................48
5.14 Other deaths associated with methadone maintenance .............................49

Section-6: Complementary treatments ..........................................................53
6.1 Psychosocial interventions .................................................................53

Section-7: Managing patients with special needs ...........................................59
7.1 HIV and opioid dependence ..................................................................59
7.2 Tuberculosis and opioid dependence: screening opioid-dependent persons for TB .................................................................60
7.3 Managing pain during methadone therapy .............................................60
7.4 Management of patients with co-existing mental health problems ..............61
7.5 Psychotic episodes due to drug use ........................................................63
7.6 Opioid dependence and pregnancy .......................................................64
7.7 Neonatal abstinence syndrome ............................................................65

Section-8: General information on related issues .........................................69
8.1 Abuse of prescription drugs ....................................................................69
8.2 Legal responsibilities ............................................................................69
8.3 Confidentiality .....................................................................................70
8.4 Driving while on methadone ..................................................................70
8.5 Forms ................................................................................................71
8.6 Record-keeping ....................................................................................71

Section-9: Methadone maintenance therapy guidelines for dispensers ............75
9.1 Background .........................................................................................75
9.2 Setting up the methadone programme: getting approval .........................75
9.3 Development of procedures ..................................................................76
9.4 Storage ...............................................................................................77
9.5 Patient’s records ................................................................................77
9.6 Records of administration .....................................................................77
9.7 Accepting new patients .......................................................................77
9.8 Prescriptions .......................................................................................78
9.9 Preparation of doses ...........................................................................78
9.10 Patients who are new to the methadone programme ...............................79
9.11 Take-away doses ...............................................................................79
9.12 Transferred patients.................................................................79
9.13 Temporary absences...............................................................80
9.14 Irregular attendance...............................................................80
9.15 Missed doses.......................................................................80
9.16 Possible intoxication............................................................80

Appendices

Appendix 1: Clinical Opiate Withdrawal Scale (COWS) ..................85
Appendix 2: Features of a methadone prescription .........................88
Appendix 3: Interactions between opioid substitution therapy and commonly used medications ......................................................89
Appendix 4: Comparative tables of opioids ......................................91
Appendix 5: Patient’s identification card (ID) ....................................93
Appendix 6: Methadone dispensing record book for patient............94
Appendix 7: Daily methadone utilization record register ...................95
Appendix 8: Monthly report form for DTC sites for methadone programme .................................................................97
Appendix 9: Methadone stock record book ......................................99
Appendix 10: Methadone client transfer facsimile...............................100
References ..................................................................................101
In 2004, the Department of Health, Ministry of Health, Union of Myanmar published, with the assistance of the World Health Organization (WHO) Myanmar Country Office, the *Guidelines on Methadone Therapy in Myanmar for Prescribers and Dispensers*. These guidelines were developed to support medical practitioners and dispensers at a time when methadone therapy was about to be implemented in various parts of the country. In September 2011, the Department of Health, Ministry of Health requested the WHO Myanmar Country Office to help organize a workshop to revisit and examine the 2004 guidelines, and to identify various topics deemed necessary for consideration for the 2012 revision, to be re-titled *Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar*.

A number of topics in the 2004 guidelines have remained unchanged in the updated version. However, in the 2012 guidelines, some specific topics have been updated and revised, in keeping with the expansion of the methadone programme in the country. New information has also been added, as requested by the participants in the workshop of 2012. New, important directions have been outlined in some topics and their implementation has been encouraged to assist with the scale-up of methadone therapy and to ensure that more patients can receive treatment. New resources and operational guidelines on opioid substitution therapy have been developed by WHO and other agencies, and this information has been incorporated into the guidelines, where necessary.

As with the 2004 guidelines, the 2012 guidelines have been prepared by practitioners with expertise in the use of methadone to treat opioid dependence. The guidelines are intended to assist medical practitioners and dispensers in the treatment of opioid-dependent patients in a safe and effective manner. The guidelines are general recommendations and are meant only for the purpose of providing information. They cannot provide detailed direction with respect to the management of every patient in every clinical situation, and do not offer specific advice on treatment. Individual medical practitioners and dispensers are responsible for decisions on the safety and effectiveness of the treatment used for each patient. The guidelines are not intended to replace professional judgement in individual cases.
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The College of Physicians of Ontario, Canada

Department of Health, Hong Kong Special Administrative Region, China
Acronyms and abbreviations

3TC  lamivudine
ABC  abacavir
AIDS  acquired immune deficiency syndrome
ART  antiretroviral therapy
ARV  antiretroviral
ATS  amphetamine-type stimulants
ATT  antituberculosis treatment
AZT  didanosine
CBT  cognitive–behavioural therapy
CNS  central nervous system
COWS  Clinical Opiate Withdrawal Scale
CPR  cardiopulmonary resuscitation
d4T  stavudine
ddi  didanosine
DOT  directly observed treatment
DTC  drug treatment centre
EC  enteric coated
EFV  efavirenz
FTC  emtricitabine
HIV  human immunodeficiency virus
IV  intravenous
IEC  information, education and communication
LPV  lopinavir
LPV/r  lopinavir/ritonavir
MAO  monoamine oxidase
MI  motivational interviewing

Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMT</td>
<td>methadone maintenance therapy</td>
</tr>
<tr>
<td>NAS</td>
<td>neonatal abstinence syndrome</td>
</tr>
<tr>
<td>NASS</td>
<td>neonatal abstinence syndrome score</td>
</tr>
<tr>
<td>NNRTI</td>
<td>non-nucleoside reverse transcriptase inhibitor</td>
</tr>
<tr>
<td>NRTI</td>
<td>nucleoside reverse transcriptase inhibitor</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>NSP</td>
<td>needle and syringe programme</td>
</tr>
<tr>
<td>NVP</td>
<td>nevirapine</td>
</tr>
<tr>
<td>OI</td>
<td>opportunistic infection</td>
</tr>
<tr>
<td>OST</td>
<td>opioid substitution therapy</td>
</tr>
<tr>
<td>PI</td>
<td>protease inhibitor</td>
</tr>
<tr>
<td>PWID</td>
<td>people who inject drugs</td>
</tr>
<tr>
<td>SC</td>
<td>subcutaneous</td>
</tr>
<tr>
<td>SQV</td>
<td>saquinavir</td>
</tr>
<tr>
<td>SNRI</td>
<td>serotonin norepinephrine reuptake inhibitor</td>
</tr>
<tr>
<td>SSRI</td>
<td>selective serotonin reuptake inhibitor</td>
</tr>
<tr>
<td>STI</td>
<td>sexually transmitted infection</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>TCA</td>
<td>tricyclic antidepressant</td>
</tr>
<tr>
<td>TDF</td>
<td>tenofovir disoproxil fumarate</td>
</tr>
<tr>
<td>TMO</td>
<td>township medical officer</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
</tr>
<tr>
<td>UNGASS</td>
<td>United Nations General Assembly Special Session</td>
</tr>
<tr>
<td>UNODC</td>
<td>United Nations Office on Drugs and Crime</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>Term</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Abstinence</td>
<td>Refraining from drug use, whether as a matter of principle or for other reasons</td>
</tr>
<tr>
<td>Addiction</td>
<td>See “dependence”. The term “addiction” was more commonly used in the past and has, to a large extent, been replaced by “dependence” as it is considered stigmatizing. It refers to the repeated and compulsive use of a psychoactive substance or substances despite knowledge of the negative consequences.</td>
</tr>
<tr>
<td>Agonist</td>
<td>A drug that binds to and activates a particular type of receptor. It produces effects similar to those of a substance/drug.</td>
</tr>
<tr>
<td>Analgesic</td>
<td>A substance that reduces pain and may or may not have psychoactive properties</td>
</tr>
<tr>
<td>Antagonist</td>
<td>A drug that blocks a particular type of receptor in the brain, preventing it from being activated. Pharmacologically, an antagonist interacts with a receptor to inhibit the action of agents (agonists) that produce specific physiological or behavioural effects mediated by that receptor. For example, naltrexone is an opioid antagonist, meaning that it blocks and prevents activation of the opioid receptors.</td>
</tr>
<tr>
<td>Brief intervention</td>
<td>A treatment strategy in which structured therapy of a short duration (typically 5–30 minutes) is offered with the aim of assisting an individual to cease or reduce the use of a psychoactive substance, or (less commonly) to deal with other life issues</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>A partial opioid agonist used for the treatment of opioid dependence</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>A severe liver condition characterized by the destruction of liver cells and their replacement with scar tissue. Liver function is markedly reduced.</td>
</tr>
<tr>
<td>Closed settings</td>
<td>Refers to any institution or centre where people are detained and not able to leave. Examples of closed settings include compulsory drug treatment centres and prisons.</td>
</tr>
<tr>
<td>Dependence</td>
<td>A syndrome characterized by compulsive use of a substance despite knowledge of the negative consequences of such use</td>
</tr>
<tr>
<td>Detoxification</td>
<td>The process by which an individual is withdrawn from the effects of a psychoactive substance. Detoxification may or may not involve the administration of medication.</td>
</tr>
<tr>
<td>Drug half-life</td>
<td>The time the body takes to remove 50% of an administered medication</td>
</tr>
<tr>
<td><strong>Human immunodeficiency virus (HIV)</strong></td>
<td>The virus that causes HIV/AIDS is transmitted through blood, semen, vaginal fluid and breast milk. There are treatments available to prevent the progression of HIV to AIDS, but there is no cure or vaccine as yet.</td>
</tr>
<tr>
<td><strong>Maintenance treatment</strong></td>
<td>Long-term provision of medication that has the same or similar action as the patient’s drug of dependence. The goal is to reduce illicit drug use and the harm resulting from it.</td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td>A synthetic opioid drug used in maintenance therapy for those dependent on opioids. It has a long half-life and can be given orally, once daily, under supervision.</td>
</tr>
<tr>
<td><strong>Motivational interviewing</strong></td>
<td>A style of interviewing that aims to increase a patient’s motivation to change their behaviour.</td>
</tr>
<tr>
<td><strong>Neuroadaptation</strong></td>
<td>The neuronal changes within the brain associated both with tolerance and the appearance of a withdrawal syndrome.</td>
</tr>
<tr>
<td><strong>Neurotransmitter</strong></td>
<td>A chemical released in the brain that blocks or activates brain receptors.</td>
</tr>
<tr>
<td><strong>Opiate</strong></td>
<td>One of a group of naturally occurring alkaloids derived from the opium poppy (<em>Papaver somniferum</em>). It activates opiate receptors in the brain and has the ability to induce analgesia, euphoria and, in higher doses, stupor, coma and respiratory depression. The term opiate includes heroin and morphine and excludes synthetic opioids.</td>
</tr>
<tr>
<td><strong>Opioid</strong></td>
<td>The generic term applied to alkaloids from the opium poppy (<em>Papaver somniferum</em>), their synthetic analogues, and compounds synthesized in the body, which interact with the same specific receptors in the brain, have the capacity to relieve pain and produce a sense of well-being (euphoria). The opium alkaloids and their synthetic analogues also cause stupor, coma and respiratory depression in high doses. Examples include codeine, methadone, buprenorphine and (dextro) propoxyphene.</td>
</tr>
<tr>
<td><strong>Peer educator or peer facilitator</strong></td>
<td>Peer education typically involves using the members of a given group to effect change among other members of the same group. The changes aimed at include modifying their knowledge, attitudes, beliefs or behaviours. A peer educator helps group members define their concerns and seek solutions through the mutual sharing of information and experiences. A peer educator not only tells the peers about a desired practice for risk reduction but also models it.</td>
</tr>
<tr>
<td><strong>Pharmacotherapy</strong></td>
<td>The use of pharmacologically active medication to treat a condition. In the case of opioid dependence, it refers to opioid substitution therapy, which is also known as opioid pharmacotherapy.</td>
</tr>
<tr>
<td><strong>Polysubstance use</strong></td>
<td>The concomitant use of multiple psychoactive substances. It is also called multiple substance (or drug) use.</td>
</tr>
<tr>
<td><strong>Problematic substance use</strong></td>
<td>The use of psychoactive substances resulting in negative consequences for the individual.</td>
</tr>
<tr>
<td><strong>Psychoactive substance</strong></td>
<td>A substance which, when ingested/inhaled/injected, affects mental processes, e.g. cognition or affect.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
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</tr>
<tr>
<td>Relapse</td>
<td>A return to drug use by a formerly dependent person after a period of abstinence, often accompanied by reinstatement of dependence symptoms. Some distinguish between relapse and lapse (“slip”), with the latter denoting an isolated occasion of drug use. Relapse is very common and most drug users relapse several times before they achieve long-term abstinence.</td>
</tr>
<tr>
<td>Substitution</td>
<td>Substitution means replacing the harmful opioid on which the individual is dependent (commonly heroin or buprenorphine in the South-East Asia Region) with a less harmful opioid.</td>
</tr>
<tr>
<td>Tolerance</td>
<td>A decrease in response to a drug dose that occurs with continued use. Increasing doses of drugs are required to achieve the effects originally produced by lower doses.</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>A group of symptoms of variable clustering and degree of severity that occur on cessation or reduction of use of a psychoactive substance which has been taken repeatedly, usually for a prolonged period and/or in high doses. The syndrome may be accompanied by signs of physiological disturbance. A withdrawal syndrome is one of the indicators of a dependence syndrome.</td>
</tr>
</tbody>
</table>
Section-1

Essentials of prescribing methadone
1 Essentials of prescribing methadone

(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 (tolerance)
   - The goals of treatment, on which both you and the patient agree

(3) Register the patient as a drug user who is participating in the methadone programme before prescribing methadone, to facilitate coordination of the patient’s treatment and avoid the risk of multiple dosing with methadone (and/or other opioids), which may have been prescribed by other practitioners.

(4) Establish an appropriate starting (induction) dose (Section 5.1). This dose should usually be 20–30 milligrams (mg) per day. It is unusual for patients to require higher doses. Patients rarely require doses of more than 40 mg at the end of the first week of treatment.

(5) Ensure that the prescription gives clear, unequivocal directions to the dispensing point. These should include (Section 5):
   - The precise dose in words and figures
   - The precise starting date
   - 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 whether there is a need for dose revision and to manage the high risk of methadone or combined drug toxicity during induction into treatment (Section 5).

(7) Do not increase the methadone dose by:
   - More than 10 mg at a time
   - More than 30 mg over any seven-day period

(8) When transferring a patient between dispensing points or drug treatment centres (DTCs), avoid the risk of duplication of dosing by providing clear instructions in writing to both sites on their respective finishing and starting dates (Section 5).

(9) Before authorizing take-away doses:
   - Contact the dispensing site to check the regularity of dosing and the patient’s progress; and.
   - Ensure that the patient is stable and meets all the criteria specified in the guidelines (Section 5).
Send a notification to the Department of Health (DoH) as soon as you terminate the treatment. 
Remember: “Start low, go slow, aim high.”

1.1 Introduction

These guidelines have been developed to assist policy-makers who make decisions on the availability of medicines and the structure and funding of services. They should also be helpful for programme managers responsible for the organization of specific health-care services, as well as health-care workers (practitioners, dispensers) treating patients within the health-care system. Patients interested in the safe and effective use of methadone to treat opioid dependence should also benefit from these guidelines. The guidelines are evidence-based and draw upon various documents. They take into consideration the specific context of opioid dependence and treatment responses in Myanmar.

1.2 The problem of drug dependence and heroin use

Drug dependence is a complex condition which has social, psychological and biological components. Dependence on illicit opiates is a serious condition, which is currently associated with severe morbidity, and the risk of the transmission of blood-borne viruses (HIV, hepatitis B and C) and of death. These risks arise from drug overdose, and the morbidity and injury resulting from chronic illicit drug use, injecting or misuse of licit opioids.

Heroin and opium are short-acting opiates with a marked tendency to develop a dependence syndrome in the user, when used in a recreational manner for their euphoric or analgesic properties. In addition, the mode of administration of these drugs may generate a risk of drug overdose or the transmission of blood-borne viruses. The fact that heroin and opium are illicit and often expensive contributes to the criminal behaviours associated with their use—primarily acquisitive crime and drug trafficking. The dependence syndrome is often associated with substantial behavioural changes, which have their own social cost. For example, the individual’s interest in other activities, relationships and their own health diminishes.

1.3 Methadone—an effective treatment for opioid addiction

Methadone has become established in many parts of the world as an effective treatment for opioid dependence. Its administration as an opioid substitution therapy (OST) is an effective evidence-based intervention, highly recommended by WHO and other United Nations agencies, to prevent the transmission of HIV among drug injectors and to treat drug dependence.

Methadone can be compared to other drugs that are effective in the treatment of serious, chronic, relapsing conditions, such as hypertension and diabetes. These conditions, like opiate dependence, are chronic, require daily treatment and put patients at a high risk of suffering adverse effects if their compliance with treatment is poor.

