

Alberta Methadone Maintenance Treatment

STANDARDS AND GUIDELINES
FOR DEPENDENCE



College of
Physicians
& Surgeons
of Alberta

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Introduction

The Alberta Methadone Maintenance Treatment Standards and Guidelines for Dependence (2014) guides physicians in the use of methadone to treat patients diagnosed with an Opioid Dependence Disorder.

The College of Physicians and Surgeons of Alberta (CPSA) plays a leadership role in establishing standards and best practices in this very complex area of practice. The main objective with this document is to increase or maintain the safety of patients in opioid dependency treatment. It is also hoped that these Standards and Guidelines raise awareness of opioid dependence with physicians and the healthcare community, and support and encourage physicians to consider MMT in the treatment of patients in their clinic or as a part of their general practice.

These standards and guidelines were developed to support: (a) experienced MMT physicians (initiating physicians) with a focused MMT practice, (b) community-based physicians (maintaining physicians) who take on stable MMT patients as a part of their regular practice, and (c) temporary prescribers of methadone who are physicians that temporarily care for an MMT patient in a hospital or corrections facility. Standards and guidelines for methadone treatment are intended to enhance patient care by improving the consistency of and access to safe clinical MMT management, and patient and community health and safety.

While the audience for this document is physicians, it is acknowledged that there are other health professionals involved in the care of opioid dependent patients. This is not intended to be a comprehensive manual, nor is it

expected to replace sound clinical judgement. Physicians are encouraged to consult with a specialist in MMT or addiction medicine as required.

These standards and guidelines are based on multiple sources of evidence on the safe and effective management of opioid dependency. This document is based on data obtained from best practice guidelines and research in the field of methadone maintenance and addictions medicine, as well as clinical experience from respected authorities and individual professionals in the field.

In March 2012, the CPSA established an expert group of physicians and healthcare professionals to revise and update the standards and guidelines for Methadone Maintenance Treatment (MMT) in Alberta. This document is the second edition of MMT standards and guidelines for Alberta, with the first standards and guidelines developed and published in 2005.

These revised standards and guidelines are the result of many months of research, consultation and discussion. We reviewed Alberta's existing standards and guidelines, as well best practices, evidence and standards and guidelines from other Canadian provinces and jurisdictions around the world. The CPSA and our expert committee reviewed, consulted, excerpted and adapted content from the following documents:

- College of Physicians and Surgeons of Nova Scotia: Methadone Maintenance Treatment Handbook, May 2012

- Methadone Maintenance Treatment Program Standards and Clinical Guidelines: February 2011, College of Physicians & Surgeons of Ontario
- Methadone Maintenance Handbook: College of Physicians and Surgeons of British Columbia, December 2009
- Saskatchewan Methadone Guidelines for the Treatment of Opioid Addiction: College of Physicians and Surgeons of Saskatchewan, June 2008
- Methadone Maintenance Treatment Guidelines for New Brunswick Addiction Services: July 2005
- Guideline - Methadone Maintenance Treatment: The College of Physicians and Surgeons of Newfoundland and Labrador
- The Use of Methadone in the Treatment of Opiate Addiction: College des Medecins du Quebec - February 2000
- Practice Guidelines for Opioid Substitution Treatment in New Zealand 2008
- Guidance for the use of substitute prescribing in the treatment of opioid dependence in primary care: Royal College of General Practitioners, United Kingdom, 2011
- Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence: Commonwealth of Australia, 2003

This Alberta-based document draws heavily on the standards and guidelines recently developed in Ontario

and Nova Scotia. We thank the Colleges of Physicians and Surgeons in these jurisdictions for the thoroughness of their work, as it gave us a foundation for our own revisions. We are particularly grateful and appreciative of the College of Physicians and Surgeons of Ontario (CPSO) and Wade Hillier (Associate Director, Quality Management, CPSO) for granting us complete access to and use of their research, standards and guidelines and accompanying materials.

These standards and guidelines were subject to public consultation, as required by the Alberta Health Professions Act - Section 133(2). The consultation period occurred between mid-September to mid-November 2013. This document was sent to 26 organizations, department and individuals for review and comment. The final document was approved by the Council of the CPSA in December 2013, and published in 2014.

We are indebted to the expert Advisory Committee that generously gave their time, knowledge and experience to help us create standards and guidelines that accurately reflects MMT in Alberta today, and where we want the practice to be in the near future. The Terms of Reference and membership of this Advisory Committee can be found in Appendix A.

We would also like to thank Dr. Don Legatt, Clinical Professor of Toxicology at the University of Alberta, for providing his expertise and perspective on key parts of these standards and guidelines.

This project was made possible through the financial support of the Council of the College of Physicians and Surgeons of Alberta.

Standards and Guidelines – Overview

The Standards of Practice of the College of Physicians & Surgeons of Alberta (hereafter referred to as the “College” or CPSA) are the minimum standards of professional behaviour and ethical conduct expected of all physicians registered in Alberta. Standards are enforceable under the Health Professions Act and will be referenced in complaints resolution and discipline hearings. Standards, which “must” be followed, define a minimum acceptable level of care to ensure patient safety. Standards are a mandatory requirement of physicians.

Guidelines provide direction that “should” be followed when managing specific issues. In MMT, guidelines provide direction and recommendations for effectiveness

and optimal patient care. Guidelines assist Initiating, Maintaining and Temporary Prescribing Physicians in making clinical decisions about patients, and may be adopted, modified, or rejected according to clinical needs, individual patient considerations, local resources, and physician discretion. A physician must exercise reasonable discretion and have justifiable reasons when there is a decision to not follow a guideline. In every instance, the reasons for not following a guideline must be well documented.

In this document, the term “physician” means any person who is registered or who is required to be registered as a member of the CPSA. The College regulates physicians, surgeons and osteopaths. All references to the “patient” in these Standards and Guidelines include the patient’s legal guardian or substitute decision maker, where applicable.

Methadone Maintenance Treatment in Alberta

The goal of Methadone Maintenance Treatment (MMT) in Alberta is to provide safe, accessible, effective and consistent treatment for individuals with opioid dependence.

MMT is a recognized therapy for an Opioid Dependence Disorder. It is not replacing one addiction with another. “Addiction” is a psychiatric and medical diagnosis, the criteria of which are not met by the patient who conscientiously adheres to a medication protocol and treatment plan.

Methadone causes physiological dependence and will result in physical and psychological withdrawal symptoms if discontinued abruptly. This in itself does not constitute “addiction”. The treatment of patients with addictions can be complicated by confusion between physiological dependence and addiction. This misunderstanding can result in a reluctance to embark on an appropriate and compassionate treatment plan.

MMT is a substitution therapy that allows a return to normal physiological, psychological and societal functioning. It is one possible treatment for an Opioid

Dependence Disorder. MMT may continue indefinitely in some people, while others may be able to eventually cease all opioid use and remain abstinent while preserving the normal functioning they attained while on MMT. Each patient must be assessed, treated and monitored on an individual basis, and MMT must consider the physiologic/biological, psychological, and social aspects of the patient’s wellbeing. Successful outcomes through MMT require knowledge, experience, vigilance and diligence on the part of the physician, the patient and everyone involved in treatment.

The demand for MMT is growing with more individuals with opioid addictions requesting treatment. This increased demand brings a corresponding need for more Initiating and Maintaining Physicians. It is hoped that these Standards and Guidelines will clarify the requirements and protocols for MMT and encourage more physicians to either become an Initiating Physician, or maintain MMT patients as a part of their current practice.

While buprenorphine/naloxone (Suboxone®) is prescribed for patient groups with opioid dependence, the drug is beyond the scope of this document.

Chronic Pain

MMT is for the treatment of opioid dependence and not for the treatment of chronic pain. The protocol for using methadone to treat chronic pain is almost always different than the protocol used for the treatment of opioid dependence.

It is important to understand that it may be impossible to differentiate between an addiction and chronic pain. In cases where comorbid pain complicates the presentation

of addiction (or vice versa), it is strongly recommended that there is consultation with a physician experienced in managing patients with both an addiction and chronic pain.

For patients with chronic pain who have lost control of their use of opioid medication, and where other methods fail to result in a return to stability, MMT can be helpful in regaining control and addressing a patient's pain issues in a healthy, manageable way.

Standards and Guidelines

1. Initiating Physicians

This section applies to physicians who deliver MMT in a private or in an Alberta Health Services (AHS) supported methadone clinic. These MMT physicians evaluate patients on their suitability for the treatment and start, or initiate, patients on MMT, working closely with an interdisciplinary team that offers a range of services and support to the patient.

Standards

1. Initiating Physicians must have a license to practice medicine in the province of Alberta.
2. Initiating Physicians must have an exemption granted by the Office of Controlled Substances, Health Canada, to prescribe methadone for the treatment of opioid dependence, endorsed by the Council of The College of Physicians & Surgeons of Alberta (CPSA).
3. Initiating Physicians will have the following training and experience:
 - a) Successful completion of a MMT workshop/course recognized by the CPSA
 - b) A period of direct training, supervision and mentorship with an experienced, CPSA-approved Initiating Physician until approved as competent in MMT
 - c) Documentation of clinical competence
4. Initiating Physicians will pursue ongoing education relevant to MMT. Physicians must provide documentation of MMT-related education that is acceptable to the CPSA. Examples of education acceptable to the CPSA are:
 - a) Completion of a recognized course on the fundamentals of addiction medicine within 2 years of acquiring a methadone exemption
 - b) A minimum of 40 hours of formal Continuing Medical Education (CME) in some aspect of addiction medicine every five years (time spent at a recognized MMT workshop/course qualifies)
 - c) Education equivalent acceptable to the Council of the CPSA
5. Initiating Physicians must access prescribing databases, including the Triplicate Prescription Program (TPP) and/or Netcare, in an effort to provide informed care to MMT patients.
6. An interview with the registrar of the CPSA or his/her designate may be required.
7. Initiating Physicians must have access to laboratory services and a pharmacy.
8. If the Initiating Physician is going to be away or is suspending their practice, they must ensure the patient receives continued care from another physician trained in MMT according to minimum standards described in the CPSA's Standards of Practice.
9. Initiating Physicians must collaborate with Maintaining Physicians that are continuing to provide MMT to former patients, and with the pharmacists that are dispensing to current patients.

Guidelines

1. Initiating Physicians should make reasonable efforts to provide non-pharmacological support to their patients (i.e.: pharmacy, addiction services, counselling, etc.).

2. Maintaining (Non-Initiating) Physicians

This section applies to physicians who provide MMT to a limited number of stabilized patients as a part of their general primary care practice.

Standards

1. Maintaining Physicians must have a license to practice medicine in the province of Alberta.
2. Maintaining Physicians must have an exemption granted by the Office of Controlled Substances, Health Canada, to prescribe methadone for the treatment of opioid dependence, endorsed by the Council of The College of Physicians & Surgeons of Alberta (CPSA).
3. Maintaining Physicians must have an ongoing association with an experienced Initiating Physician who serves as a resource to the Maintaining Physician.
4. Maintaining Physicians shall have an understanding of methadone pharmacology and will undertake the following education prior to taking on a MMT patient:
 - a) Successful completion of a MMT workshop/course recognized by the CPSA
 - b) Attendance at the original MMT workshop/course or another educational course relevant to addiction medicine and approved by the CPSA, within 5 years of acquiring a methadone exemption
5. Maintaining Physicians must access prescribing databases including, the Triplicate Prescription Program (TPP) and/or Netcare, in an effort to provide informed care to MMT patients.
6. An interview with the registrar of the CPSA or his/her designate may be required.
7. If a Maintaining Physician is going to be away or is suspending their practice, they must ensure the patient receives continued care from another physician trained in MMT.
8. A Maintaining Physician must work collaboratively with the Initiating Physician and other caregivers that provide an interdisciplinary network of resources to the MMT patient (i.e.: pharmacy addiction services, counselling, laboratory, etc.)