Some long-term heroin users can be treated successfully with detoxification and abstinence-based treatments, but studies have shown that more than 70% will relapse, resuming the use of illicit opiates within one to two years. Methadone can prove valuable in assisting these people to successfully manage physical dependence, craving for the drug and compulsive drug use.
Methadone has been used for more than 40 years for detoxification as well as maintenance therapy for patients dependent on opioids for the following reasons.

- It has cross-tolerance with other opioids, which makes it suitable for use as a substitute 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, which makes it possible to take just one dose a day.

The daily supply of an adequate dose of methadone in a supervised manner, as part of a structured programme, has demonstrated substantial benefits for the individual, their family and society. These are:

- It reduces or limits illicit heroin use.
- It reduces the occurrence of illness or death resulting from illicit drug use.
- It discourages the high-risk practice of sharing needles.
- It decreases criminal activity.
- It stabilizes the patient’s life and reduces the tendency to take drugs chaotically.
- It makes it possible for heroin and opium users to lead productive lives.

Maintenance treatment with methadone may be delivered in a variety of 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 different disciplines and backgrounds, including medicine, substance use treatment, nursing, social work and mental health, may be involved in programmes for delivering maintenance treatment with methadone. Their roles vary, depending on factors such as qualifications, the setting of the programme, resources available and geographical location.

The goals of methadone treatment include normalizing the patients’ lives, integrating them back into their family and the community, and keeping them in treatment when necessary. Patients on methadone should be treated in the same way as other patients, as far as possible.

1.3.1 Methadone maintenance therapy in Myanmar

The Myanmar methadone programme commenced in 2006 and has been based on delivering services through specialist drug treatment centres and selected hospitals. It is anticipated that over time, methadone will become more readily available and that it will help in the integration of the treatment of opioid dependence with general medical care. This is important because many opioid-dependent patients suffer from serious illness, HIV infection or injury as a result of their years of injecting drug use and dependence.
Under the coordination of drug treatment centre (DTCs) acting as coordinating agencies, methadone may be dispensed under community-based programmes. This would allow the treatment of drug dependence to be normalized and de-stigmatized, and would also avoid the congregation of large numbers of patients around DTCs.

A wider spread of medical and dispensing services would help improve accessibility and choice. It is also expected that co-location of treatment services for opioid dependence, tuberculosis and HIV will make the process of accessing services more efficient and improve adherence to treatment for these common comorbid conditions.

**HIV and methadone maintenance therapy in Myanmar**

Myanmar has entered its third decade of the HIV epidemic among people who inject drugs (PWID). The prevalence of HIV among PWID remains unacceptably high. In 2010, it was 28%, the highest among all the high-risk groups (the other groups include female sex workers and men who have sex with men). In 2009, the prevalence of HIV among PWID was 34%. It is likely that the decline in prevalence was due to deaths from HIV-related illness and hepatitis C. In some parts of the country, the prevalence of HIV among PWID is 50% or above. In 2011 the estimated number of PWID was 75,000. The methadone maintenance therapy (MMT) programme commenced in early 2006 and enrolled 260 people in that year. Till September 2011, up to 1227 patients had received MMT from 13 sites: Yangon (2 sites), Mandalay (2 sites), Lashio, Myitkyina, Mogauk, Bamaw, Namti, Tachileik, Muse, Namkham and Kukkhai. It was felt that the progress in getting more patients to receive methadone was relatively slow. The need to enrol many more opioid-dependent people in the MMT programme to halt and reverse the HIV epidemic among PWID was acknowledged.

The Myanmar methadone programme places emphasis on initiating treatment and increasing doses with care, together with supervised dosing, to minimize the risks involved. It also aims to 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”. According to the programme’s aims, the beginning of the process of detoxification, as well as the progress, should be progressive and carefully monitored. The therapeutic levels of methadone expected to be reached in the case of most patients in the Myanmar context are in the range of 80 mg to 120 mg per day.

### 1.4 Risks associated with the methadone programme

Despite the proven success of methadone programmes, there are some risks. These are as follows.

- Methadone is an opioid drug and as such, is prone to misuse and capable of causing toxicity.
- Methadone is a potentially toxic drug with a low therapeutic index (the therapeutic dose is close to the toxic dose).
- Treatment with methadone is provided to a high-risk population, among whom the misuse of prescription drugs and alcohol is highly prevalent, and who may have a history of using drugs compulsively and recklessly. Given these circumstances, considerable caution is necessary.
- 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 risks of methadone treatment and the counter-measures that can be taken to minimize them are presented in Table 1.

**Table 1: Risks of treatment with methadone**

<table>
<thead>
<tr>
<th>Risks</th>
<th>Countermeasures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated pharmacokinetics, prescriber/dispenser unfamiliarity with the pharmacokinetics</td>
<td>Prescriber/dispenser training; a registration system</td>
</tr>
<tr>
<td>Dosing by multiple prescribers and dispensers</td>
<td>Development and implementation of a standardized registration system for patients</td>
</tr>
<tr>
<td>Poor compliance and diversion of syrup for illicit use and trafficking</td>
<td>A supervised dosing programme; monitoring and placing a limit on the number of take-away doses</td>
</tr>
<tr>
<td>Trafficking and consequent overdosing of non-tolerant people not on the methadone programme</td>
<td>Tight control over take-away doses; discretion in judging patient’s suitability for take-away doses</td>
</tr>
<tr>
<td>Illicit injection of take-away doses</td>
<td>Dilution of take-away doses to at least 200 millilitres; discretion in judging patient’s suitability for take-away doses</td>
</tr>
<tr>
<td>Child poisoning with methadone</td>
<td>Informing patients or guardian about the danger and encouraging them to lock up take-away dose and keep it out of children’s reach</td>
</tr>
<tr>
<td>Multiple dosing at time of transfer</td>
<td>Meticulous arrangements for transfer of registration</td>
</tr>
<tr>
<td>High risk of drug overdose in the first 10 days of treatment</td>
<td>Meticulous care and frequent reviews of patients in the first 10 days; alertness of dispenser to signs of toxicity</td>
</tr>
<tr>
<td>High risk of combined drug toxicity; death</td>
<td>Alertness of dispenser to signs of toxicity; comprehensive assessment, understanding the management of poly-drug abuse, warning patients about risk, educating family/friends on signs of overdose and coma (unrousable, “snoring”, respiratory depression, cyanosis)</td>
</tr>
<tr>
<td>Greater risk of overdose with respiratory problems</td>
<td>Careful assessment, lower starting doses, smaller and slower dose increases, inpatient treatment and appropriate medications for all respiratory problems, such as asthma, bronchitis and tuberculosis</td>
</tr>
<tr>
<td>Injury</td>
<td>Warning patients about the risks of driving/using machinery before dose stabilization and while the dose is being adjusted</td>
</tr>
<tr>
<td>Psychiatric comorbidity, including risk of suicide</td>
<td>Assessment of patient’s psychiatric status and risk of suicide; maintenance of a high index of suspicion, and timely response to suicide risk; referral to specialist methadone service for management of dual disability, if appropriate</td>
</tr>
<tr>
<td>Discontinuation of treatment</td>
<td>Provision of supervised dosing to be as convenient as possible; discrete use of take-away doses</td>
</tr>
</tbody>
</table>

### 1.5 Types of methadone treatment

**Withdrawal.** Methadone can be used to mediate patients withdrawing from opioid dependence. A dosage schedule that reduces the dose of methadone over 10-30 days can help in reducing withdrawal symptoms significantly.
**Maintenance.** A high proportion of patients who have withdrawn from opioid dependence will relapse. A programme of maintenance on methadone for several months to years can help these patients.

In Myanmar, the methadone programme is delivered under the Ministry of Health, with psychiatrists or township medical officers lending their support for the assessment and management of complicated cases.

### 1.6 Opioid dependence and harm reduction

The harm reduction approach involves an acceptance of the fact that despite all efforts to control supply and reduce demand, many people will continue to have access to and use licit and illicit drugs.

The term “harm reduction” refers to policies, programmes and projects that aim to reduce the harmful consequences, in the health, social and economic spheres, associated with the use of psychoactive substances. The harm reduction approach is an evidence-based and cost-effective approach, and brings benefits to the individual, community and society.¹

The policy of harm reduction was endorsed by the United Nations, at the United Nations General Assembly Special Session (UNGASS) in 2006,² and by WHO, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the United Nations Office on Drugs and Crime (UNODC).³

WHO, UNAIDS and UNODC have identified nine interventions, as part of a comprehensive package, which have the greatest impact on HIV prevention, and treatment of and care for PWID.⁴

<table>
<thead>
<tr>
<th>The comprehensive package on HIV prevention, and treatment of and primary health care for PWID includes the following nine interventions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Needle and syringe programmes (NSPs)</td>
</tr>
<tr>
<td>(2) Opioid substitution therapy (OST) and other treatment for drug dependence</td>
</tr>
<tr>
<td>(3) Targeted information, education and communication for PWID</td>
</tr>
<tr>
<td>(4) Counselling and testing for HIV</td>
</tr>
<tr>
<td>(5) Treatment and care for HIV patients</td>
</tr>
<tr>
<td>(6) Promoting and supporting condom use</td>
</tr>
<tr>
<td>(7) Detection and management of sexually transmitted infections</td>
</tr>
<tr>
<td>(8) Prevention and treatment of viral hepatitis</td>
</tr>
<tr>
<td>(9) Prevention, diagnosis and treatment of tuberculosis.</td>
</tr>
</tbody>
</table>

The package is of the maximum benefit when all the interventions are delivered together, but not all countries have sufficient resources to do this. It is advised that in countries with limited resources, at least six of the nine interventions be delivered, i.e. NSPs, OST, promoting condom use, HIV testing and counselling, prevention, diagnosis and treatment of tuberculosis, and antiretroviral treatment (ART).
In the context of harmful use of and dependence on opioids, harm reduction means preventing the transmission of HIV and hepatitis B and C through the practice of using sterile injections, reducing injection-related injuries through safe injection techniques, and reducing engagement in illegal activities through the use of methadone and another OST called buprenorphine, which is used in some countries.5

Methadone treatment obviates the need for patients to obtain and inject heroin. This is useful for individuals in whose case abstinence-based methods of dealing with heroin addiction have failed because they continue to relapse.
Section-2

Clinical pharmacology and toxicology of methadone
2.1 Methadone pharmacology

- Methadone has a complex range of effects that can vary widely among individuals. It is used as a long-acting analgesic and a substitute treatment for opioid (mostly heroin) addiction.
- It is necessary to understand the pharmacology of methadone so that it can be used safely by patients with problems of compulsive drug use, often complicated by co-abuse of other drugs that depress the central nervous system (CNS).

The safe and effective use of methadone requires a familiarity with three characteristics of its pharmacology:

1. a slow onset of peak blood levels (4 hours);
2. a long half-life (25 hours); and
3. a low therapeutic index (overlap of toxic and therapeutic blood levels)

- Methadone acts by binding to the opioid receptors in the brain.
- Oral methadone is well absorbed from the gastrointestinal tract and 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.
- The risk of overdose is the highest in the first few days of treatment as the ingested methadone equilibrates with tissue stores, and the patient’s drug-taking stabilizes.

2.2 Metabolism and drug interactions

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

- Renal clearance. Renal clearance makes for a small proportion of the total clearance at a urine pH of 7. If the urine is acidic (pH below 6), then the proportion of renal clearance increases to about 30% of the total clearance; if the urine is alkaline (pH above 7.8), renal clearance is reduced to zero. Patients should be advised on the use of urinary alkalinizers or acidifiers, including aspirin.
- Pregnancy. Methadone clearance increases during pregnancy, resulting in a corresponding decrease in plasma concentrations. This may increase the risk
of the failure of treatment, self-medication and toxicity. Pregnant women may benefit from split-dosing. Given the variability of methadone clearance among pregnant women, they are regarded as a high-risk group.

2.2.1 Pharmacokinetic drug interactions

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

Potential inhibitors of methadone metabolism

- SSRIs (sertraline, fluvoxamine, etc.)
- SNRIs (venlafaxine, nefazodone)
- Broad-spectrum antifungals and antibacterials (clotrimazole, etc.)
  - HIV drugs (zidovudine, ritonavir, etc.) (See Appendix 3)
  - Hormones (progesterone, ethinylestradiol, dexamethasone)
  - Calcium channel antagonists (nifedipine, verapamil, diltiazem)
  - Antibiotics (erythromycin, ciprofloxacin, chloramphenicol, etc.)
  - Miscellaneous (quinidine, midazolam, cyclosporin, vinblastine, bromocriptine, cimetidine)

Potential inducers of methadone metabolism

Some anti-epileptics and anti-convulsant drugs (phenobarbitone, phenytoin, primidone, carbamazepine, but not valproate or benzodiazepines), and HIV drugs (nevirapine [Figure 1], efavirenz) may induce methadone metabolism. For more information on glucocorticoids and antituberculosis drugs (rifampicin, rifabutin), refer to Appendix 3.

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

During induction into treatment with methadone, one should avoid commencing any drug that inhibits or induces the activity of CYP3A4. When commencing methadone treatment in the case of patients who use medications that inhibit CYP3A4, one should prescribe conservative doses of methadone, review the patient carefully for signs of toxicity during induction, and advise the patient about the potential for drug interaction.
2.2.2 Pharmacodynamic drug interactions

Almost all methadone-related deaths occur if the patient is on 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 being used.
- Alcohol is a CNS depressant that is capable of causing respiratory depression and death. The combination of non-fatal doses of alcohol and methadone may cause fatal toxicity, particularly in males.
- High doses of tricyclic antidepressants (TCAs) can cause respiratory depression and pulmonary oedema, and these drugs may interact with methadone and increase the risk of toxicity. One must assess patients on TCAs for the risk of suicide, and review them carefully for signs of toxicity during induction into treatment.

2.3 Side-effects and precautions

The side-effects of methadone are similar to those of other opioid analgesics (dependence, nausea, vomiting, constipation, respiratory depression, coma). Patients develop tolerance to most of these effects after long-term use. However, the pharmacology of methadone differs from that of most other opioids. There is a long interval between ingestion and the time that
it reaches the peak level in the blood; it has a long half-life, which varies considerably from individual to individual; it has considerable tissue distribution; and there is accumulation after successive doses.

2.3.1 Pharmacokinetic factors

These are relevant in the context of side-effects and the safe prescription of methadone.

- Peak plasma concentration occurs one to five hours after oral dosing.
- Metabolism to inactive metabolites occurs in the liver, so before prescribing, consider whether the patient’s liver function is impaired.
- The elimination half-life varies considerably (the range being 15–60 hours).
- Plasma concentration varies greatly among patients and wide fluctuations occur in individual patients. The dose should be adjusted carefully when the drug is administered repeatedly.

2.3.2 Contraindications

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

2.3.3 Precautions

Precautions need to be taken in the case of elderly patients and those with hepatic impairment.

For further information on the common side-effects of methadone, see Section 5.5.
Section-3

Preparing to become a methadone prescriber
Preparing to become a methadone prescriber

3.1 Training

It is necessary for health professionals prescribing and dispensing methadone to be familiar with the pharmacology of methadone and the management of drug dependence, so they should ideally receive regular training in the management of opioid dependence (see also Section 9.3).

3.2 Approval

A health professional is granted approval as a methadone prescriber by the DoH after 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 are to provide supervised dosing. It is important for dispensers to familiarize themselves with all the options for supervised dosing because they generally see patients more often than do medical practitioners and can provide useful advice on the patient progress.

3.4 Dosing fees

Many argue that opioid pharmacotherapy should be free in order to encourage uptake, while others argue that charging a minimal fee for the medication can put greater value on the therapy. Whatever the case, the main determinant should be to maximize access to the therapy and see to it that those affected remain under treatment. If a dosing fee is charged, it should be kept to a minimum to allow equity of access. It should also be consistent with the socioeconomic situation of patients. In the future, subject to approval by the DoH, some dispensing sites may be entitled to charge a fee for dispensing methadone through a cost-sharing process.

3.5 Arrangements to cover prescriber’s absence

Methadone prescribers are responsible for the management of each patient they have registered, and they should remain the main person treating these patients.
When a prescriber is unavailable to supervise the treatment of patients (due to planned leave, sudden/unexpected absences or duty travel to other locations), the patients run the risks associated with unsupervised treatment; the treatment may be interrupted; and the patients may be treated by a colleague who has little experience with methadone treatment, or who is unfamiliar with the patients being treated.

To minimize the risks faced by patients due to the absence of the prescriber, the following arrangements should be made.

### Arrangements for anticipated or unexpected absence of methadone prescriber

- Document and maintain up-to-date management plans for individual patients in your patient records, to enhance communication between your colleagues and yourself.
- Make arrangements for a colleague (preferably an approved methadone prescriber) to deputize for you and continue with the documented management plan for each patient.
- Request any colleague deputizing for you to record changes in the treatment in the patient’s notes.