Guidelines

1. Maintaining Physicians are encouraged to pursue a minimum of 20 hours of formal Continuing Medical Education (CME) in some aspect of addiction medicine every 5 years (time spent at a recognized MMT workshop/course qualifies).

3. Temporary Prescribing Physicians – In Hospitals and Corrections

This section applies to physicians who do not normally engage in MMT as a part of their practice, but may require brief, patient-specific exemptions to prescribe methadone for the treatment of opioid dependence. Temporary prescribing physicians may work in hospitals or in a corrections facility. If a physician is not a patient's current methadone prescriber, they are considered a Temporary Prescribing Physician. Whatever the situation, these physicians may not have specialized knowledge of opioid dependence but are responsible for patients who actively receive MMT.

A. Hospital-based Temporary Prescribing Physicians

Standards

1. A license to practice medicine in the province of Alberta.
2. An exemption specific to in-patient treatment, granted by the Office of Controlled Substances, Health Canada, to prescribe methadone for the treatment of opioid dependence, endorsed by the Council of The College of Physicians & Surgeons of Alberta (CPSA). A Temporary Prescribing Physician must apply for this exemption within 2 business days of starting MMT for a hospitalized patient.
3. In an urgent or emergency situation where an Initiating Physician is not available, the Temporary Prescribing Physician must consult their hospital policy or the College of Physicians and Surgeons of Alberta.

4. Prescribing of MMT is only for the duration of the patient's hospital admission.
5. Carried doses are not permitted, except in consultation with the Initiating or Maintaining Physician.
6. Temporary Prescribing Physician must collaborate with the current methadone prescriber and any other treating prescribers for all changes to the methadone dosage, frequency, or addition of medications that have the potential to interact with methadone.
7. Prior to the patient's discharge from hospital, the Temporary Prescribing Physician must collaborate with the Initiating or Maintaining Physician on:
 - a) discharge plans
 - b) any changes in dosage
 - c) the prescribing of short-term opioid analgesics, psychoactive or medications with the potential for interaction with MMT
8. Must review the overview of methadone and MMT. [See Appendix B: Highlights of Methadone Maintenance Treatment (MMT) in Alberta for Dependence]

Guidelines

1. The Temporary Prescribing Physician should be familiar with the basics of MMT, as obtained through previous education, such as an introductory workshop/course, or mentorship by an Initiating Physician.

2. Any physician who manages patients on MMT on a routine basis should apply for a general exemption to prescribe methadone for the treatment of opioid dependence. In this case, the Standards and Guidelines for an Initiating or Maintaining Physician apply.

B. Corrections-based Temporary Prescribing Physicians

Standards

1. A license to practice medicine in the province of Alberta.
2. An exemption specific to in-patient treatment, granted by the Office of Controlled Substances, Health Canada, to prescribe methadone for the treatment of opioid dependence, endorsed by the Council of The College of Physicians & Surgeons of Alberta (CPSA). A Temporary Prescribing Physician must apply for this exemption within 2 business days of starting MMT for an incarcerated patient.
3. In urgent or emergent situations where an Initiating Physician is not available, the Temporary Prescribing Physician must consult their facility's policy or the College of Physicians and Surgeons of Alberta.
4. Prescribing of MMT is only for the duration of the patient's incarceration. An exception to this may be made only when a patient is discharged from the facility on a weekend. The physician is then permitted to prescribe methadone for a maximum duration of 72 hours after discharge and the community methadone prescriber must be notified at discharge that methadone was prescribed to avoid double dosing.
5. Carried doses are not permitted, except in consultation with the Initiating or Maintaining Physician.

6. The Temporary Prescribing Physician must collaborate with the current methadone prescriber and any other treating prescribers for all changes to the methadone dosage, frequency, or addition of medications that have the potential to interact with methadone.
7. Prior to the patient's discharge from a corrections facility, the Temporary Prescribing Physician must collaborate with the Initiating or Maintaining Physician on:
 - a) discharge plans
 - b) any changes in dosage
 - c) the prescribing of short-term opioid analgesics, psychoactive or medications with the potential to interact with MMT
8. Must review the overview of methadone and MMT. [See Appendix B: Highlights of Methadone Maintenance Treatment (MMT) in Alberta for Dependence]

Guidelines

1. The Temporary Prescribing Physician should be familiar with the basics of MMT, as obtained through previous education, such as an introductory workshop/course, or mentorship by an Initiating Physician.
2. Any physician who manages patients on MMT on a routine basis should apply for a general exemption to prescribe methadone for the treatment of opioid dependence. In this case, the Standards and Guidelines for an Initiating or Maintaining Physician apply.

4. Methadone Prescriptions

The safe dispensing of methadone begins with a well-written prescription. Collaboration and communication between physician and pharmacist enhances patient safety. This section outlines what must be present in any prescription for methadone.

Standards

1. Methadone prescriptions must be written on the physician's personalized triplicate prescription pad, or by CPSA approved electronic prescribing, unless dispensed from a hospital pharmacy for in-patient use.
2. Prescriptions must specify all of the following:
 - a) start/end dates
 - b) days of the week to be supervised by daily witnessed ingestion (DWI)
 - c) carried doses (with the number and days of week that are to be given as take home doses specified)
 - d) methadone dose written in numbers and words
 - e) any special instructions and extraordinary situations
3. Methadone must be dispensed in crystalline suspension or in a form that reduces its diversion and potential for abuse.
4. If a patient requests methadone in a form that can be more easily diverted or abused, the Maintaining Physician must consult with the Initiating Physician. Only an Initiating Physician can change a prescription to a non-crystalline suspension.
5. Initiating and Maintaining Physicians must communicate with the patient's pharmacist on the management of spoiled, lost and missed doses, either with each prescription or as general instructions for all methadone prescriptions.
6. With any change in dosage, the physician must:
 - a) cancel the existing prescription, and
 - b) issue a new prescription based on the Standards cited above.

Guidelines

1. To improve a patient's adherence to treatment, the duration of a methadone prescription should not exceed the interval between clinical visits.
2. Physicians should fax the methadone prescription directly to the pharmacy and to VOID the original prescription in an effort to deter prescription alteration and diversion if possible.

5. Patient Assessment for Admission to an MMT Program

This section details the steps physicians must complete before starting a patient on MMT. The patient must be assessed to determine their suitability for MMT, their history documented, appropriate investigations completed and informed consent obtained. The patient is made aware of treatment options and if it is decided that the patient will benefit from MMT, an agreement between patient and physician and a detailed treatment plan are developed.

Standards

1. The patient must have a diagnosis of an Opioid Dependence Disorder, as based on the most current DSM criteria for opioid dependence, and be assessed by a physician as likely to benefit from MMT. [See Appendix E – Diagnostic Criteria for Substance Dependence]
2. The patient must understand the rights, responsibilities, risks and the daily requirements of MMT treatment.
3. Before admitting a patient to an MMT program, the physician must explicitly discuss all appropriate and available treatment options other than MMT, including opioid substitution, tapering, and abstinence.
4. The patient must be informed and understand the impact of methadone on their health and activities, and all of the significant risks of methadone, particularly during initiation and with any increase in dosage.
5. Patients must provide informed consent to treatment. [See Appendix U: CPSA Standards of Practice: Informed Consent]
6. Prior to initiating methadone, the Initiating Physician must assess the patient and ensure the following information has been reviewed and documented:
 - a) medical history, including cardiovascular history
 - b) appropriate physical examination
 - c) pattern of drug use
 - d) addiction treatment history
 - e) psychiatric history and mental status
 - f) high-risk behaviour
 - g) social situation
 - h) details on chronic or recurrent pain
7. The patient must sign an MMT agreement that will be kept as a part of the patient's medical record. A copy must be given to the patient and to the dispensing pharmacy. [See Appendix M: Methadone Maintenance Treatment Agreement – Sample]
8. Prior to methadone initiation, the Initiating Physician must obtain the patient's prescribing profile from the Triplicate Prescription Program (TPP) and/or Netcare.
9. The Initiating Physician must make every reasonable effort to notify the patient's family physician and any other healthcare providers that have prescribed to the

patient in the 3 months prior, that the patient is being initiated on methadone.

10. If the patient prohibits the Initiating Physician from communicating with their primary care physician or other prescribers, the Initiating Physician must not begin methadone initiation.
11. The Initiating Physician or MMTP clinic staff must notify the CPSA within 2 business days of any patient's admission to or discharge from MMT. [See Appendix T: Admission and Discharge Form - Submitted to CPSA]
12. The patient's treatment plan must be documented and kept as a part of the patient's medical record.
13. All women of child-bearing potential must be offered a pregnancy test prior to initiation. If the patient does not consent to a pregnancy test, the Initiating Physician must document why the patient has refused.
14. Physicians must inform patients of arrhythmia risk when they prescribe methadone.
15. All patients must have an ECG prior to initiation.
16. An initial UTT must be obtained prior to initiation of methadone and this must include both screening and confirmation testing (GC/MS or tandem MS).
17. The physician must encourage the patient to include non-pharmacological measures (i.e.: addiction counselling) as a part their treatment plan.
18. Pregnant women requesting MMT are to be given priority over other applicants for MMT.
19. Risks to the individual, society and public health must be evaluated when considering priority access to MMT.

Guidelines

1. The initiation of MMT should not be delayed pending the UTT results when not immediately available.

6. Clinical Visits

This section outlines the frequency an MMT patient must be seen by an Initiating or Maintaining Physician.

Standards

1. Patients must be seen at least once a week during the first 14 days of treatment by the Initiating Physician or another physician with a methadone exemption that permits the initiation of methadone in opioid dependence. This is in addition to the patient's daily witnessed ingestions at either the pharmacy or at an MMT clinic.
2. After the first 14 days of treatment, patients must be seen by a physician on a weekly basis until the dose is stable.
3. After the patient is stable, the patient must be seen by a physician at least every 3 months.
4. If the patient shows a sign(s) of instability, the patient must have clinical contact with the initiating physician or another physician with a methadone exemption that permits the initiation of methadone in opioid dependence.
5. For dose increases, the patient must be seen by the physician within one week of the change in dose.

Guidelines

1. For stable patients, the following schedule of clinical visits is recommended:

Length of Time Patient is Stable on Methadone	Frequency of Visits with a Physician
Less than 3 months.....	At least every 2 weeks
Less than 6 months.....	At least monthly
Less than 12 months.....	At least every 2 months
Greater than 12 months.....	At least every 3 months

7. Dosages

A) Initiation Phase

Patients are at the highest risk of methadone overdose (and overdose death) in the first 2 weeks of MMT. This section outlines the starting dose and subsequent dose increases for patients in the first few weeks of MMT (the same information is presented in chart form in Appendix I). The initial dose is based on the patient's opioid tolerance and underlying risk for methadone toxicity. It is important to note that methadone, particularly in combination with other CNS depressants or substances that increase serum methadone levels, can be dangerous. Rapidly escalating increases in dose bring increased risk and do not necessarily benefit the patient, and should be treated with caution.

The risk of increasing a dose in the initiation phase needs to be balanced with the recognition that increasing methadone doses to effective levels can increase patient retention rates and decrease the use of illicit drugs, alcohol and psychoactive medications.