Note: A deputizing practitioner may or may not be already approved to prescribe methadone.

Patients who develop complications while their medical practitioner is absent should be referred to a DTC or medical practitioner with experience in the treatment of substance dependence. In all cases, the dispenser and allied health staff involved in the care of patients should be contacted.

### 3.5.1 Deputizing by approved methadone prescribers

A prescriber deputized in the absence of the regular prescriber must follow the procedures mentioned below.

- Take history and examine the patient in the case of stable patients who require only the renewal of an expired prescription and no increase in dose or the frequency of take-away doses.
- Check with the dispensary whether the patient has been attending the dispensary regularly for daily dosing.
- Contact the officer-in-charge of a major DTC if there are any problems with the management of the patient or concerns his/her safety. 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” (given at the beginning of these guidelines).
### Management by deputizing prescribers

- Continue the usual prescriber's management plan and dosage regimen as documented in the clinical record. However, it is acceptable to reduce the dose if it is believed that it is causing toxicity.
- Note on the prescription that the prescriber is temporarily deputizing for the patient’s usual prescriber.
- Limit the duration of the prescription to the expected period of absence of the usual prescriber, making sure you indicate precise starting and finishing dates.
- Document the details regarding consultations and methadone prescriptions in the patient’s notes.
- Arrange for the usual prescriber to review the patient as soon as possible thereafter.

### 3.5.2 Deputizing by a practitioner who is not an approved methadone prescriber

- Being unfamiliar with the risks of methadone treatment, these prescribers must adopt a cautious approach to the treatment of patients.
- Only approved methadone prescribers can commence patients on methadone treatment.
- Take history and examine the patient in the case of stable patients who require only the renewal of an expired prescription and no increase in dose or the frequency of take-away doses.
- Check with the dispensary whether the patient has been attending the dispensary regularly for daily dosing.
- Contact the officer-in-charge of a major DTC if there are any problems with the management of the patient, there are concerns about the patient’s safety or if it seems necessary to increase the dose or give a take-away dose.
- Do not provide a higher dose or take-away dose unless advised to do so by a 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” (given at the beginning of these guidelines).
PREVENTING ADVERSE EVENTS DURING TREATMENT

Adverse events can and do occur during treatment. Many are preventable. The main steps to avoid adverse events during treatment are:

- Educating patients
- Training the staff
- Familiarizing oneself with the drug interactions, particularly with benzodiazepines, and TB and HIV medications (see Appendix 3)
- Taking special care in the case of
  - Liver disease or hepatitis
  - HIV, considering the possible interactions between antiretroviral drugs (ARVs) and methadone (see Appendix 3)
  - Elderly patients
  - Poly-substance use (to prevent overdose)
- Regularly reviewing the patient, at intervals determined by the patient’s progress. Poor progress indicates the need for more frequent review.
Section-4

Intake procedures and assessing suitability for treatment
4 Intake procedures and assessing suitability for treatment

The assessment of a patient’s suitability for treatment should be carried out in a consistent manner from patient to patient to reduce errors. Clinical protocols can enhance consistency. Although an assessment can be completed by any trained clinical staff member, generally the diagnosis of opioid dependence should be made by the doctor.

4.1 Establishing the patient’s identity

The patient’s identity should be established to avoid dual dosing of the same person. The patient must be requested to provide a document of identification (for example, a national registration card). The patient should also provide four recent 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.

4.1.1 Establishing an effective therapeutic relationship

A strong therapeutic relationship with the patient is crucial to effective treatment. Establishing such a relationship is particularly important as many drug users are uncomfortable while giving a history of drug dependence. If one successfully engages the patient, it can help them feel at ease and assist in gathering a complete history. Treating the patient with empathy, sensitivity, respect and warmth, and being aware of their cultural context helps in building a rapport with the patient. The rapport should be based on respect, knowledge and the willingness to work through issues in a systematic fashion. Clinical decision-making should, where possible, be the result of an agreement between the patient and practitioner to maximize adherence to therapy. The extent to which this occurs may depend on the local context.

4.2 Assessing suitability for treatment

A patient’s suitability for the treatment of opioid dependence is determined by the diagnosis and assessment. A diagnosis which points to pharmacotherapy as the form of treatment should be made by trained medical personnel.
<table>
<thead>
<tr>
<th>History</th>
<th>Key components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current and past use of drugs and alcohol</td>
<td></td>
</tr>
<tr>
<td>• Opioids</td>
<td>Type of drug</td>
</tr>
<tr>
<td>• Amphetamines</td>
<td>Age at first use</td>
</tr>
<tr>
<td>• Benzodiazepines</td>
<td>Age at daily use</td>
</tr>
<tr>
<td>• Alcohol</td>
<td>Amount currently being used/frequency of use</td>
</tr>
<tr>
<td>• Other drugs commonly used locally</td>
<td>Age at first injection</td>
</tr>
<tr>
<td>Mental health, including</td>
<td>Current and past treatment</td>
</tr>
<tr>
<td>• Depression</td>
<td></td>
</tr>
<tr>
<td>• Anxiety</td>
<td></td>
</tr>
<tr>
<td>• Mania</td>
<td></td>
</tr>
<tr>
<td>• Psychosis</td>
<td></td>
</tr>
<tr>
<td>• Self-harm</td>
<td></td>
</tr>
<tr>
<td>Comorbid medical conditions</td>
<td>Viral hepatitis and chronic liver disease</td>
</tr>
<tr>
<td>Past episodes</td>
<td>Injury and disease related to injecting</td>
</tr>
<tr>
<td>Current and past treatment</td>
<td>HIV infection</td>
</tr>
<tr>
<td>Psychosocial issues</td>
<td>TB</td>
</tr>
<tr>
<td>Living conditions</td>
<td></td>
</tr>
<tr>
<td>Legal issues, including history of incarceration</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
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<tr>
<td>Educational status</td>
<td></td>
</tr>
<tr>
<td>Support from family and relationships</td>
<td></td>
</tr>
<tr>
<td>Other cultural issues</td>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
<td>Cellulitis and abscesses, thrombophlebitis,</td>
</tr>
<tr>
<td>Injection marks, inflammation, infection or vascular damage</td>
<td>septicaemia, musculoskeletal infections,</td>
</tr>
<tr>
<td>associated with injecting sites, evidence of TB, opportunistic infections (OIs) or liver disease</td>
<td>endovascular complications, viral hepatitis,</td>
</tr>
<tr>
<td></td>
<td>respiratory tract infections</td>
</tr>
<tr>
<td>Mental state examination</td>
<td>Psychiatric disorders, disorders related to</td>
</tr>
<tr>
<td>May reveal depression, anxiety, hypomania or a psychotic illness.</td>
<td>substance use</td>
</tr>
<tr>
<td>Depression and anxiety are the most common psychiatric comorbidities.</td>
<td></td>
</tr>
</tbody>
</table>
The medical history is the most important component of the examination. An open dialogue between the patient and the prescriber is crucial to obtaining the medical history.

4.2.1 Previous treatment for substance use

The patient’s account of previous treatment and relapse can provide valuable information in helping to determine appropriate treatment and preventing relapses in the future. It can also provide an insight into the patient’s reasons for requesting treatment.

Request information on:

- The types of treatment received by the patient (detoxification, methadone, unsupervised withdrawal) and the reasons for failure and relapse, as well as the number of attempts at joining a methadone programme;
- The length of time that the patient has been on treatment;
- The patient’s perception of the benefits of treatment;
- The maximum dose they have taken;
- The end of treatment and the reasons for terminating the treatment.

It is advisable to verify the information given by the patient with the DTC.

4.2.2 Psychiatric and medical co-morbidity

Many patients seeking methadone maintenance to resolve substance abuse problems have pre-existing psychiatric conditions (including psychosis) or mood disorders, such as depression and anxiety disorders. A history of injecting drug use and poly-drug 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 methadone service centre for assessment and treatment, or for the initiation of methadone treatment which can be continued by a general practitioner later.

4.3 Brief interventions during assessment

The aim of brief interventions is to help patients understand that their substance use is putting them at risk and to encourage them to reduce or give up their substance use. Brief interventions can be conducted on any relevant topic during the initial assessment of the patient. The major areas in which brief interventions are conducted are:

- Risky behaviour (sharing needles and syringes, unsafe sex)
• Poly-substance use (making the patient aware of the interactions between different drugs)
• Overdose (enabling patients to reduce the risk).

Further details of brief interventions are given in Section 6.1.4.

4.4 Establishing suitability for treatment by diagnosing opioid dependence

Methadone treatment is usually appropriate for people who are dependent on opioids. According to the WHO International Classification of Diseases (ICD)-10, opioid dependence is present if three or more of the following have been experienced or exhibited at some time during the previous 12 months: 7

1. A strong desire or compulsion to take opioids
2. Difficulty controlling the urge to take opioids
3. The development of opioid withdrawal syndrome on giving up the opioid, and relieving this by intentionally reusing opioids
4. Tolerance to the effects of opioids
5. Preference for taking opioids neglecting other normal activities
6. Persistent use despite a knowledge of the serious harmful consequences.

Harmful opioid use is defined as a pattern of use which damages the health and for which the criteria for dependence may not be met. The adverse consequences of such use may be physical, psychological or social. Patients engaging in harmful use can also be candidates for OST.
Patients’ eligibility for methadone

- A patient who has been using opioids in a dependent fashion for at least six months, and who has made at least one serious attempt at withdrawal over that period, can be considered suitable for treatment.
- Patients engaging in harmful use are eligible for treatment with methadone.
- All those who are dependent on opiates are eligible.
- Those with previous treatment failures (medical or non-medical), including those who have been on methadone in the past, are eligible.
- If the patient has the ability to access methadone on a daily basis, they are considered eligible for methadone treatment.
- The patient should have the motivation to undergo longer term treatment (those on treatment for 12 months and longer have better outcomes).
- The patient should have a strong desire to give up opiate use.
- Special attention should be paid while considering the eligibility of those who are infected with HIV, those receiving antiretroviral therapy (ART) or anti-TB treatment, and pregnant women.
- Generally, the patient should be 16 years of age or older. However, there needs to be flexibility with respect to the age of the drug user and determining the patient’s eligibility is ultimately up to the doctor. It is extremely important to consider the risk behaviours and harmful opioid use of the patient. It should be kept in mind that the potential benefit to the individual’s health and social functioning outweighs the potential disadvantage of methadone treatment.

Patients’ non-eligibility for methadone (Important: there are no fixed exclusion criteria)

- Acutely psychotic drug users are not eligible.
- Those for whom opioids are not the prime drugs of dependence, such as those who are dependent on alcohol, benzodiazepines, amphetamine-type stimulants (ATS) or marijuana alone, are not eligible for methadone treatment.
- Patients with acute medical conditions (severe hepatic disease, respiratory illness or head injury) are not eligible.
- Patients with a high risk of overdosing are not eligible for treatment with methadone.

Note: If there are any doubts about a patient’s suitability for methadone treatment, a second opinion may be sought from a psychiatrist or township medical officer (TMO).

In general, patients with a diagnosis of opioid dependence are suitable for either substitution or withdrawal therapy using OST. A psychosocial intervention alone may be undertaken when the patient does not wish to commence on medication or when the harm resulting from the use of pharmacotherapy may be greater than the resultant benefit. An example is a young person who uses an opioid intermittently and who is brought to a drug treatment service by the family for the first time. Chronic, opioid-dependent patients (e.g., after several years of dependence) will almost certainly need long-term substitution therapy.
4.5 Considering treatment options

A diagnosis of dependence or harmful substance use indicates that the patient is in need of treatment. In case a person is engaging in non-problematic substance use, such as occasional opium smoking in an elderly male in a rural area, a case might be made that treatment may not necessarily provide any benefit. In such cases, it is important that patients are followed up to ensure that use does not become problematic or harmful.

Discuss treatment options, including detoxification, withdrawal using methadone, and methadone maintenance programme, with the patient (see Section 4.5.4). In consultation with each other, the prescriber and the patient can decide whether a methadone programme will help them to achieve their treatment goals. The level of support and treatment required by different patients varies. Some require a high level of medical, case-work and other services, while others can be treated satisfactorily without extensive additional services. A total abstinence from the unsanctioned use of opioids is only one among the range of treatment objectives, which the patient may achieve during the course of treatment.

4.5.1 Providing the patient with information on treatment

A strong therapeutic relationship will strengthen the exchange of information. All members of the treatment team should contribute to educating the patient on opioid dependence, its treatment and other relevant issues.

Information should be provided to the patient in the following forms.

- Verbal discussions, including answering the patient’s questions
- Written information, such as pamphlets (keeping in mind the level of literacy)
- Posters on the walls of the treatment centre and relevant video displays providing messages on health promotion
- Where appropriate, and if infrastructure is available, patients may be referred to websites

The prescriber should provide the following information to the patient:

- Explanation regarding the causes of opioid dependence
- The occurrence of peak effects two to four hours after the administration of methadone
- The accumulation of methadone over time, which results in a greater effect after 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 10 days of treatment, the risks related to combining methadone with the unsupervised use of other CNS depressant drugs (particularly benzodiazepines) and alcohol, and the special risk associated with binge drinking
- The fact that some medications can induce or inhibit CYP3A4 enzyme activity on methadone concentrations (Section 2.2)
- The interactions of methadone with TB medicines (rifampicin) and some HIV medicines (particularly nevirapine and efavirenz)
- The effects and side-effects of methadone use
Guidelines for and conditions of participation in the methadone programme

The impairing effects of methadone on driving ability (until the patient is stabilized on a constant dose)

The addictive nature of methadone, with an emphasis on the potential benefit to the individual’s health and social functioning outweighing the potential disadvantage of methadone treatment

The behaviour expected during the programme

The likely duration of the treatment, the benefits of which are maximized if the patient remains under treatment for at least 12 months

The cost of treatment (medical and pharmaceutical) if required

The length of time required to withdraw from methadone and the fact that the patient may experience slight discomfort during this period

The causes of drug overdose, the high-risk situations associated with overdose, the symptoms and signs of overdose, and the action to be taken when overdose is suspected. The patient needs to inform family, friends and/or associates about the symptoms and signs of overdose, and about the urgency with which a response is required when they suspect an overdose.

The process of resolution of complaints during treatment

Support and information services

Harm reduction (including how to prevent the transmission of blood-borne viruses and how to inject safely)

### Important information provided to and understood by patient

- The dynamics and processes of stabilization
- The hazards of poly-drug use, particularly in the first week of treatment
- The effects and side-effects of methadone use
- Programme guidelines and conditions
- The risks of driving while stabilizing
- Expected behaviour while on treatment
- Risks and symptoms of an overdose

### 4.5.2 Options for treatment

A diagnosis should lead to the development of a treatment plan. The options for the management of harmful opioid use and opioid dependence are psychosocial interventions, non-opioid withdrawal therapy, and opioid withdrawal or opioid maintenance pharmacotherapy. Preference should be given to OST in the case of patients with opioid dependence.

### 4.5.3 Psychosocial or pharmacological treatment (or both)

Psychosocial treatment is generally recommended as an adjuvant to pharmacotherapy. If a patient is to be given psychosocial treatment alone, it is important to ensure that they have strong social support from family or close friends. Given that many drug users are homeless and alienated from their families and communities, this is frequently not easy to ensure. Commencing an individual on methadone may not necessarily be beneficial in this early phase.

### 4.5.4 Substitution versus withdrawal

Most patients presenting for treatment of opioid dependence request withdrawal therapy in the false belief that when they have completed withdrawal they will be “drug-free” and be
able to get on with their lives. Families often reinforce this view. The rate of relapse following withdrawal from opioids is very high. However, there are several reasons to provide a patient with withdrawal treatment:

- It supports the patient in the decision to seek treatment.
- It maintains engagement.
- It reduces opioid use.
- It allows the patient to remain abstinent.
- It helps to stabilize people for the commencement of ART or TB treatment and improves their health status.

Patients may unsuccessfully attempt withdrawal several times before embarking on substitution therapy. OST is more successful than withdrawal therapy in reducing illicit opioid use and retaining patients in treatment. Most patients with a history of opioid dependence benefit from substitution therapy in that it stabilizes their drug use and its consequences.

4.6 Obtaining consent for treatment

This may be done at any stage during the assessment process. Consent should be voluntary and should be obtained after the patient has been given an explanation about the risks, benefits and expectations of the treatment. Ideally, information should be provided in both verbal and written forms, keeping in mind the patient’s level of literacy. The consent should be signed by the patient and carry a date. Consent for minors under the age of 16 years should be obtained from a parent or guardian. If this is not possible, before commencing treatment, the treatment team should seek appropriate information regarding significant adults or family members who have previously acted as guardians for the child.