Standards

1. The risk of methadone toxicity must be assessed by a physician prior to initiation. [See Appendix X: Managing Potential Methadone Overdose]
2. For patients at **LOW RISK** for methadone toxicity:
 - a) the starting dose is 30mg or less
 - b) the initiating physician shall prescribe dose increases of no more than 10mg every 3 days during the early and late stabilization phases
3. For patients at **MODERATE RISK** for methadone toxicity:
 - a) the starting dose is 20mg or less
 - b) the initiating physician shall prescribe dose increase of no more than 10mg every 4 days during early and late stabilization phases
4. For patients at **HIGH RISK** for methadone toxicity, or who have been abstinent from opioids for 7 or more days:
 - a) the starting dose is 10mg or less
 - b) the initiating physician shall prescribe dose increases of no more than 5mg every 5 or more days during the early and late stabilization phases
5. Patients must receive Daily Witnessed Ingestion (DWI) during the initiation phase.

Guidelines

1. Patients should not be on other prescribed opioids during the initiation phase.
2. Physicians should be cautious with patients who ask for increases in their dose during the initiation phase. There are significant risks with increasing dosages beyond what is cited in the standards listed above.

B) Stabilization Phase

This section details how to manage the stabilization phase, where physicians work towards a dose and treatment plan to stabilize the patient's condition, social environment and overall wellbeing.

Standards

1. The Initiating Physician must ensure doses are increased only after the patient has been assessed in person, and it is determined that the patient is experiencing cravings or ongoing opioid use, and/or a constellation of withdrawal symptoms.
2. The Initiating Physician shall not increase the patient's dose by more than 10mg every 5-7 days during the stabilization phase.
3. The Initiating Physician must adhere to the Standards and Guidelines in Section 12: ECGs.

Guidelines

1. The typical methadone dose to reduce cravings and withdrawal symptoms is between 60-120mg.
2. Changes to any concurrent medications should prompt a review of the current methadone dosage. Collaboration with a knowledgeable pharmacist is recommended.
3. The physician must evaluate the possibility of pregnancy and discuss contraception options during every clinical visit.

C) Maintenance Phase

When both the dose and the patient are adequately stable, the patient can be considered to be in the maintenance phase. This section details the requirements of physicians when their patient is maintained on methadone. The optimal maintenance dose of methadone will relieve withdrawal symptoms, prevent opioid-induced euphoria and reduce cravings for 24 hours without causing

sedation or other significant side effects. With experience, an MMT physician can reach the correct maintenance dose within 2-8 weeks of initiating MMT, with an optimal dose range of 60-120mg.

Standards

1. The Initiating Physician must document adequate stability in the patient and the dose for 3 months before transferring to a Maintaining Physician.
2. The Maintaining Physician must consult with the Initiating Physician before any change in dose and/or if the patient shows more than one indicator of instability. [See Appendix D: Key Indicators of Stability and Instability]
3. The Initiating Physician must resume care of the patient from the Maintaining Physician in the following situations:
 - a) When the Maintaining Physician requests a transfer back to the Initiating Physician
 - b) When the patient shows more than one indicator of instability
 - c) When the Maintaining Physician is unable to provide appropriate care to the patient
 - d) When the pharmacist to the patient indicates that the patient is having issues maintaining their prescription
4. The Maintaining Physician should administer a UTT a minimum of every 3 months for a stable, maintaining patient.

Guidelines

1. The patient should have clinical contact with the Maintaining Physician at least every 3 months, or as otherwise recommended by the Initiating Physician. The Maintaining Physician may wish to see the patient more frequently than every 3 months until they are comfortable with the patient and the required care.

8. Split Dosages

Split doses are occasionally used in the management of pregnant or chronic pain patients, or in patients with intrinsic rapid methadone metabolism or who are on medications that induce rapid metabolism of methadone. This section details how split dosages should be managed.

Standards

1. The prescribing and dispensing of split dosages of methadone must be supported by documented withdrawal signs and symptoms within 24 hours of the daily dose, and/or signs and symptoms of excessive methadone dose in the four hours following a single daily dosage.

Guidelines

1. Split dosages may be required under certain clinical conditions. In these situations, it is recommended that physicians consult with an experienced toxicologist, pharmacist or knowledgeable expert.

2. Rapid metabolizers of methadone are rare; evaluation of the peak and trough serum methadone level, or calculating the half-life, is recommended.
3. Twice-daily observed ingestion may be necessary.
4. Split doses do not necessarily have to be equal. A lower dose of 1/4 to 1/3 the total daily dose, provided as a carry, may be satisfactory to the patient, and reduce the amount of methadone prone to diversion or misuse.
5. It is important to recognize these guidelines are intended for the treatment of the opioid-dependent patient. Patients with concurrent chronic pain may require special consideration, and consultation is advised to ensure optimal care.
6. Split dosages are common for pregnant patients in the third trimester, and consultation with an expert is recommended.

9. Spoiled, Lost and Missed Doses

This section outlines how physicians and pharmacists must manage a spoiled, lost or missed dose (the same information is presented in chart form in Appendix J). When there is uncertainty about whether a dose had been spoiled, lost, vomited or missed, it is important to remember that the risk of death from overdose is much greater than the risk of harm from mild withdrawal symptoms. Ongoing communication and collaboration between the physician and pharmacist is essential. Rapid decline in tolerance to methadone necessitates careful management of missed doses. Failure to adjust a dose in this context can result in overdose death.

Standards

1. Unwitnessed vomited doses must not be replaced without documentation of withdrawal signs and symptoms.
2. All reports of vomited, lost or missed doses must be documented on the patient's medical file.
3. If the patient misses 1 dose and attends the following day, a change in the dose or prescription is not required but should be considered.
4. If the patient misses 2 consecutive doses, the prescription must be cancelled and a new

prescription must be written and the dose must be reduced by 25%.