4.7 Registering a patient for prescribing methadone

A drug user must be registered and a notification of the registration should be sent to a DoH, DTC. Treatment should not be commenced until the prescriber has registered the user and confirmed that they are not already receiving methadone treatment from another DTC. The initiation of methadone treatment should also be notified to the DoH, DTC at the time of commencement and mentioned in the monthly summary report of new patients commenced on treatment.
Section-5

Opioid substitution therapy
5.1 Induction into treatment: careful induction and review during the first week

Patients should be counselled not to consume opioids or sedatives (including alcohol) for 24 hours before the commencement of methadone treatment. However, the first dose of methadone should not be delayed because of a patient’s use of heroin the same day, though the actual time of the first dose maybe postponed an hour or two if there are signs of sedation. It is important to start treatment and begin working on behavioural change when the opportunity presents itself. If a patient is intoxicated with heroin, the first (or any) dose of methadone should be delayed by some hours and be chosen keeping in mind the higher risk faced by the patient. The initial dose should be administered in the morning. The induction dose depends on:

- The severity of opioid dependence and the degree of recent tolerance to opioids;
- The use of other drugs, such as sedatives, and the misuse of alcohol;
- Concurrent medical conditions, including respiratory illness and impaired hepatic function;
- The time since the patient last used a drug and signs of withdrawal or intoxication; and
- Anticipated interactions with other prescribed medications.

The maximum induction dose should be 30 mg. Patients should be reviewed four hours after the first dose for signs of withdrawal or intoxication in order to inform changes of dose in the first week of treatment. It is recommended that an additional 5–10 mg be given 3–4 hours after the induction dose if the Clinical Opiate Withdrawal Scale (COWS) tool (Appendix 1) indicates moderate or severe withdrawal. After the starting dose(s) on the first day, ensure that the patient spends three days on each dose before considering an increase in the dose, as it may take up to five days for a change in dose to have its full effect owing to the long half-life of methadone.

<table>
<thead>
<tr>
<th>Induction dose</th>
<th>Clinical condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–20 mg</td>
<td>Opioid dependence with use of alcohol or other sedatives; relevant concurrent medical conditions; low or uncertain levels of tolerance</td>
</tr>
<tr>
<td>20–25 mg</td>
<td>Moderate level of opioid tolerance or some lower level risk factors</td>
</tr>
<tr>
<td>25–30 mg</td>
<td>Higher level of opioid tolerance with minimal use of other drugs; patient well known to doctors with no special risk factors; prior methadone treatment with no special risk factors</td>
</tr>
</tbody>
</table>
Patients should be reviewed 3-4 days after the first dose to determine whether the initial dose needs to be increased. A review enables the prescriber to determine the most effective dose and provides an opportunity for the management of the high risk of methadone or combined drug toxicity during induction. It also provides an opportunity to reinforce treatment education and to assess the patient for side-effects. If the patient has been experiencing withdrawal symptoms for most of the period, the dose can be increased by a maximum of 10 mg. If, on the other hand, the patient has been experiencing withdrawal symptoms only just before taking the next dose, the dose may be increased by less. The dose should be increased only after reviewing the patient and where clinically indicated.

**Induction as out-patient or in-patient**

The induction phase usually lasts 10–14 days. It was common for patients to be admitted to the DTC during this time for observation. Now, in line with the common international practice, a person is inducted into treatment as an outpatient. However, the patient may also be admitted, if this is considered more suitable and appropriate for the patient.

5.1.2 Writing prescriptions

The prescription book must be used for writing prescriptions, which should be written clearly and signed by the prescriber. The following information should be contained in the prescription.

- Name of the patient and other identifying pieces of information, such as address and date of birth
- Type of treatment and dosage
- Dates between which the prescription is valid
- Doses should be written in milligrams (mg) to avoid confusion in dosing where methadone is mixed at variable concentrations

An example of a prescription is given in Appendix 2 (see also Section 9.8).

**Prescription**

- Indicate the initial dose, not a range of doses, on the prescription. Do not increase the dose without personally reviewing the patient.
- Limit the duration of the prescription to less than one week to encourage the patient to return for review frequently during the first week (the period of the highest risk during the treatment).
- Do not prescribe commencement doses of above 30 mg for patients seeking treatment for dependence on prescription opioids (morphine, codeine, oxycodone or pethidine).

5.2 Establish an effective maintenance dose

As with the treatment of other medical conditions with drugs, the dose is an important determinant of the effectiveness of treatment. Prescribing should not focus on reducing the dosage to a level that minimizes the risk of adverse effects or decreases 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 mg per day is more effective than lower doses in achieving treatment outcomes such as decreased illicit drug use and better retention of patients in treatment.
Reaching an effective maintenance dose usually takes a few weeks.

### Flexibility with maintenance dose

Establishing an effective maintenance dose requires a degree of flexibility. Some patients will be comfortable and tolerate 40 mg per day, while others need 200 mg or more per day. HIV-infected patients receiving antiretroviral therapy are likely to require adjustments in the dose of methadone (commonly higher dose). In the context of Myanmar, most patients would need to be maintained on a dose of 80 to 120 mg per day.

The two most important findings of clinical assessment that guide dose changes of dose are:

- The presence of withdrawal symptoms or signs of intoxication; and
- The use of illicit opioids.

The dose of methadone should be increased until the patient is not experiencing withdrawal symptoms but does not show signs of intoxication, such as drowsiness or pinpoint pupils, and until illicit opioid use is generally less than once a week.

Doses should be increased by a maximum of 10 mg, with a gap of at least four days separating each dose, in order to reduce the risk of overdose. If there is evidence of intoxication, enquiries should be made about other drug use (particularly benzodiazepines) or alcohol and, if necessary, the methadone dose should be reduced by 5–10 mg.

### 5.3 The methadone prescription

As in the case of any other controlled drug, a dispenser or pharmacist cannot dispense methadone without holding a valid prescription. The prescription for methadone must be in writing. The usual requirement that the quantity to be dispensed be written in words and figures applies. In the first two months of treatment, when the patient is being stabilized and the risk of toxicity is high, a precise dose should be prescribed. Any adjustment of the dose requires a review of the patient. To avoid misunderstanding, it is essential that the following information is specified 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 go for a review after an appropriate interval)
- The name of the dispensing site at which the methadone is to be dispensed

### 5.4 Reviewing the patient’s progress regularly

Patients should be reviewed regularly by the treating doctor. The treatment team should discuss the patient’s progress on at least two occasions in the first week of treatment, about two times per month for 2nd and 3rd month, and monthly thereafter. Patients should be clinically reviewed on:

- Day 1, four hours after the first dose
- Day 3 or 4
- End of week 1
- At least once a week for the first month or until a stable dosage has been achieved
- At least every two weeks for the first two and three months
- At least monthly thereafter
This schedule should be revised if a patient’s condition deteriorates.

The purpose of the review is to gain a better understanding of the clinical and psychosocial issues affecting the patient, and develop a strong therapeutic relationship with them. Although patients are usually preoccupied with the length of the treatment, emphasis should be placed on the importance of clinical and psychosocial progress in determining the duration of the treatment. Each review should also focus on matters such as the patient’s history of drug use, comorbid medical conditions, physical and mental health examinations, and the management plan (Section 4).

### Factors to be considered during annual review of individual treatment programme

- The effect of the treatment on illicit opioid use
- The patient’s use of other drugs
- Changes in the patient’s lifestyle, social functioning and situation
- The patient’s physical health and well-being
- The achievement of goals agreed upon mutually
- 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 Side-effects of methadone

It is not uncommon for methadone to have side-effects. Patients should be educated on the potential side-effects before the commencement of the treatment. This will allow for early detection and management. The key side-effects that should be discussed are:

- Sedation, particularly in combination with other sedatives
- Constipation—fluids and osmotic laxatives, e.g. lactulose, are the treatment of choice
- Sweating
- Nausea and possibly vomiting
- Reduction in libido
- Dry mouth

### 5.5.1 Risks of methadone toxicity

Some patients are at a greater risk of methadone toxicity than others, particularly during induction into treatment. The toxicity of methadone resembles that of other opioids: sedation, coma, respiratory depression and miosis (pinpoint pupils) can occur following an overdose. However, the pharmacokinetics of methadone is unique, particularly the long interval between ingestion and the time that it reaches its 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 risks of overdose and death are the highest in the first 10 days of treatment. This is because during this time, the patient may misuse other CNS depressants (including alcohol and benzodiazepines) or continue with illicit drug use in an effort to minimize the withdrawal symptoms before becoming stabilized in treatment.
5.5.2 Methadone toxicity: symptoms and signs

Methadone is a potentially toxic substance. Death occurs because of hypoxia due to respiratory depression, usually the result of interactions with other sedatives, of which benzodiazepines are the most common.

- Pinpoint pupils
- Slurred speech
- Unsteady gait
- Poor balance
- Drowsiness
- Slow movement
- Coma
- Pinpoint pupils
- Respiratory depression
- Hypoxia and death

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

5.5.3 Treatment of methadone overdose

The highest risk of drug overdose occurs in the first two weeks of treatment, when the ingested methadone is equilibrating with tissue reservoirs and accumulating in the body. The level of methadone in the blood during this period may not be sufficient to prevent craving, or may reach a toxic level if the clinical judgement regarding tolerance is incorrect. The patient may continue using illicit opioids or high doses of prescription drugs to self-manage the symptoms.

Patients who are on long-term methadone treatment and appear to be suffering from a methadone overdose can be observed for 4-6 hours at the dispensing centre. If there are no signs of toxicity, the patient can be discharged and asked to return the next day. Patients who are naive to the effects of methadone or are experiencing a clinical overdose of methadone, as described in the figure above, should be referred to the drug dependency treatment hospital.

Naloxone should be used with caution due to its short half-life, as methadone will continue to produce respiratory depression after the effects of naloxone have worn off.

A patient suffering from a methadone overdose should be treated as follows:

- Provide respiratory support
- Administer naloxone, if appropriate

The patient has a high risk for methadone toxicity in the following circumstances:

- This is the patient’s first presentation as a drug user, and their medical history and history of drug use are unclear.
- The patient has a high risk of poly-drug abuse and dependence.
- The degree of neuro-adaptation 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.
Methadone-related drug deaths due to methadone toxicity alone are rare: most (about 90%) involve prescription drugs and alcohol. Prescription drug abuse is common, and these drugs contribute to potentially dangerous toxicity, cognitive impairment and anterograde amnesia.

### Key messages about induction and effective maintenance dose

- The initial dose should be 15–30 mg per day, depending on opioid tolerance over the previous week and overdose risk factors.
- Review the patient 3–4 hours after the first dose is given.
- The patient can be given an additional dose of 5 mg 3–4 hours after the first dose, if there is clear evidence of opiate withdrawal and severity of withdrawal.
- The Clinical Opiate Withdrawal Scale (COWS) is a relatively reliable tool to measure the severity of withdrawal.
- The maximum induction dose should be 30 mg, except for patients starting methadone soon after stopping treatment with a therapeutic dose (for example, first 10 days if over 100 mg when it can be up to 40 mg). If a patient has missed methadone doses for some days, a urine test should be done and their status should be reassessed using COWS. If the urine test is negative, the patient should be dispensed 30 mg. If the patient relapsed within the period during which they missed doses, the dosage should be decided in accordance with COWS.
- Review the patient every day for 3–4 days after the first dose. After that, review at least before each potential increase in dose.
- Be aware that there is a small number of individuals with low tolerance (particularly heroin smokers) and those with respiratory conditions (i.e. infection, asthma) who can become dangerously intoxicated at a dose of 20 mg.
- Increase the daily dose by 5–10 mg after the patient has been on the dose for three days. It is important to keep the patient on each dose for at least three days before deciding to increase the dose again. Increase the dose after 3-5 days on each dose.
- For a patient experiencing withdrawal symptoms during the induction phase, the daily dose can be increased by a maximum of 5 mg (to 50 mg or first 10-15 days).
- The maximum daily dose of methadone in the first week of treatment should be 40 mg.
- When the client reaches a daily dose of 50 mg, it is safe to increase the dose by 10 mg/day after 5-7 days on the stable dose.
- The dose of methadone should be increased once or twice a week till the patient reaches an effective substitution dose. The administration of methadone at a higher dose is associated with better retention rates and greater suppression of opioid use.
- As for the maintenance dose, some patients are comfortable with and tolerate 40 mg per day, while others need 200 mg or more per day. Flexibility is essential. Most patients can be maintained on 80–120 mg per day.
- Encourage doctor participation and observation of the client in the decision-making processes during the 10–14-day induction period.
- The patient can go through the induction period as an inpatient or outpatient.
5.6 Counselling

Counselling may help the patient address their drug addiction problem. It is for the prescriber to choose whether they will counsel the patient themselves or whether to refer the patient to another counsellor. The patient’s dispenser may also provide limited counselling. Patients with special counselling needs may need to attend a specialist DTC or consult a psychiatric service. The other matters on which counselling should be provided are risk behaviours, and the prevention of the transmission of blood-borne viruses (HIV and hepatitis B and C) and testing for these diseases.

5.6.1 Allied health staff

A range of organizations fund professionals to support methadone patients and those who are dependent on substances. They should be encouraged with the following.

- The inpatient management staff must follow the national programme policy and guidelines.
- Only trained and approved methadone prescribers can commence patients on methadone treatment.
- The roles and responsibilities of those involved must be clearly documented and understood.
- Proper recording and regular reporting (monthly), in keeping with the national guidelines, are a must (Appendix 8).
- As far as the management of methadone therapy in new DTC sites is concerned, a senior consultant must monitor the situation. To contribute towards uniformity of the reporting and recording of national data, all DTC sites should use a standardized monitoring system.

5.7 Dispensing arrangements

Health professionals dispensing opioid pharmacotherapy to patients are an integral part of the treatment team, particularly as frequent contact with patients facilitates the development of a good rapport.

5.7.1 Supervised dosing at Drug Treatment Centres

Written instructions on dosing are to be documented in a patient’s daily dispensing book, which is kept in the dispensary. The format of the daily dispensing book may vary across DTCs. The dispensing book shall contain details of the patient including a photograph.

- The daily dispensing book is to be used at the DTC to review the attendance of the patient, and changes in dose are to be noted directly on the prescription and in the dispensing books by the prescriber.

5.7.2 Supervised dosing arrangements through outside dispensing sites and hospital pharmacies

The following important issues are required to be addressed when supervising dosing arrangements:

- After it has been agreed upon that the patient will attend a particular dispensing site, contact the site to arrange for daily supervised dosing.
• Keep a record at the DTC of the dispensing site at which dosing is to be done.
• Forward the following 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 the 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, following which a fax of the prescription may be sent to the dispensary, endorsed with the name of the dispensary to which it is being sent. The fax must be confirmed in writing by forwarding the original prescription to the dispensary as soon as possible.
• Alternatively, place the documentation and prescription in a sealed envelope, to be given by the patient to the dispensing site. The envelope must be marked “confidential”, with a sign across the seal. The prescription must be endorsed by the 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 DTC should be informed of any change in methadone dispensing location

5.7.3 Communication between prescriber, patient and dispensing site

Good communication should be maintained between the prescriber and the patient and among the members of the treatment team. Each party has particular information that is useful to the other.

• Other than taking the history, examining the patient and running laboratory tests, the prescriber should be aware of the patient’s medical condition and social circumstances.
• The dispenser, who sees the patient daily, may establish a good rapport with them and even provide counselling. The dispenser may notice irregular attendance for dosing, unprescribed drug use, abuse of medication and evidence of drug toxicity. They may refer the patient back to the prescriber for a review of management.
• The patient may have had previous experience with methadone, which may prove useful for those involved in treatment.

It is desirable for dispensers to be able to contact the prescriber at all times. For this reason, it is recommended that they be provided with full contact details (including after-hours contact numbers) of the prescriber. It is of vital importance that all information on dosing is communicated in writing, and telephone conversations are recorded 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

Split-dosing refers to twice-daily dosing. A small minority of patients may benefit from split-dosing. Split-dosing is indicated when a patient experiences withdrawal symptoms within 12 hours of the administration of methadone, despite being on a high dose of the drug. This may be more common in the third trimester of pregnancy or when a patient is taking other medications which alter the metabolism of methadone. While dispensing split-doses, the morning dose is usually administered under supervision and the afternoon dose is taken at home. In cases in which a take-home dose is not safe, both doses should be administered under supervision.

5.8 Dispensing of methadone in closed settings: prison or police custody

Specific issues need to be considered when dispensing opioid pharmacotherapy in closed settings. A system for treating opioid dependence must include the provision of OST in closed settings to ensure the continuity of treatment/care since many patients often spend time in jail due to the illicit nature of their activities. Methadone is not yet provided within closed settings in Myanmar. However, it is anticipated that it will be provided in the future.

It is often unexpected that a patient will be detained in a closed setting. Dispensing arrangements should commence as soon as practicable. Ideally, custodial arrangements should not interrupt treatment. Dispensing the patient’s dose within the closed setting is usually more convenient than transporting the patient to a DTC every day. Only supervised dosing should be provided in closed settings to minimize the risk of diversion and harm through illicit injecting.

Continuity of treatment should also be ensured after the sentence has been completed and the patient is due to return to the community. Arrangements should be made so that there is minimal interruption of treatment as the chances of overdose, relapse and risky behaviour are higher in the few weeks immediately after the patient returns to the community. There is often a lot of mobility and transfer to different systems that can occur post-release from closed settings, which may lead to disruptions in treatment. Every attempt should be made to ensure the continuity of treatment and, where ongoing OST is not possible, the patient should be medically assisted in withdrawal.

The practice of initiation into OST prior to discharge is desirable in the case of patients who have relapsed earlier and have chronic, refractory opioid dependence. It helps to reduce the risk of overdose and ensures a better clinical outcome on return to the community. Typically, it is commenced in the final months of detention, allowing for time to achieve a stable dose prior to discharge. Individuals who are not opioid-tolerant need to be inducted into OST carefully to minimize the risk of overdose.

5.9 Take-away (take-home) doses

Methadone, which is subject to misuse and trafficking, is a strictly controlled drug. People with a history of substance abuse may misuse it by mixing it with other psychoactive drugs, such as benzodiazepines and/or alcohol. Patients may also share it with associates who are not tolerant to the drug, with serious adverse consequences. Another risk is that drug-dependent friends or partners may steal a patient’s take-away dose. This has been known to cause deaths. Children are particularly vulnerable to overdose, calling for special care in the safe storage of methadone.
Despite the risks, incidents of misuse and adverse consequences arising from take-away dose in Myanmar as well as in most other countries, are rare. Take-away doses can help stable patients normalize their lives, integrate into the community, and meet work and family commitments by freeing them from the demands of travel for daily supervised dosing. They are important not only for those who wish to maintain employment, but also in the management of a chronic medical condition as well as in situations such as court appearances, visiting distant sick relatives, holidays or conferences, and so on. Most importantly, take-away doses contribute to compliance with prolonged methadone maintenance and the retention of patients in treatment.

The provision of take-away doses is important in many (rural as well as urban) areas of Myanmar because of the geographical and logistical difficulties associated with patients attending a dispensing service daily.

Take-home medication should be identical in dose to supervised doses. The patient should be assessed for stability before take-home dosing is commenced. The assessment of a patient’s stability (usually a month or two before commencing take-home dosing) should take the following into account:

- Current adherence to supervised dosing
- Current adherence to appointments with the treatment team
- Infrequency of use of additional illicit opioids or other drugs (may or may not be confirmed with a random urinary drug screen)
- Stability of mental health
- Stability of accommodation
- The availability of a secure area to store medication (particularly if there are children at home)
- Little evidence of intention to divert or inject take-home doses

It may be difficult to assess the suitability of a patient for take-home dosing. The entire treatment team, including the dispenser, must take the decision in consultation with each other.
Key issues for prescriber-authorized take-away doses

In order to scale up the number of opioid-dependent patients onto methadone greater emphasis and authorization for take-away dose is needed. Take-away dosing might progress as follows:

- No take-home doses in the first three months of treatment
- Assess stability and family support
- First take-home dose should not be for more than two days per week
- Assess stability over one month - should not be more than three days per week.

However, if the entire treatment team, including the dispenser, is fully convinced of the stability criteria of the patient take-away dose of up to **seven days** should be permitted in circumstances such as travel, family and employment commitments.

Note: Take-away dosing should be supported by appropriate documentation to protect the prescriber.

- Where possible, efforts should be made to find an alternative to just providing doses to the patient, for example, encouraging the involvement of the family or guardian to play a role in collecting and handling take-away dosing for the patient. This would be done in consultation with treatment team.

Take-home dosing is not recommended in the following situations:

- Poly-substance use
- Recent overdoses or presenting for dosing in an intoxicated state
- Unstable psychiatric conditions
- Risk of injecting take-home doses

5.10 Transfer to another methadone treatment centre

Patients may transfer to other dispensing locations (towns) temporarily for work, holiday or other reasons. The patient’s suitability for transfer must be assessed before making arrangements for it. The 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. The transfer may be intrastate, interstate or international. Proper communication between the transferring and receiving prescribers and dispensing sites is vital in each case. Without such communication, there is a risk of confusion about when the last dose was administered at the transferring dispenser, and the possibility of dual dosing on the same day, with resultant methadone toxicity. The transferring doctor who makes the arrangements for the transfer of dosing points must ensure that clear, written instructions are provided to both dispensaries about the timing of the last dose at the transferring dispensary and the first dose at the receiving dispensary.

The local DTC can provide details of the local dispensing sites to be considered for transfer. The receiving prescriber should be provided with details such as the patient’s name, date of birth, methadone dose, dates of doses, 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 with the transfer form, the patient’s prescription book and the methadone dispensing record book to the receiving prescriber.
5.10.1 Procedures for arranging international transfers

- For information and advice on arranging international transfers for patients receiving methadone, check the following link: www.euromethwork.org.
- Enquiries for information that is more up to date and regarding a particular international transfer can be sent to the following e-mail: info@q4q.nl.

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

5.10.2 Receiving transfers

A prescriber who accepts a transferred patient must obtain adequate information from the transferring prescriber to ensure safety of treatment and continuity of care, and to facilitate decisions on take-away doses. It may be necessary to contact the transferring prescriber and request for the appropriate documents. The documents should include:

- The patient’s full name, date of birth, and old and new address;
- Current methadone dose in milligrams; and
- 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 given over a long term. Patients should be encouraged to remain in treatment for as long as they benefit from the programme and preferably for more than three years. Even though they will not be “drug-free”, they will still benefit from reduced drug use, decreased risky behaviours and decreased risk of opioid overdose. The programme offers patients relief from the need to obtain drugs and an opportunity to stabilize their lives and withdraw from the drug-taking culture. Evidence suggests that the benefits increase when the patient remains in treatment for more than 12 months.

5.11.1 Voluntary withdrawal from methadone

Despite the fact that methadone is an effective treatment for opioid dependence, 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 a rapid reduction of the dose. Complete cessation is recommended only when the patient is socially engaged with family or friends, ideally, has employment or is engaged in regular extracurricular activities, and is not engaging in opioid and, ideally, other drug use. Cessation is usually not recommended in the first 12 months of treatment.

The decision to withdraw and the rate of withdrawal may be determined by consultations between the patient, the prescriber and others in the treatment team (including the dispenser and the counsellor). Monitor the patient closely during withdrawal, and if they experience difficulties, cease the dose reduction until they stabilize.
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. The general guidance is that a reduction of the daily dose by 1 mg per fortnight or 25 mg per year is usually achievable when all social factors are favourable.

Methadone should be reduced at the following rate:
- Dose of >50 mg by a maximum of 5 mg/week
- Dose of 30–50 mg by a maximum of 2.5 mg/week
- Dose of <30 mg by a maximum of 1-2 mg/week

Patients may experience withdrawal symptoms for a number of weeks after cessation despite very gradual tapering of the dose during the final 5 mg of therapy.

5.11.2 Involuntary cessation of methadone

It may be decided to discontinue a patient’s methadone treatment because the patient is making unsatisfactory progress or is putting themselves or others at risk. In this situation, the potential risks to the individual from cessation of therapy need to be balanced against the potential risks to others (patients and staff) if the patient continues. All reasonable attempts should be made to retain the patient in treatment or transfer the patient to another service that may be more accommodating.

The reasons for involuntary cessation may include:
- Violent threats to or abuse of staff or other patients
- Confirmed drug dealing or other illegal activities around dosing points
- Continued use of dangerous quantities of other central nervous system (CNS) depressant drugs
- Repeated failure to attend for treatment
- Diversion of methadone
- Trafficking of take-away doses.

An abrupt termination of treatment or a dramatic reduction in dosage is associated with a marked deterioration in behaviour, drug use and emotional stability, and is rarely warranted.

5.11.3 Methadone dosing for opioid withdrawal

Methadone-assisted opioid detoxification regimens are generally longer and the withdrawal symptoms are more intense than those associated with other OST, such as buprenorphine.

Methadone dosing should be flexible. The initial dose sequence and the rate of withdrawal should be based on:
- Previous experience of opioid withdrawal
- Current level of opioid use
- Degree of psychosocial support

The principle is to commence treatment, and then increase the dose of methadone to a level that reduces symptoms. The dose is then reduced gradually to zero over 10–14 days.
Table 3: Suggested methadone-assisted out-patient withdrawal regimen

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Days 2–4</th>
<th>Days 5–14</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–30 mg</td>
<td>20–30 mg</td>
<td>2.5 - 5 mg a day*</td>
<td></td>
</tr>
</tbody>
</table>

*Hold the dose at the same level for 2 days if discomfort unmanageable

The period of withdrawal for in-patient withdrawal should be 5-7 days of methadone, followed by several days without methadone prior to discharge to prevent relapse. Non-opioid medication should be used to control withdrawal symptoms during methadone detoxification.

A limited extension of the planned schedule of dose reduction may be allowed at the patient’s request; however, if it seems likely that withdrawal will extend beyond 10-14 days, the intent to withdraw should be reviewed with the patient so they fully understand the implications of extending the withdrawal period. One should discuss with the patient’s ability to accept the level of discomfort and to control the use of opioids. If the withdrawal period has to be extended or the dose of methadone needs to be increased to control the use of heroin, there is a strong need to consider maintenance.

Patients undergoing opioid detoxification may experience withdrawal symptoms that are unpleasant enough to contribute to a relapse to heroin use. Symptomatic treatment may limit the level of discomfort. One should prepare the patient to be ready to face some discomfort owing to withdrawal, particularly as the dose of methadone is being reduced and in the two to four days after the last methadone dose. Most individuals will experience symptoms of opioid withdrawal during this regimen, with the symptoms occurring with reduced intensity for a number of weeks afterwards.

A review of the patient must be arranged for after they complete the methadone treatment, to assess their progress and discuss the prevention of a relapse.

5.12 Dealing with specific clinical situations

5.12.1 Intoxication

Patients intoxicated with sedatives, such as alcohol, opioids or benzodiazepines, should be assessed clinically before the administration of OST.

- Moderately intoxicated patients should be asked to return later in the day, when they are not intoxicated, or to wait at the dispensing agency or treatment centre until such time as they are alert.
- Mildly intoxicated patients should be assessed prior to the administration of a dose, and given a reduced dose (e.g. 50% of the methadone dose).

5.12.2 Overdose

The risk of an overdose is the highest in the first two weeks of treatment. Overdoses are usually associated with the use of other sedatives, particularly benzodiazepines. After stabilization of the methadone dose, those on a higher dose are at a lower risk of overdose than those on lower (<60 mg) doses. This is thought to be due to the fact that high-dose methadone increases the individual’s tolerance to opioids.
The treatment of overdoses in individuals on opioids, including methadone, consists of cardiopulmonary resuscitation (CPR), with initial drug therapy with naloxone, as well as monitoring in hospital. Naloxone has a short duration of action, which can be lengthened by intramuscular administration. Failure to rouse the patient following the administration of naloxone indicates an overdose from another sedative. As respiratory support with oxygen and ventilation may be needed, the patient has to be transported to a hospital.

The signs of an opioid overdose are:

- Pinpoint pupils
- Peripheral cyanosis (blue tinge on the fingers)
- Respiratory depression (not breathing)

Naloxone should be stocked as an emergency drug to combat opioid overdoses in general hospitals, DTCs and drop-in-centres (DIC). Further information on the management of overdoses during OST may be found in Section 5.5.3.

5.12.3 Missed doses

It is not uncommon for patients to miss supervised doses of methadone. The reasons may be valid (commitments related to the family or employment), or be related to continued drug use. It is often difficult to confirm why doses have been missed. If a patient misses doses intermittently (one to two a month), it does not necessarily indicate instability. Patients who regularly miss one or more doses a week should be reviewed by the treating team. If patients are missing doses to use opioids, the dose of methadone should be increased.

In these circumstances, dispensers are advised to notify the prescriber, who should consider:

- The reasons for failure to attend the hospital/centre
- The patient’s use of drugs during this period
- The patient complaining of opiate withdrawal
- Physical evidence of withdrawal or intoxication

Table 4: Management of missed doses during opioid substitution therapy (OST)

<table>
<thead>
<tr>
<th>Number of days missed</th>
<th>Recommended action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day</td>
<td>Continue current dose, review at next appointment</td>
</tr>
<tr>
<td>2 days</td>
<td>Review by treatment team</td>
</tr>
<tr>
<td></td>
<td>Continue at current dose</td>
</tr>
<tr>
<td>3 days</td>
<td>Review by treatment team</td>
</tr>
<tr>
<td></td>
<td>Give half dose of methadone and resume normal dosing the following day</td>
</tr>
<tr>
<td>4 days</td>
<td>Review by treatment team</td>
</tr>
<tr>
<td></td>
<td>Give half dose of methadone and resume normal dosing the next day</td>
</tr>
<tr>
<td></td>
<td>Keep patient under close observation the next few days</td>
</tr>
<tr>
<td>5 days</td>
<td>Begin new induction</td>
</tr>
</tbody>
</table>
5.12.4 Administration of incorrect doses

Errors commonly occur when a patient is seen by a new, inexperienced dispenser who is unfamiliar with the patient. It is not uncommon for new dispensers to confuse the methadone dose, mistaking milligrams for millilitres. This can result in the administration of very high doses. Patients should be monitored for signs of sedation for four hours after the incorrect dose has been administered. It is not recommended to induce vomiting.

5.12.5 Vomited doses

Methadone is absorbed rapidly, so vomiting more than 20 minutes after the administration of a dose probably does not result in much loss of the dose.

**Table 5:** Management of vomited doses during opioid substitution therapy

<table>
<thead>
<tr>
<th>Time of vomiting</th>
<th>Witnessed or unwitnessed</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting &gt;20 minutes after dose</td>
<td>Witnessed or unwitnessed vomiting</td>
<td>Methadone has probably already been absorbed so no action required</td>
</tr>
<tr>
<td>Vomiting &lt;20 minutes after dose</td>
<td>Witnessed vomiting of methadone dose</td>
<td>Re-administer same dose of methadone</td>
</tr>
<tr>
<td></td>
<td>Unwitnessed vomiting of methadone dose</td>
<td>Review patient in 4 hours’ time to assess whether he/she is experiencing withdrawal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Signs of withdrawal—give normal dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No signs of withdrawal—give no dose, resume dosing the following day</td>
</tr>
</tbody>
</table>

Patients sensitive to the emetic effects of opiates may require anti-emetic treatment (for example, pre-dose domperidone, prochlorperazine and metoclopramide) for a few days in the initial phase of treatment. Additional care is warranted in the case of pregnant patients because opioid withdrawal can cause foetal distress.

5.13 Combined drug toxicity

Deaths due to methadone alone are rare; they 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 commonly identified in methadone-related drug deaths. Some methadone-related deaths occur due to the misuse of methadone tablets prescribed for pain, or the misuse of methadone following diversion from legitimately prescribed doses.

**Countermeasures**

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

Deaths from combined drug toxicity involving methadone may be preceded by a long period of coma, during which the patient is left to “sleep it off” and subsequently dies. A methadone patient who cannot be roused and makes noises suggestive of a blocked upper airway and depressed reflexes (snoring, gurgling, spluttering) has a very high risk of dying from a drug overdose.

**Countermeasures**

- Inform the patient, family, friends and associates about the signs of coma, and the need to take urgent action if it is suspected. They should be made aware that it is a medical emergency if the patient cannot be roused and is snoring (or making other sounds that suggest airway obstruction).
- Comatose patients should be positioned on their side, with the 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 intravenous infusion, over 24-36 hours. This can best be provided in an intensive care or high-dependency inpatient setting.

5.14 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 diseases, such as ischaemic heart disease and stroke. The illicit use of drugs 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 among methadone patients (following a drug overdose). Some methadone patients 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 when they were injecting drugs, and these may become evident once they are stabilized with methadone maintenance therapy.

**Countermeasures**

- Make a psychiatric assessment as part of the initial assessment of the patient.
- Maintain a high index of suspicion for signs of suicidal intent, depression and other psychiatric complaints throughout the 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

Complementary treatments
6.1 Psychosocial interventions

Psychosocial interventions are most effective when used in combination with methadone. Retention in treatment is the most important factor in achieving effective outcomes of psychosocial interventions. Patients are more likely to participate in and continue with psychosocial interventions if they enjoy them. For this reason, they should be encouraged to engage in a number of psychosocial treatments over time in order to discover those that are appropriate to their needs.

6.1.1 Contingency management

Contingency management is a method used to change behaviour by rewarding desirable behaviour. In some techniques, undesirable behaviour leads to negative consequences. In essence, contingency management is a structured system of boundaries agreed upon by patients and the treatment team prior to the initiation of treatment. It can be administered by any staff with relatively little training. The major elements of contingency management are as follows:

- Clear definitions of desirable behaviours, such as abstinence from opioids
- Regular monitoring for the presence or absence of the desired behaviour, for example, looking for evidence of fresh injecting sites
- Specified rewards, such as money, vouchers, take-home methadone doses and lottery tickets, for desired behaviour
- Positive personal feedback from the staff on the desired behaviour.