5. If the patient misses 2 out of 7 non-consecutive doses, the patient must be reassessed by the physician.
6. If the patient misses 3 or more doses, the prescription must be cancelled and the patient must be assessed by the Initiating Physician for consideration of dose reduction by at least 50% or reinitiation on methadone.
7. Replacement doses must be given only as witnessed ingestion.
8. If the patient has emesis after taking methadone, the initiating/maintaining physician should not replace the dose unless the emesis was witnessed by the pharmacist or staff, and it occurred less than 15 minutes after consumption. The replacement dose must be no more than 50% of the regular dose.
9. Communication with the Initiating Physician must occur for all missed doses, regardless of cause, duration or number.

Guidelines

1. Doses vomited 15 minutes or more after ingestion are not replaced.

10. Carries

This section outlines the parameters for patients carrying 1 or more doses of methadone. Take-home doses are referred to as “carries”. The decision to permit carried doses must consider the safety of the patient and the community. Patients cannot be granted carries until adequate stability is achieved, which is based upon a combination of clinical data, urine toxicology results and a thoughtful consideration of social, psychological and other circumstances impacting the patient. It is important to recognize that some patients may never achieve adequate stability, due to underlying mental illness, co-existing addictions, or social conditions such as unstable housing.

Any deviation from the Standards and Guidelines for Carries requires clear documentation of the rationale. Serious harm to the patient and others can result from inappropriately used, lost, stolen or spoiled carries. Patient requests for replacements may indicate clinical instability, and necessitates a thorough clinical evaluation. Decisions to replace doses should be made only after diligent consideration and evaluation of the risks and benefits.

Standards

1. Carries must not be granted in the initiation and stabilization phase, and until adequate clinical and social stability has been achieved and documented. Exceptions may only be made when the pharmacy is closed for statutory holidays or in exceptional circumstances.
2. The MMT physician shall not prescribe take-home doses if:
 - 1) the patient is at risk of taking more than prescribed
 - 2) the patient is not able to safely store the methadone
 - 3) there is suspicion that the patient is diverting methadone
 - 4) the patient does not understand the risks of methadone diversion
3. Patients on MMT who continue to use prohibited drugs and other potentially harmful interacting substances such as alcohol and other CNS depressants must not be granted carry doses.
4. Patients on MMT who are prescribed medications with potentially harmful interactions such as benzodiazepines, other CNS depressants including other opioids, should not be granted carries. If carried doses are granted in an exceptional situation, the physician must evaluate the risks and document the rationale for the decision to grant carries.
5. The MMT physician must ensure the first take-home dose is prescribed only after the patient has been in the program for a minimum of 3 months, and the patient has had at least 3 consecutive random negative UTT.
6. Take home doses must be prescribed at a rate of no more than 1 dose per week every 4 weeks, to a maximum of 6 take-home doses per week. Fourteen take-home doses can only be given after 2 years of stability and negative urine tests.
7. Prescriptions must clearly define witnessed ingestion days and carry intervals.
8. All carries must include a witnessed ingestion. There may be rare, exceptional circumstances where witnessed ingestions with carries cannot occur. In

these situations, prescribers must consider:

- a) the patient's circumstances
 - b) storage of methadone carries
 - c) the environment in which they live and work
9. Physicians must clearly document any decision to provide a patient with carries.
 10. The prescribing physician must be satisfied that carried doses will be securely transported and stored by the patient. A locked box or storage container for any carried doses is required, and empty bottles should be returned to the pharmacy for proper disposal.
 11. Carries must be suspended for a patient that misses a dose.
 12. Inappropriately used, lost, stolen or spoiled carried doses require complete withdrawal of carry privileges until adequate clinical and social stability is established. Replacement dosing is provided only upon documentation of physiological signs of withdrawal, and only as a daily witnessed ingestion.
 13. The MMT physician shall cancel all carry privileges immediately when any of the circumstances listed below occur. The daily observed dose should be reduced if the MMT physician suspects the patient

may not have been taking the full take-home dose.

- a) There is reasonable suspicion that the patient has diverted their methadone dose, or has tampered with their UTT.
- b) The patient has relapsed to using drugs and/or prescription medications either by self report, observed intoxication or by a positive UTT.
- c) The patient has unstable housing, and can no longer safely store their methadone.
- d) The patient is actively suicidal, cognitively impaired, psychotic, or is otherwise at risk for misuse of their methadone dose.
- e) The patient has recently been released from incarceration.

Guidelines

1. Carries should be provided as individual doses rather than in bulk form, which would require the patient to apportion the daily dosage.
2. Resumption of carry privileges after reports of inappropriately used, lost, stolen or spoiled carried doses should take into account the circumstances of the incident, as well as the patient's clinical and social situation. A cautious and conservative approach is recommended.

11. Urine Toxicology Testing (UTTs)

Urine Toxicology Testing (UTT) is the analysis of urine for the presence of medications and illicit drugs or their metabolites. This section outlines how UTT results are used as one tool to verify patients' self-reported substance use, assess response to MMT and determine suitability for take-home doses.

False positives and false negatives may occur in UTT as in any other medical test. In addition, different substances may be detected in the urine for a variable period after their use depending on the type of lab methodology used.

Consultation with the clinical toxicology laboratory before initiation of testing is recommended to ensure it will meet expectations of the UTT program as it pertains to the particular individual.

Standards

1. The UTT program for a patient must include random screenings: that is UTTs that are unscheduled with no fixed dates and where the patient has no more than 24 hours' notice that a urine collection is required.
2. Routine UTT can be more focused but will include methadone metabolite, opiates, cocaine metabolite, amphetamines, alcohol, benzodiazepines, barbiturates and other psychoactive drugs for reasons of patient safety and as an indication of patient instability.
3. Frequency of collection:
 - a) Initiation: at least 1 UTT before a patient is initiated
 - b) Stabilization: collected at least monthly
 - c) Maintenance: collected at least every 3 months
4. Unexpected UTT results should prompt physicians to evaluate the withdrawal of take-home carries, increasing the frequency of UTTs and the return of the patient back to the Initiating Physician.
5. If the patient has provided a tampered urine sample or has failed to attend a requested UTT within 24 hours (48 hours in occasional exceptional circumstances), this is considered a positive UTT result. The patient must be considered unstable and treated with caution.