Contingency management can be related to any desirable behaviour that has specific outcomes with a potential for reward.

6.1.2 Cognitive–behavioural therapy (CBT)

Cognitive–behavioural therapy (CBT) should be administered by trained clinical psychologists. In the case of opioid dependence, CBT focuses on the notion that behaviours are a function of beliefs. For example, substance dependence is a learned behaviour capable of being modified through the correction of distorted belief patterns. The “cognitive” component of CBT aims to change distorted, negative thinking styles and rationales for substance use. It follows that once a patient has “reprogrammed” their thinking on drug use, they will make better decisions on the use of drugs, resulting in reduced levels of use and harm. An example is being able to identify, and hence avoid, high-risk situations which might lead to relapse. The “behavioural” component of CBT aims to reinforce positive behaviour associated with good outcomes. Contingency management is an example.
6.1.3 Brief motivational interviewing

Motivational interviewing (MI) was used primarily to treat tobacco smokers but is now applied to amphetamine-type stimulants (ATS) users. Its underlying assumptions are that people change their thinking and behaviour in a series of identifiable stages, and it is possible to influence the natural change process with MI. The key components of MI include establishing a “therapeutic alliance”, showing empathy, providing feedback, helping the client to reframe their behaviour and thus reinforcing change. The five basic stages of change are the pre-contemplation, contemplation, determination, action and maintenance stages.

6.1.4 Brief interventions

Brief interventions should always be a part of therapy. Brief interventions can cover any topic of relevance and importance to the patient, and are best carried out in the context of a strong, respectful professional relationship. There are a number of different schemata for brief interventions. One example is FRAMES (an acronym), which applies to substance use.

<table>
<thead>
<tr>
<th>Feedback</th>
<th>Personal feedback on the risks associated with continued substance use, based on the current pattern of use, problem indicators and health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsibility</td>
<td>Emphasis on the individual’s personal responsibility and choice to reduce or seek treatment for substance use</td>
</tr>
<tr>
<td>Advice</td>
<td>Clear advice on the importance of changing current substance use patterns</td>
</tr>
<tr>
<td>Menu</td>
<td>A menu of alternative change options. This emphasizes the individual’s choice and allows them to choose the approach best suited to their own situation.</td>
</tr>
<tr>
<td>Empathy</td>
<td>The expression of empathy by the person providing the intervention is an important determinant of how far the patient will feel motivated and change. A warm, reflective and understanding brief intervention is more effective than an aggressive, confrontational or coercive one.</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>This component involves instilling optimism in the patient that their chosen goals can be achieved. It is in this step, in particular, that motivation-enhancing techniques are used to encourage patients to change.</td>
</tr>
</tbody>
</table>

6.1.5 Peer programmes

Peers are well accepted by other peers within the drug-using community. For this reason, peer programmes, including peer education and peer group work, can be helpful in building strong relationships with opioid-dependent individuals. Peer education officers may not have formal health qualifications and thus not too expensive for a clinic to employ them. Peer programmes are based on the concept that individuals who have good interpersonal skills, and who are interested in health-related learning, can be trained to provide information and education to their drug-using counterparts. Training is generally given in a step-wise manner and knowledge is built over time.

The role of a peer educator is:

- To develop relationships with drug users in the community
- To provide information on health to drug users in the community
• To provide information on and facilitate access to harm reduction interventions
• To provide referrals and link drug users to local health services, such as the DTC.

To maintain a strong ethical framework, peer educators should:

• Provide accurate, unbiased information to drug users
• Provide drug users with information in a respectful, confidential manner
• Provide information which will help drug users maintain their health
• Maintain confidentiality, except with the treatment team.

Peer educators have the following limitations.

• Peer educators are not nurses or doctors and cannot be expected to know everything. They are not able to provide treatment.
• Drug use occurs at all hours and on all days of the year. Peer educators cannot be expected to work all hours as this may lead to burnout and diminished capacity.
• Inaccurate information can be counterproductive and sometimes dangerous. Therefore, peer educators should only give information relating to their specific areas of training.

If in doubt, peer educators should refer their patients to somebody more knowledgeable.

6.1.6 Self-help groups

These groups are voluntary, run by peers and generally small. The members meet regularly. Patients may find that self-help groups provide emotional support and may derive comfort from knowing that they are not alone in the struggle against opioid dependence. One of the roles of peer educators may be to help a self-help group.
Section-7

Managing patients with special needs
Managing patients with special needs

7.1 HIV and opioid dependence

The sharing of injecting equipment is a common mode of HIV transmission across Myanmar. All people who inject drugs should be provided, where possible, with access to new, sterile injecting equipment. It is a key function of peer educators, outreach workers and others agencies to provide people who inject with information on harm reduction and other methods of reducing the risk of acquiring HIV. Similarly, HIV-positive individuals should be counselled on the importance of using their own injecting equipment and ensuring its safe disposal.

7.1.1 Offering HIV testing and counselling to persons with opioid dependence

HIV testing and counselling should be offered to all patients with opioid dependence, as they are at high risk for acquiring the virus. The normal clinical activity of prescribers and the drug treatment team should include developing a relationship with the local HIV testing and counselling service to facilitate easy referral. Patients with a positive HIV status should be given priority access to methadone treatment, where it is appropriate. If illness or behavioural problems complicate the management of the patient, they may be referred to a specialist DTC or a respiratory or infectious disease unit, or advice may be sought from these specialists.

7.1.2 Stabilizing opioid-dependent persons on methadone before initiating antiretroviral therapy

Optimal HIV treatment is dependent on strict adherence to antiretroviral therapy (ART). Adherence to ART among populations using drugs can be improved by first stabilizing such patients on OST for the treatment of opioid dependence. The stabilization period before the initiation of ART may be around two months, although there is little evidence to support a fixed period of stabilization.

7.1.3 Counselling patients regarding interactions between methadone and antiretroviral (ARV)

Methadone interacts with a number of ARV medications and may reduce the effectiveness of some of them, while increasing the side-effects of others. On the other hand, ARV medications can alter the level of methadone in the blood, so careful monitoring of symptoms is required during the commencement of ART in patients on methadone. Dose adjustments may be necessary. A table on the interactions between ARV medications and methadone is given in Appendix 3.
7.2 Tuberculosis and opioid dependence: screening opioid-dependent persons for TB

TB is not uncommon among drug users because of the low socioeconomic status, and poor general health and nutrition of many opioid-dependent patients. Many drug users are also HIV-positive, which further compromises their nutritional and health status.

7.2.1 Stabilizing opioid-dependent persons on methadone to improve adherence to anti-TB medication

Patients with opioid dependence may adhere better to the complex anti-tuberculosis treatment (ATT) regimen once their drug use has been stabilized with methadone. This also helps to improve retention in treatment. Patients taking supervised or directly observed OST and needing treatment for TB should be supported with both medicines.

7.2.2 Counselling patients on interactions between methadone and anti-TB medication

Several medications used for the treatment of TB, in particular rifampicin, can interact with methadone. For a full discussion of these interactions see Appendix 3. To know more about the prevention, treatment and care of TB in people who inject drugs, refer to other guidance documents.12

7.3 Managing pain during methadone therapy

7.3.1 Management of patients with acute pain

Patients suffering from acute pain during methadone therapy should be treated with simple non-opioid analgesics, such as paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs (NSAIDs), especially when there is an inflammatory component to the pain. A short-acting opioid analgesic is often required concurrently. The management of severe acute pain in patients who are on methadone and require hospitalization should be similar to that of other patients (i.e. by using parenteral opioids), except that higher doses of the treating opioid may often be required due to opioid tolerance. Where possible, the methadone dose should be continued during the hospital stay, with additional opioid analgesics if necessary.

7.3.2 Management of patients with chronic pain

The use of methadone (or another long-acting opioid) is preferable to the drug buprenorphine, when treating chronic pain as it has greater analgesic properties. When a patient is suffering from chronic pain, the origin of the pain should be clinically investigated prior to treatment with methadone. Referral to a specialist in the DTC is recommended, and a second opinion may be sought if the management plan is not clear. Patients who have been stabilized on methadone and experience acute severe pain may require opioid doses that are higher than normal to overcome tolerance. In some cases, they may also require a temporary increase in their methadone dose. It may be worthwhile to discuss such cases with an experienced drug treatment specialist at a major DTC because these treatment situations are frequently difficult to handle. Patients suffering from chronic pain often have significant psychosocial and mental health problems, which should be managed during treatment. Depression, in particular, is common. Such patients can be co-managed by the prescriber and a clinical specialist from the DTC.
7.4 Management of patients with co-existing mental health problems

People who inject drugs and those who are opioid-dependent commonly have psychiatric comorbidities, which need to be managed. It is often difficult to tell whether there is a causal relationship between substance use and mental health problems. Such patients may need to be referred to a psychiatrist or a health professional with a mental health background.

7.4.1 Depression and anxiety in persons with opioid dependence

Depression is a common mental health problem, affecting 20% or more of the population at some point during their lifetime. It is more prevalent among people who use drugs and is the most common comorbid psychiatric disorder among such people. Anxiety is also a widespread problem and is often associated with substance use. Anxiety may be related to withdrawal symptoms and may subside with OST. Depression can be more difficult to manage. Patients diagnosed with depression should be treated pharmacologically where possible (most antidepressants are off-patent and are becoming increasingly accessible). The pharmacological treatment of depression takes around two to six weeks to have an initial impact. The treatment should be continued for at least six months in the case of a first episode of depression.

7.4.2 Management of depression

Recognizing depression and treating it effectively has a considerable impact. The clinical features of depression include depressed or sad mood, crying, irritability, low self-esteem, guilt or pessimism, suicidal ideation, difficulty in concentrating or forgetfulness, lack of interest in pleasurable activities, lack of energy, sleep disturbance, appetite disturbance and agitation.

Risk assessment and management

The most important aspect of depression is the risk of suicide. It is important to assess this risk in all patients presenting with depressive symptoms. People who use drugs, particularly those with comorbid depressive disorders, have a higher risk of suicide.
Assessment of suicidal risk

1. What is the current degree of suicidal ideation?
   a. Actively suicidal (any plans?)
   b. Ambivalent about suicide
   c. Passively suicidal
   d. No ideation

2. Previous attempts at suicide
   a. Number of previous attempts
   b. Those that required medical intervention

3. What is the psychiatric status?
   a. Is the person psychotic?
   b. Is there drug or alcohol dependence?

4. What is the level of social support?

5. What are the other risk factors (older, male, living alone, unemployed)?

Depressive patients who are suicidal may be helped by hospitalization and specialist care, including the prescription of antidepressants. It is extremely important to be vigilant, and the patient’s family members have to be educated and counselled on the suicidal behaviour of the patient.

Pharmacotherapy for major depressive disorder

Antidepressants are the first choice for moderate-to-severe depressive disorder. For those who experience additional psychotic symptoms, the addition of second-generation antipsychotics may be considered.

**Antidepressants**

*Tricyclic antidepressants:* imipramine, amitriptyline, dothiepin, trazodone  
*Selective serotonin reuptake inhibitors (SSRIs)*: fluoxetine, sertraline, citalopram, escitalopram, paroxetine  
*Serotonin norepinephrine reuptake inhibitors (SNRIs)*: venlafaxine

7.4.3 Management of anxiety

Persistent anxiety is manifested as fear of unknown origin, a feeling of tremulousness, palpitation, racing of the heart and profuse sweating (evident on a handshake with an anxious
The duration of anxiety may vary depending on the cause. The common causes of persistent anxiety among people who use drugs are alcohol withdrawal, benzodiazepine withdrawal and generalized anxiety disorder. The frequent causes of acute anxiety attacks are panic disorder, substance-induced panic episodes, hypoglycaemia and hyperventilation.

Distress and the risk of suicide secondary to anxiety can be greatly alleviated with sedation, administered orally (diazepam 5-10 mg or lorazepam 1-2 mg) or intramuscularly (lorazepam 1-2 mg).

The diagnostic features of generalized anxiety disorder include restlessness or nervousness, fatigue, difficulty in concentrating, irritability, tension, trembling, sweating, palpitations, dizziness, sleep disturbance and discomfort in the abdomen.

**Treatment**

- Relaxation techniques (e.g. Jacobson muscle relaxation technique)
- Supportive psychotherapy (reassurance, explanation, expert advice, suggestions, guidance, ventilation, support and facilitating emotional support from key people)
- Pharmacotherapy

SSRIs are effective in controlling the symptoms and should be used as the first line of therapy.

The other treatments include mirtazapine, venlafaxine, beta blockers (useful for somatic symptoms, particularly tachycardia), imipramine, and clomipramine.

Benzodiazepines are prescribed only for a short period of time. It is better to avoid their use in the treatment of generalized anxiety disorder, as they should not be used to alleviate symptoms caused by the minor stresses of everyday life. Alcohol and CNS depressants potentiate the effects of benzodiazepines. Driving should be avoided. Educating the patient is critical to the effective management of generalized anxiety disorder.

### 7.5 Psychotic episodes due to drug use

Psychosis can be primary or associated with the use of drugs. It can be induced by amphetamine-type stimulants (ATS), other substances or alcohol, among other things, or it can be a result of several disorders, such as acute psychotic disorder, schizophrenia, bipolar disorder, depression, delirium and head injury. ATS are the most common psychoactive substances that induce psychosis. It has been estimated that the prevalence of psychosis is 11 times higher among regular ATS users than among the general population, and that 23% of regular ATS users will experience symptoms of psychosis within a given year.

Opioids generally have an antipsychotic effect. Opioid-dependent patients who have had psychotic episodes should be formally evaluated to exclude drug use as a cause of the psychosis. Normally, medication is not required to resolve drug-induced psychosis. Patients who have psychosis and who do not have a recent history of the use of stimulants or hallucinogens may have a primary psychosis, such as schizophrenia. Primary psychoses are difficult to manage and the patient should be referred to a mental health-specific service.
7.6 Opioid dependence and pregnancy

The demographics of opioid dependence show that opioid-dependent females tend to be in the fertile years, which means that pregnancy is not uncommon among female patients. All attempts should be made to engage women in the early stages of pregnancy and retain them in treatment to optimize antenatal care. This includes screening for other substance use and mental health issues, as well as for blood-borne viruses. Folate supplementation and psychosocial support should also be provided. Opioid withdrawal is generally not recommended during pregnancy as it results in poorer pregnancy outcomes. Where possible, substitution therapy using methadone should be recommended for pregnant women as it is associated with the most favourable outcomes. As pregnancies in this population are not planned in most cases, advice on family planning and birth control, including effective contraception, needs to be offered to women seeking treatment for opioid dependence.

In general, methadone treatment for pregnant women should consist of the following.

- Stabilize the patient on an appropriate dose that is sufficient to cease the use of illicit drugs.
- Maintain the patient at a level which is comfortable for her and which avoids drug withdrawal during pregnancy. Do not encourage a reduction of the dose.
- Reassess the dose in the days immediately following delivery to avoid oversedation. Keep the patient on the maintenance dose for a minimum of two to three months postpartum before reducing the dose.
- Consider the need to address other substance abuse problems (smoking, alcohol, benzodiazepines) that have adverse effects on pregnancy outcomes.

7.6.1 Increasing methadone dose during and after pregnancy

As pregnancy proceeds and fluid retention increases the volume of distribution, the dose of methadone may need to be increased. Generally, there are two phases: during the first trimester, when the effects of hormonal changes and fluid dilution are the greatest, and during the last trimester, when the sheer bulk of body mass and the foetal liver contribute to rapid metabolism. For this reason, and due to other metabolic changes, the dose of methadone may have to be increased by 5 mg to 10 mg or occasionally, by more in the latter half of pregnancy. The need for split-dosing (twice daily) is still relatively rare even in late pregnancy, but such dosing may be required in some cases. The situation is assessed by considering whether the patient is experiencing withdrawal symptoms and over-sedation symptoms in the same 24-hour period (for further information on split dosing, see Section 5).