Guidelines

1. There should be a discussion between the Maintaining Physician and the Initiating Physician about how to manage and when to share UTT results.
2. Consultation with the clinical toxicology laboratory performing the testing should be considered if a result requires clarification or follow-up discussion.
3. A physician should consult prescribing data, including Netcare and/or TPP to understand all prescribed medications when interpreting a UTT result.
4. Physicians should be aware of all medications prescribed to the patient as certain medications can purposefully or unintentionally mask the presence of other substances in UTT results.
5. Confirmatory UTT has an important role to play in drug testing as it rules out false positives and false negatives. These situations may result from techniques that laboratories use in the initial screening. The physician should request confirmation of a positive or negative result if the initial screen is not consistent with patient history.
6. Where there is a concern for the integrity of urine samples, an observed collection may be considered.
7. Laboratory results should be made available to all caregivers to the patient in an effort to improve patient care and safety.

12. ECGs

This section outlines the frequency for ECGs in methadone patients. Methadone may prolong the QTc interval and result in torsade de pointes.

Standards

1. Initiating Physicians must obtain an ECG prior to initiation to measure the QTc interval.
2. A follow-up ECG must be obtained within 30 days of initiation.
3. An ECG must be obtained annually for all MMT patients.
4. Additional ECGs must be obtained in the following situations:
 - a) If the methadone dose meets or exceeds 100mg, and thereafter at every dose that meets or exceeds a multiple of 20mg (i.e., 120mg, 140mg, 160mg)
 - b) If the patient has unexplained syncope or seizures, or other symptoms that are suggestive of cardiac involvement
 - c) When a patient is initiated on medications known to prolong the QTc interval
5. If the QTc interval is greater than 450msec but less than 500 msec, physicians must review the potential risks and benefits with patients and monitor them more frequently, including more frequent ECGs. There is an increased risk of cardiac dysrhythmia as the QTc exceeds 450msec.
6. If the QTc interval exceeds 500 msec, the physician must carefully consider the risks and benefits of continued treatment at the current dose, and discuss alternatives with the patient, including discontinuing or reducing the methadone dose, or eliminating contributing factors or medications.

Guidelines

1. Medications should be reviewed prior to initiation of methadone and on a regular basis to identify any medications that are known to prolong the QTc interval, in an effort to reduce risk.
2. The patient's other prescribers should be advised of this issue, and encouraged to avoid medications that have the potential to prolong the QTc interval.

13. Methadone and Other Medications

This section discusses how to manage potential interactions between methadone and other medications.

Patients receiving MMT frequently have other medical conditions, including psychiatric diagnoses, for which they receive medication. People with a history of addiction to one substance have a much greater risk of developing other addictions. Methadone has a narrow therapeutic window and can prolong the QTc interval, suppress respiration and can interact with many medications. Every patient on MMT requires a thorough evaluation of all medications on an on-going basis. Information and communication between all healthcare providers is essential for patient safety and wellbeing.

Standards

1. Prescribing physicians must be familiar with other medications that interact with methadone due to prolongation of the QTc interval and/or CNS depression, and/or inhibition or induction of those cytochrome systems involved in the metabolism of methadone.

2. Prescribing physicians must access prescribing databases, including Netcare and/or TPP, as a part of their ongoing patient management.
3. Prescribing physicians must advise patients about the interactions of benzodiazepines and other opioids with methadone. Caution should be exercised in prescribing benzodiazepines in MMT, and a patient's history, examination findings and diagnoses leading to treatment with benzodiazepines should be well documented.

Guidelines

1. If the risk of continuing to prescribe methadone outweighs the benefits, the prescribing physician should discontinue methadone treatment. Maintaining Physicians are encouraged to consult with the Initiating Physician as necessary.
2. Patients that are prescribed methadone for the ongoing management of concurrent chronic pain and addiction need a comprehensive management plan. With such patients, it is recommended the advice of a physician with a specialization in chronic pain be considered.

14. Discontinuation

A) Involuntary Withdrawal

Involuntary withdrawal should be considered when continuation of treatment presents unreasonable risk to the patient, treatment staff, prescribers, pharmacy staff or the public.

Standards

1. The Initiating/Maintaining Physician may transfer or cease a patient from MMT if:
 - a) the patient has been threatening or disruptive, or has shown violent behavior towards a staff member or others
 - b) the patient is consistently non-compliant with the treatment agreement
 - c) the patient is at high risk for adverse outcomes and attempts to reduce the risk have failed
 - d) the patient is believed to have diverted their methadone prescription
2. All doses during involuntary withdrawal must be Daily Witnessed Ingestion, with no carries except as pharmacy closure requires.
3. Involuntary withdrawals are unstable patients and their withdrawal must be managed by an Initiating Physician only. Maintaining Physicians with a patient that must be involuntarily withdrawn from MMT must

transfer the patient back to an Initiating Physician who will manage their withdrawal and ongoing care.

4. The Initiating Physician must notify the CPSA within 2 business days of any patients' admission to and or discharge from MMT.
5. The Initiating Physician must warn the patient about the loss of tolerance and the risk of toxicity if they relapse to opioids.

Guidelines

1. The Initiating/Maintaining Physician should explain the reasons for cessation to the patient and document the rationale.
2. A typical schedule for involuntary withdrawal is as follows: a 10% reduction of the daily dose per day, or 1mg per day, whichever is greater. This results in complete cessation within 30 days for any dose under 150mg, and within 40 days for any dose less than 500mg.
3. The Initiating Physician may use pharmacotherapy in the final 1-2 weeks of the decrease to relieve withdrawal symptoms.
4. The Initiating/Maintaining Physician should encourage the patient to engage with other health care professionals or an addiction treatment program for counselling and support.