The dose may need to be reduced postpartum. The dose is decreased after delivery in response to maternal sedation, if it occurs (one should anticipate it and observe the patient for it). The dose will need to be reduced by 5 mg to 10 mg (depending on how much the dose was increased). If there is pain (e.g. after a caesarean section) or severe emotional distress, the dose should be reduced less aggressively. If the methadone dose is reduced in the absence of opiate-induced sedation, the resulting opiate withdrawal can induce severe insomnia, exacerbation of the depression or a return to opioid use. If the methadone dose is not reduced after delivery (because there were no signs of sedation), the reduction in dose should be delayed until some months after birth and till the healthy routines of breastfeeding and infant sleeping patterns have been established.
7.7 Neonatal abstinence syndrome

Neonatal abstinence syndrome (NAS) is an opioid withdrawal syndrome commonly experienced by the newborn following birth when the mother is opioid-dependent. Withdrawal generally commences within 48 hours of delivery, though it may be delayed in cases of poly-substance dependence, particularly that involving other sedatives such as benzodiazepines. Not all newborns suffer from NAS and although NAS is more likely to develop in the infants of mothers with a higher level of opioid dependence, this is not necessarily the case. When possible, infants should be kept with their mothers to encourage breastfeeding.
Section-8

General information on related issues
8.1 Abuse of prescription drugs

Abuse of prescription drugs is widespread among people who inject drugs. The psychoactive drugs preferred include the benzodiazepines and prescription opiates, such as tramadol, codeine and pentazocine. The doses in which the drugs are taken often far exceed those required for normal therapeutic use.

8.2 Legal responsibilities

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

Prescription and supply of controlled drugs

- Prescribing doctors should take all reasonable steps to ascertain that there is a need for the therapeutic use of a controlled drug, and then prescribe/supply it only for the medical treatment of a patient under their care.
- Before prescribing 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 the full details of the prescriber, the patient and the drug, as well as the quantity prescribed and the maximum number of repeats doses (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 that the name of the drug and the dose are handwritten and provided that they are signed).
- In an emergency, a doctor may contact doctors at the local DTC for the supply of controlled drugs.
- When doctors supply 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 with the DoH as being drug-dependent.
- 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).

**Other matters to be notified**

- The police and DoH must be notified if any controlled drugs or a register on a drug-dependent patient is lost.
- If there is a suspicion that a person has obtained a controlled drug (or a prescription for one) by fraud, 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.
- The 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, records of transactions involving controlled drugs must be such that they can be readily sorted by drug. Further, they must show a true and accurate stock of each drug.

### 8.3 Confidentiality

Confidentiality is of paramount importance in the provision of good clinical care. It can also increase the rate of retention in treatment. Clinical information should be provided to others only with the patient’s written consent. Special care must be taken to prevent access to clinical or other records which may reveal that the patient is being treated with methadone.

### 8.4 Driving while on methadone

Patients should be counselled on the risk of driving while on opioids. Opioids are sedating and may impair the patient’s ability to perform complex tasks, particularly when the dose level peaks, e.g. two hours after taking the methadone dose. Particular care should be taken when OST is initiated or the dose of the opioid is changed. The impairment may be more severe in the case of patients engaging in poly-substance use involving other sedatives. 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 patients are stabilized on treatment, their ability to perform complex tasks such as driving is unlikely to be impaired (provided their dose has not been increased recently). For those on methadone who are well controlled, it is recommended that they may drive if they are stable and under regular review. However, such patients need to be warned about the effects of changes in dosage.
8.5 Forms

The Drug Treatment Service uses a number of forms for recording standardized data, reporting and monitoring the programme.

**Forms for Treatment of Opiate-Dependent Patients with Methadone Solution**

- Registration of a drug user for methadone program and patient’s identification card is completed and endorsed “Methadone Treatment” for the patient to carry.
- Patient’s prescription book for clinician
- All DTC sites must complete the standardized “methadone treatment programme monthly report” form to provide an up-to-date record of the number of patients actively engaged in treatment and their doses to the Yangon DTC national drug abuse control unit and DoH.
- Register on patients utilizing methadone to record daily data on attendance, absences, drop-outs, take-away doses, transfers out, transfers in, therapy completed and total methadone consumed per day. (Cumulatively to record)
- Methadone dispensing patients record book for individual patients.
- Main and sub-stock register book for methadone received, issued and balance
- Patients transfer form for temporary and permanently outpatients.

It is recommended that patients be given certain essential information on methadone during the provision of normal clinical services. The documents which contain such information are:

- Manual for Methadone Maintenance Therapy Patient [Myanmar version]
- Flip chart and pamphlet containing the necessary information on introducing methadone.

8.6 Record-keeping

The patient’s prescription book should be adequately maintained and legible to another clinician who may be involved in the care of the patient. A patient’s records are confidential and should be stored with care. They are generally stored for a number of years after the patient has been discharged from care. Electronic systems for maintaining patients’ records are emerging as an alternative to paper-based systems; however, these require substantially greater resources and are, therefore, available only in major centres, if at all.
Section-9

Methadone maintenance therapy guidelines for dispensers
9.1 Background

The ongoing HIV epidemic among people who inject drugs has prompted Myanmar to adopt a harm reduction comprehensive package of interventions and address the health needs of those that consume drugs. One of the essential HIV interventions is the use of methadone to reduce or limit the use of illicit opioids. The availability and accessibility of methadone has resulted in a decrease in the high-risk practice of needle-sharing. Treatment with methadone is associated with certain risks, but there are countermeasures that can be taken to minimize these risks (see Section 1). To better understand the clinical pharmacology and toxicology of methadone, see Sections 2 and 5.5.1.

Key factors in dispensing methadone

- correctly identify the patient before dosing.
- Ensure that the dose is authorized by the prescriber.
- Confirm whether it is safe to administer the dose.
- Supervise the dosing.
- Communicate with the prescriber regarding any irregularities in the patient’s attendance.
- Maintain proper records.

Right person - right drug - right dose - right time - write down!

9.2 Setting up the methadone programme: getting approval

It is recommended that the participating nurses, medical staff and dispensers be provided with training and education. A person may be granted approval as a methadone dispenser by the consultant at the DTC after he/she has received appropriate training. If a dispensing site is not open seven days a 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).
9.3 Development of procedures

The methadone programme may be implemented in a number of ways, and all dispensers employed in the dispensary should have access to accurate information about the programme.

Certification for dispenser

It is strongly recommended that all dispensers employed in the clinic, dispensary or pharmacy be required to complete training and receive certification to confirm that they are familiar with the guidelines on the methadone programme and the principles of methadone administration. Signed certification documents should be kept in a designated file, and a copy should be readily available to all dispensers for reference.

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: .............................................

Certificate

Methadone Maintenance Therapy Programme
Myanmar (Date……………..)

This is to certify that Dr/ U/ Daw ................................ has successfully participated in the training on methadone maintenance therapy treatment guidelines as prescriber / dispenser in ........ (site), Division from ........ (date to date).

Methadone training is organized by the National Drug Control Programme.

Signature

Training of dispensers

It is strongly recommended that all dispensers employed in the dispensary be encouraged to complete the education and training course on methadone maintenance therapy treatment.
9.4 Storage

Methadone is a controlled drug and according to the regulations, must be stored in a locked metal cabinet (or safe). The bottle in use should be kept in a secure location and replaced in the locked cabinet when it is not being used. Methadone solution has a shelf-life of 12 months and does not require refrigeration.

9.5 Patient’s records

- A separate patient’s record should be maintained for each patient. It should include the name and date of birth of the patient (or another identifier to differentiate between patients who have identical names); a photograph of the patient (firmly attached inside the front cover of the record book); the current prescription (firmly attached inside the back cover); and the dosage, which may also be written in words to reduce the chances of error.
- A patient’s record should not be visible to other patients.
- The patient’s record should mention the dates between which the prescription is valid.
- All prescriptions should be written in milligrams (mg) to avoid confusion in dosing where methadone is mixed at variable concentrations.
- There should be a record of each dose dispensed, signed by the dispenser and patient.
- The patient’s record should have space for ancillary notes on adverse events or situations.

Each dispenser should have access to all the relevant details of patient, including details of communications with the prescriber, variations in dosage and the authorization of take-away doses. It is recommended that such details be recorded in a permanent, readily retrievable and consistent manner, and that they should not be readily accessible to patients; for example, they could be recorded in chronological order on a separate page of the patient’s book (see Appendix 6).

9.6 Records of administration

In addition to patients’ records, a dispensary must maintain an accurate record of each dose administered to each patient. These records may be computerized or manually prepared. It is the volume of methadone solution (expressed in millilitres) that is commonly recorded, but the records should also clearly mention the dose of methadone (expressed in milligrams) so that there is no scope for misinterpretation. For a methadone dispenser, it is necessary to record the remaining stock on at least a daily basis. The records of administration may be in a form that enables the daily reconciliation to be carried out there in or within the Daily Attendance Register. (see Appendix 7). Records must show the actual balance of stock, not merely a calculated balance, and both these should be reconciled on a regular basis.

9.7 Accepting new patients

When accepting a new patient, contact should be made with the prescriber to ascertain whether the patient is new to the methadone programme or is merely transferring from another dosing point. Special management issues apply in each case. To ensure that potential
patients are fully aware of the structure and requirements of the methadone programme, they may be interviewed before being accepted as methadone patients. A new patient should be carrying their drug user registration card, marked “Methadone Programme”, 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.

9.8 Prescriptions

Patients should not be administered doses without a valid prescription. In emergencies, a verbal order from the prescriber may be necessary, with a valid prescription being forwarded as soon as possible. Similarly, there should be no increase in the dose administered unless the prescriber has provided an original written authorization (prescription). In an emergency, a verbal communication of instructions by the prescriber is sufficient for increasing the dose. Following this, a confirmation should be faxed and the original prescription forwarded as soon as possible.

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. The expiry date should be recorded clearly on the cover and/or-appropriate page of the patient’s book, for example, or reminder notes should be provided to patients to alert them to the impending expiry date. Expired prescriptions should be retained for three years, and should be filed in a secure manner which precludes the possibility of confusing these prescriptions with the current prescription (for example, in a separate file or a pocket in the patient’s book).

9.9 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 the use of a syringe or displacement pump is recommended. It is recommended that the methadone dose be prepared during the patient’s visit. Some dispensaries transfer the methadone syrup to another container (e.g. a bottle with a displacement pump) and some dilute the syrup to create a consistent strength (e.g. 5 milligram or 10 milligram per 1 milliliter). In such instances, the container should be clearly labelled to indicate the concentration of the methadone syrup being used, so as to prevent the administration of an incorrect (under or over) dose.

9.9.1 Administration of doses

Supervised doses should always be directly observed to prevent diversion.

The patient should be engaged in conversation to ensure that they have consumed the dose.

Dispensing areas should be discrete to avoid stigma and ensure confidentiality.

Methadone should be consumed in full view of the dispenser. There should be no remaining methadone visible in the patient’s mouth. It is recommended that methadone doses be administered in disposable containers. Alternatively, the dispensary should have some appropriate means of sterilizing glass or similar vessels used for administering doses. The aim is to ensure a satisfactory standard of hygiene. The patient should be observed for signs of toxicity from methadone or other drugs (Section 2), and dosing must be delayed if they appear intoxicated (Section 5.5.2).
9.10 Patients who are new to the methadone programme

During the initial period of stabilization, there is a significantly greater risk of toxicity/overdose due to a lack of recognition of the long half-life of methadone and the possibility of concurrent poly-drug use. The dispenser must make sure that the patient has been appropriately informed about these risks.

For further information on patients who are new to treatment, induction into treatment and the risks, see Sections 5.1 and 5.5.

9.11 Take-away doses

Only the prescriber may authorize take-away (take-home) doses. Such doses should be authorized in writing and the details of the authorization must be recorded in a prominent place (for example, in the patient’s book).

To deter injecting or consuming take-away doses (especially by a child), the take-away dose should be diluted with fruit juice or other particulate matter (for example, cordial) to a volume of 20 millilitres, and supplied in a container with a child-resistant closure. A container with a take-away dose should be labelled with the patient’s name, the name of the drug and the date on which the dose is to be consumed. See the example below.

<table>
<thead>
<tr>
<th>Methadone Liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>This bottle contains a single daily dose of methadone to be taken on 15 January 2012 by Maung ABC (patient)</td>
</tr>
<tr>
<td>Dispensary details……………………</td>
</tr>
<tr>
<td>Date of supply ………………..</td>
</tr>
</tbody>
</table>

Also, the following warnings must be attached 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 the reach of children.’
- ‘May cause death or serious injury if taken by another person.’

The details of take-away doses should be clearly recorded in the patient’s dispensing book and the prescription book. Patients should be advised to store their take-away doses in a secure place that is out of the reach of children and other drug users. If a person claims that their take-away dose has been lost or stolen, the dose cannot be replaced without the prescriber’s written authorization. For further details on the guidelines for prescribers and the schedule for the authorization of take-away doses, see Section 5.9.

9.12 Transferred patients

When patients are transferred from another dispensing site, the dispensers should confirm the time of dosing, type of medication and quantity of the last dose. The confirmation should be written or verbal with follow-up written (faxed) information (Appendix 10). This approach minimizes the risk of the patient being administered doses at two different sites on the same day, and thus reduces the risk of overdose.
When accepting a patient who has previously received a dose at another location, one must confirm the date and the amount of the final dose administered at the transferring dispensary. It should also be confirmed whether the patient has received any take-away dose. This is necessary to reduce errors in dosing. Transfer from one dispensing site to another 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 received a dose for more than three days and their tolerance for opioids would be reduced, putting them at a risk of potentially dangerous opioid toxicity if they are administered the regular dose.

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

For further information on transfers, see 5.10.

### 9.13 Temporary absences

Some patients might be admitted to hospital, taken into police custody or temporarily transferred to another dosing point. In such cases, there may be a dispenser to whom the patient is transferred. The dispenser should inform the prescriber and mark as transfer out temporarily [T/OT] and calculated as one patient at the end of the month.

### 9.14 Irregular attendance

Regular attendance by the patient makes for less fluctuation in the levels of methadone and greater stability of the patient. Irregular attendance may be indicative of the ongoing use of illicit drugs, or it could point to the possibility that the patient needs counselling or review.

It may not be significant if the patient misses merely one dose, but the prescriber must be informed when a client attends the dispensary irregularly for methadone doses.

### 9.15 Missed doses

For further information on missed doses, see Section 5.12.3.

### 9.16 Possible intoxication

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

*The 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 DTC.

*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 go to a hospital (severe intoxication)
- Administer a reduced or placebo dose (when the patient refuses to accept advice).

It must be remembered that though a prescription represents authorization to administer the drug, professional judgement must be exercised with respect to the appropriateness of dosing. Caution should be exercised in situations in which there are doubts regarding safety or there appears to be a risk of overdose. The dispenser has the final word and must administer an authorized dose only if it is safe to do so.
Appendices
# Clinical Opiate Withdrawal Scale (COWS)

## Flow-sheet for measuring symptoms over a period of time during methadone induction

For each item, write the number that best describes the patient’s signs or symptoms. Rate only those with an apparent relationship to opiate withdrawal. (For example, if the heart rate is increased because the patient was jogging just before assessment, the increased pulse rate would not add to the score.)

<table>
<thead>
<tr>
<th>Patient’s name: ___________________________</th>
<th>Date: __________</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone induction:</td>
<td></td>
</tr>
<tr>
<td>Enter scores at time zero, 30 minutes after the first dose, 2 hours after the first dose, etc.</td>
<td></td>
</tr>
<tr>
<td>Times</td>
<td></td>
</tr>
</tbody>
</table>

### 1. Resting pulse rate (record beats per minute)

*Measured after patient is sitting or lying for one minute*

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>pulse rate 80 or below</td>
</tr>
<tr>
<td>1</td>
<td>pulse rate 81–100</td>
</tr>
<tr>
<td>2</td>
<td>pulse rate 101–120</td>
</tr>
<tr>
<td>4</td>
<td>pulse rate greater than 120</td>
</tr>
</tbody>
</table>

### 2. Sweating

*(Over past ½ hour not accounted for by room temperature or patient activity)*

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no report of chills or flushing</td>
</tr>
<tr>
<td>1</td>
<td>subjective report of chills or flushing</td>
</tr>
<tr>
<td>2</td>
<td>flushed or observable moistness on face</td>
</tr>
<tr>
<td>3</td>
<td>beads of sweat on brow or face</td>
</tr>
<tr>
<td>4</td>
<td>sweat streaming off face</td>
</tr>
</tbody>
</table>

### 3. Restlessness

*(Observation during assessment)*

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>able to sit still</td>
</tr>
<tr>
<td>1</td>
<td>reports difficulty sitting still, but is able to do so</td>
</tr>
<tr>
<td>3</td>
<td>frequent shifting or extraneous movements of legs/arms</td>
</tr>
<tr>
<td>5</td>
<td>unable to sit still for more than a few seconds</td>
</tr>
</tbody>
</table>
4. Pupil size
0: Pinpoint pupils or normal size pupils for room light
1: pupils possibly larger than normal for room light
2: pupils moderately dilated
5: pupils so dilated that only the rim of the iris is visible

5. Bone or joint aches
*(If the patient was having had pain previously, only the additional component attributed to opiate withdrawal is scored)*
0: not present
1: mild, diffuse discomfort
2: patient reports severe, diffuse aching of joints/muscles
4: patient is rubbing joints or muscles and is unable to sit still because of discomfort

6. Runny nose or tearing
*(Not accounted for by cold symptoms or allergies)*
0: not present
1: nasal stuffiness or unusually moist eyes
2: nose running or tearing
4: nose running constantly or tears streaming down cheeks

7. GI upset
*(Over past ½ hour)*
0: no GI symptoms
1: stomach cramps
2: nausea or loose stool
3: vomiting or diarrhoea
5: multiple episodes of diarrhoea or vomiting

8. Tremor
*(Observation of outstretched hands)*
0: no tremor
1: tremor can be felt, but not observed
2: slight tremor observable
4: gross tremor or muscle twitching

9. Yawning
*(Observation during assessment)*
0: no yawning
1: yawning once or twice during assessment
2: yawning three or more times during assessment
4: yawning several times/minute
### 10. Anxiety or irritability

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>none</td>
</tr>
<tr>
<td>1</td>
<td>patient reports increasing irritability or anxiousness</td>
</tr>
<tr>
<td>2</td>
<td>patient obviously irritable or anxious</td>
</tr>
<tr>
<td>4</td>
<td>patient so irritable or anxious that participation in the assessment is difficult</td>
</tr>
</tbody>
</table>

### 11. Gooseflesh skin

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>skin is smooth</td>
</tr>
<tr>
<td>3</td>
<td>piloerection of skin can be felt or hair on arms standing on end</td>
</tr>
<tr>
<td>5</td>
<td>prominent piloerection</td>
</tr>
</tbody>
</table>

**Total scores with observer’s initials**

Score:

- 5-12 = mild
- 13-24 = moderate
- 25-36 = moderately severe
- More than 36 = severe withdrawal
# Appendix 2

## Features of a methadone prescription

### Patient's prescription book

<table>
<thead>
<tr>
<th>Drug treatment centre</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of the patient</td>
<td></td>
</tr>
<tr>
<td>Date of birth</td>
<td></td>
</tr>
<tr>
<td>National registration number</td>
<td></td>
</tr>
<tr>
<td>Narcotic registration number</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical records</th>
<th>Drug treatment centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Name of the patient</td>
<td></td>
</tr>
<tr>
<td>Methadone solution</td>
<td>5 or 10 mg/ml</td>
</tr>
<tr>
<td>Dispense mg</td>
<td>(in words)</td>
</tr>
<tr>
<td>From</td>
<td>(start date)</td>
</tr>
<tr>
<td>To</td>
<td>(end date)</td>
</tr>
<tr>
<td>At</td>
<td>dispensary</td>
</tr>
</tbody>
</table>

Prescriber’s signature
Appendix 3

Interactions between opioid substitution therapy and commonly used medications

Interactions between methadone and commonly used medications for HIV and TB generally occur as a result of an alteration in the metabolism of the opioid substitution therapy (OST) by the hepatic cytochrome p450 system. ART–OST interactions may result in symptoms of withdrawal or over-sedation, requiring an adjustment in the dose. The effect of methadone on some ARVs may result in reduced viral suppression or an increase in side-effects. Patients on ART should be monitored when commenced on methadone, or when the ART regimen is changed. Further information on the management of HIV among people who inject drugs can be found in various guidance documents.14–16

A.3.1 Interactions between ARVs and methadone15

<table>
<thead>
<tr>
<th>ARV</th>
<th>Effect of ARV on methadone</th>
<th>Effect of methadone on ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside reverse transcriptase inhibitors (NRTIs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>None reported; no dosage adjustment necessary</td>
<td>Concentrations increased (43%); clinical significance unclear; adverse events possible</td>
<td>Monitor for adverse events of AZT; monitor for anaemia, neutropenia, nausea, myalgia, vomiting and headache</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>None reported</td>
<td>None reported</td>
<td>No known interactions</td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>Not studied</td>
<td>Not studied</td>
<td>No known interactions</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>None reported</td>
<td>May reduce d4T levels by 27%</td>
<td>No dose adjustment usually required</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate (TDF)</td>
<td>None reported; no dosage adjustments necessary</td>
<td>None reported; concentration decreased (18%–27%)</td>
<td>No known interactions; no dose adjustment of d4T required</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>Slight decrease in methadone level; risk of opioid withdrawal low; dosage adjustments unlikely, but some patients might require increase in methadone dose</td>
<td>Concentration decreased by 34%</td>
<td>Risk of opioid withdrawal low; adjustment of methadone dose might be needed; no adjustment of ABC dose required</td>
</tr>
</tbody>
</table>
### ARV

<table>
<thead>
<tr>
<th>Drug (indication)</th>
<th>Effect of ARV on methadone</th>
<th>Effect of methadone on ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didanosine (ddI)</td>
<td>None reported; no dosage adjustments necessary</td>
<td>Concentration decreased by 60% with buffered tablet, but not with EC capsule</td>
<td>Avoid use of ddI buffered tablets; use EC capsule, if available</td>
</tr>
</tbody>
</table>

**Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**

<table>
<thead>
<tr>
<th>Drug (indication)</th>
<th>Effect of ARV on methadone</th>
<th>Effect of methadone on ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz (EFV)</td>
<td>Decrease in methadone level by up to 60%; symptoms of opioid withdrawal common</td>
<td>Unknown</td>
<td>Observe for symptoms of methadone withdrawal and increase dose as necessary</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>Decrease in methadone level by 46%; symptoms of opioid withdrawal common</td>
<td>None reported</td>
<td>Considerable increase (50%) in methadone dose usually required</td>
</tr>
</tbody>
</table>

**Protease inhibitors (PIs)**

<table>
<thead>
<tr>
<th>Drug (indication)</th>
<th>Effect of ARV on methadone</th>
<th>Effect of methadone on ARV</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>Decrease in methadone level by 26%-53%</td>
<td>None reported</td>
<td>May require increase in methadone dose</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>None reported</td>
<td>None reported</td>
<td>Studies limited, but monitor for need to increase methadone dose</td>
</tr>
</tbody>
</table>

### Interactions of methadone with other medications†

<table>
<thead>
<tr>
<th>Drug (indication)</th>
<th>Effect on methadone</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin (TB)</td>
<td>Decrease in methadone level by 33%-68%; may induce symptoms of opioid withdrawal</td>
<td>Increase in methadone dose required if withdrawal symptoms present</td>
</tr>
<tr>
<td>Sertraline (antidepressant)</td>
<td>Increase in methadone level by 26%</td>
<td>Associated with cardiac rhythm disturbances, exercise caution when using with methadone; no dose adjustment required</td>
</tr>
<tr>
<td>Carbamazepine and phenytoin (anticonvulsants)</td>
<td>Decrease in methadone levels; may cause symptoms of methadone withdrawal</td>
<td>Increase in methadone dose may be required; consider using sodium valproate as an alternative</td>
</tr>
<tr>
<td>Fluconazole (antifungal)</td>
<td>Increase in methadone level by 35%</td>
<td>Clinical significance Unknown</td>
</tr>
</tbody>
</table>


Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar
Appendix 4

Comparative tables of opioids

The following table gives approximate conversions between different opioid agonists.

### A.4.1 Opioid equivalence table

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose equivalent to 10 mg oral morphine&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Approximate duration of action (hours)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine&lt;sup&gt;c&lt;/sup&gt; (analgesic only)</td>
<td>65 mg oral</td>
<td>3-4</td>
</tr>
<tr>
<td>Dextropropoxyphene&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Unknown</td>
<td>4-6</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>30-50 μg IV/SC</td>
<td>0.5-1</td>
</tr>
<tr>
<td>Hydromorphone&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.5-0.7 mg SC/IM; 2-2.5 mg oral</td>
<td>2-4</td>
</tr>
<tr>
<td>Methadone (analgesic only)</td>
<td>10 mg SC/IM; 20 mg oral&lt;sup&gt;d&lt;/sup&gt;</td>
<td>8-24 (chronic dosing)</td>
</tr>
<tr>
<td>Methadone (chronic use in maintenance)</td>
<td>1 mg oral</td>
<td>8-24 (chronic dosing)</td>
</tr>
<tr>
<td>Morphine&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3-4 mg SC or IM</td>
<td>2-3; 12-24 (controlled release)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>5-7 mg oral</td>
<td>3-4; 12-24 (controlled release)</td>
</tr>
<tr>
<td>Pethidine&lt;sup&gt;c&lt;/sup&gt;</td>
<td>25-35 mg IM</td>
<td>2-3</td>
</tr>
<tr>
<td>Tramadol&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30-40 mg IM/IV; 50 mg oral</td>
<td>3-6</td>
</tr>
<tr>
<td><strong>Partial agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine (analgesic only)</td>
<td>0.3 mg sublingual</td>
<td>6-8&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Doses given are a guide only
<sup>b</sup>Duration of action depends on dose and route of administration
<sup>c</sup>Active metabolites which may prolong action
<sup>d</sup>Based on single-dose studies
<sup>e</sup>Duration of action is extended in higher doses used in OST

Adapted from *Australian medicines handbook, 2007*<sup>17</sup>
### Benzodiazepine comparative table

The following table gives approximate conversions between different benzodiazepines.

#### A.4.2 Benzodiazepine equivalence table

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equivalence of oral dose (mg)</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triazolam</td>
<td>0.25</td>
<td>Short</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.25</td>
<td>Long</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0.5</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>2</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>1</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Diazepam</td>
<td>5</td>
<td>Long</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>15</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Temazepam</td>
<td>10</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>15</td>
<td>Long</td>
</tr>
<tr>
<td>Zolpidem(^a)</td>
<td>0</td>
<td>Short</td>
</tr>
<tr>
<td>Zopiclone(^b)</td>
<td>7.5</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

\(^a\) Approximate
\(^b\) Zolpidem and zopiclone are not benzodiazepines but they act in a fashion similar to benzodiazepines.

Adapted from *Goodman and Gilman’s pharmacological basis of therapeutics, 2007; Micromedex® healthcare series, 2007*\(^{18,19}\)
Appendix 5

Patient’s identification card (ID)

Front

Ministry of Health
Department of Health
Methadone Client ID Card

Name…………………………………………………………
Father’s name………………………………………………
Date of birth………………………………………………
Card number………………………………………………
Address……………………………………………………

Back

Issue date ……………………………

Team Leader
(Methadone Dispensing Centre)

Remarks:
• Always bring this card when you visit the methadone dispensing centre.
• Do not pass on this card to another person.
• Inform the DTC when you lose your card so that a new card could be issued.
Appendix 6

Methadone dispensing record book for patient

Cover

<table>
<thead>
<tr>
<th>Drug treatment centre/dispensary</th>
<th>Patient’s name</th>
<th>Registration no.</th>
</tr>
</thead>
</table>

Inside

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Dose (mg)</th>
<th>Dose (ml)</th>
<th>Patient’s signature</th>
<th>Dispenser’s signature</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>
## Daily methadone utilization record register

<table>
<thead>
<tr>
<th>SR</th>
<th>Name</th>
<th>Reg : No</th>
<th>Age</th>
<th>Old / new</th>
<th>Date:</th>
<th>Remark</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10–19</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
<th>24</th>
<th>25</th>
<th>26</th>
<th>27</th>
<th>28</th>
<th>29</th>
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</tr>
</tbody>
</table>

In order to fit the format in one page, dates 10 -19 have been merged.

- Total methadone consumed
- Total patients
- Absent
- Drop-outs
- Transfers out
Guideline instructions for data entry

This is for DAILY methadone taking record and total clients attending dispensary, the total amount of methadone oral solution consumed, number of absence cases, number of take-away patients, transfer out, transfer in, referrals, arrested, drop out etc. This can be checked at any time.

<table>
<thead>
<tr>
<th>Indicator:</th>
<th>Number of people CURRENTLY on methadone maintenance therapy (not cumulative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerator:</td>
<td>Number of people who inject drugs currently on MMT on the last day of the specific quarter</td>
</tr>
<tr>
<td>Data source:</td>
<td>MMT programme registers and clients’ records at DTCs;</td>
</tr>
<tr>
<td>Method of measurement:</td>
<td>Data can be obtained from facility: hospital registers, data bases, patient/client records.</td>
</tr>
</tbody>
</table>
- Counts should be of individuals not number of contacts.
- Only those “currently” on MMT should be counted. Cumulative figures must not be recorded.
- Clients who died, stopped using methadone, transferred out (permanently) and were lost to follow-up have to be EXCLUDED from the numerator.
- Loss to follow-up defines 5 days

The following abbreviations must be used to record data. (Attended patients will be recorded as his/her dose in ml)

Absence = A (more than 5 A should be counted as drop-out and marked by a red line; if known, the reason for drop-out should recorded, e.g. moved or arrested; If the fifth day of A falls on the last day of the reporting month, the patient should be excluded from the number of current patients.)

Take away = H
Completed = C
Transfer out (permanent) = T/O
Transfer out (temporary) = T/OT (for travelling/hospitalization)
Referral = T/IT (if absent for more than 5 days due to hospitalization = T/TI, so that he or she can rejoin after discharge and continue with the prescribed treatment by the hospital [physician or psychiatrist]); to be included in the current number of patients even if still in hospital at the time of reporting
Transfer in = T/I (entering the programme permanently, having moved from another DTC)
Transfer in = T/ TI (temporary, just for taking methadone for a short duration); dose should be marked; not to be included in the number of patients reported at the end of the month; he/ she will be in the resident DTC number.
Expired = E
### Monthly report form for DTC sites for methadone programme

Monthly report from .............................................. DTH/DTC

.............................................. Month ................. Year

Total number of **current and new** patients for MMT by age group and by gender

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–24</td>
<td></td>
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<tr>
<td>25–29</td>
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<tr>
<td>30–34</td>
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<tr>
<td>35–39</td>
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<td>40–49</td>
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<td>50–59</td>
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<tr>
<td>60 and above</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Number of **current** patients according to type of treatment by gender

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detoxification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMT (in-patients) at the end of reporting month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMT (out-patients) at the end of reporting month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Integrated service provision to reduce harms related to drug use

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Type of activities</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methadone dispensing</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Counselling</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Health education</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>IEC</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>VCCT</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Condom distribution</td>
<td></td>
</tr>
<tr>
<td>7 (i)</td>
<td>Referrals for ART</td>
<td></td>
</tr>
<tr>
<td>7 (ii)</td>
<td>Referrals for anti-TB drugs</td>
<td></td>
</tr>
<tr>
<td>7 (iii)</td>
<td>Referrals for OIs</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Referrals (total)</td>
<td></td>
</tr>
</tbody>
</table>

Monthly report from ........................................... DTH / DTC

...........................................Month...............Year

<table>
<thead>
<tr>
<th>Total no. registered (cumulative)</th>
<th>Current MMT</th>
<th>Completed</th>
<th>Transfer out</th>
<th>Transfer in</th>
<th>Cessation of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Imprisoned</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Social problems</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Psychosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hyper-sensitivity</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Death</td>
</tr>
</tbody>
</table>

Minimum dose  Mg
Maximum dose  mg
Average dose  mg
Total methadone used  ml
Total stock at end of month (5-mg bottle) [Main store + sub-store]  bottles
Total stock at end of month (10-mg bottle) [Main store + sub-store]  bottles
## Methadone stock record book

### Drug treatment centre/ dispensary

<table>
<thead>
<tr>
<th>Date From/to</th>
<th>Quantity received</th>
<th>Quantity dispensed or delivered</th>
<th>Balance</th>
<th>Doctor/dispenser name</th>
<th>Signature</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>
Appendix 10
Methadone client transfer facsimile

To (Prescriber/drug treatment centre): ................................................
Fax: ..........................
From (Name of prescriber): .................................................................
Subject: Transfer of methadone patient

Details of patient and prescriber

Hospital registration number .................................
Patient’s name: ........................................
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: ................. mg
Prescriber’s signature: .................................

Place prescriber / DTC site label or stamp here with prescriber and dispensary names, addresses, telephone numbers and fax numbers.
<table>
<thead>
<tr>
<th></th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>International Harm Reduction Association. What is harm reduction? Available at: <a href="http://www.ihra.net/what-is-harm-reduction">http://www.ihra.net/what-is-harm-reduction</a> (accessed on 27 August 2012)</td>
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Methadone is established in many parts of the world as an effective treatment for opioid dependence. The administration of methadone as an opioid substitution therapy is an evidence-based intervention, highly recommended by WHO and other United Nations agencies, to prevent the transmission of HIV among people who inject drugs and to treat drug dependence. As the HIV epidemic among people who inject drugs enters its third decade in Myanmar, expanding the use of opioid substitution therapy is of increasing importance. The Myanmar methadone programme commenced in 2006 and has been based on the delivery of services through specialist drug treatment centres and selected hospitals.

The revised Guidelines on Methadone Therapy and Treatment of Drug Dependence in Myanmar give some new directions to the programme and add updated information considered relevant to strengthen service delivery. The use of these guidelines will assist in the scale-up of methadone therapy and ensure that more patients receive treatment in Myanmar.

These practical 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 in providing safe and effective treatment to opioid-dependent patients.