B) Voluntary Withdrawal

This section outlines how to manage a patient's voluntary withdrawal from MMT.

Any change in methadone dose, including voluntary tapering, may increase the risk of instability. It is prudent to discuss with the patient the preparation for this process, including ongoing or enhanced counselling or a reduction in the number of carried doses.

Standards

1. The Initiating/Maintaining Physician must notify the CPSA within 2 business days of any patients' admission to and or discharge from MMT.
2. The Initiating Physician should warn the patient about the loss of tolerance and the risk of toxicity if they relapse to opioids.
3. The Initiating Physician must see the patient regularly during withdrawal to assess the patient's mood and withdrawal symptoms, and provide supportive counselling.

Guidelines

1. For voluntary tapers, the Initiating Physician should taper patients slowly. However, the rate of the taper should be patient driven, even if the patient desires a more rapid taper.
2. The Initiating Physician should attempt to decrease the dose more slowly at doses below 20-30mg daily, as withdrawal symptoms become more pronounced.
3. The Initiating/Maintaining Physician should identify patients who are good candidates for a successful methadone withdrawal, and discuss the risks and benefits of withdrawal with them.
4. The Initiating Physician should decrease the methadone dose slowly. The decrease should be stopped or reversed at the request of the patient, or if the patient experiences severe dysphoria, cravings, or withdrawal symptoms, or relapses to opioids or other drugs.
5. The Initiating Physician should offer to follow the patient for at least a few months after the completion of the decrease.
6. The Initiating Physician should offer to reinstate MMT if the patient requests it during voluntary withdrawal.
7. The Initiating Physician may use pharmacotherapy to relieve withdrawal symptoms.
8. The Initiating/Maintaining Physician should encourage the patient to engage with other health care professionals or an addiction treatment program for counselling and support.

15. Special Situations: Transfer of Care

This section outlines the requirements of physicians transferring a patient to another physician, whether it is a patient being transferred between opioid dependency programs, or from an Initiating Physician to a Maintaining Physician. Patient convenience and preference should not outweigh concerns for patient and community safety. Patients that are high risk, are not adequately stable and do not yet have a stable dose should not be transferred to a community that does not have a pharmacy open 7 days a week.

Standards

1. The Initiating Physician must provide detailed information on the patient and their treatment plan to the Maintaining Physician, including:
 - a) the dose of methadone
 - b) all prescribed medications
 - c) details on how many carries are permitted
 - d) frequency of UTT screens
 - e) a copy of the treatment agreement
 - f) relevant clinical history of the patient
 - g) contact information for the Initiating Physician
2. The Initiating/Maintaining Physician will continue to provide services to MMT patients until they are no longer required or desired, or until involuntary withdrawal is completed.
3. When an Initiating/Maintaining Physician is closing their practice, they must initiate a transfer of care and assist the patient in finding alternate MMT services.
4. The current Initiating/Maintaining Physician must provide the new, receiving physician with sufficient clinical information to permit the safe and effective continuation of MMT.
5. When a patient is undergoing involuntary withdrawal, the Initiating/Maintaining Physician is under no obligation to find another Initiating/Maintaining Physician. However, the current Initiating/Maintaining Physician must provide the receiving physician with appropriate clinical information to permit the safe and effective continuation of MMT.
6. If a patient is stable and is moving to a community where they cannot access a pharmacy open 7 days a week, the Initiating/Maintaining physician and the local pharmacy must collaborate on a treatment plan prior to the patient transferring to the new community.
7. The physician initiating transfer of care must make all reasonable efforts to ensure the receiving physician has access to the patient's information at the time of transfer and anytime thereafter.
8. Patients that continue to be high risk, as they are not adequately stable and are not on a stable dose, must not be transferred to a maintaining methadone prescriber or to a community that does not have a pharmacy open 7 days a week.

Guidelines

1. When a patient on MMT moves to another community, region or country, it is the patient's responsibility to arrange ongoing MMT. However, the current Initiating/Maintaining physician should provide reasonable assistance to the patient.

16. Special Situations: Incarceration

Necessary medical treatment, including MMT, should be provided to any individual incarcerated in a provincial correctional centre or remand centre.

Community resources, including MMT programs and primary care physicians knowledgeable in MMT should be readily available resources for methadone prescribers in correctional or remand centres.

Standards

1. MMT prescribers practicing within provincial correctional or remand institutions must adhere to these Standards and Guidelines.
2. MMT prescribers practicing within federal correctional institutions must adhere to these Standards and Guidelines. If a prescriber feels that a conflict might exist between the Alberta Standards and Guidelines and the CSC Methadone Guidelines, it is recommended that the prescriber contact the Director General of Health Services for CSC at National Headquarters in Ottawa for clarification, at which point follow-up with the CPSA may occur, if required.
3. The prescriber/program providing MMT to the patient at the time of incarceration must provide all information necessary for safe and effective MMT upon the request of the correctional or remand centre.
4. The prescriber/program providing MMT to the patient at the time of incarceration and the prescriber during incarceration will collaborate to ensure continuity of care prior to and at the time of release.
5. Prior to release, the methadone prescriber or designate within the correctional or remand centre will assist the patient in making arrangements for continuation of MMT upon release.
6. The prescriber/program providing MMT to the patient at the time of incarceration will resume MMT at the time of release unless other arrangements have been made. Under extraordinary circumstances the prescriber may continue to prescribe during the incarceration.
7. Prior to the patient's discharge from a corrections facility, the Temporary Prescribing Physician must collaborate with the Initiating or Maintaining Physician on:
 - a) discharge plans
 - b) any changes in dosage
 - c) the prescribing of short-term opioid analgesics, psychoactive or medications with the potential to interaction with MMT

Guidelines

1. Patients entering a provincial correctional or remand centre who are on a stable dose of methadone should be maintained on an appropriate dose for the duration of their incarceration, except where patient behaviour incurs involuntary withdrawal as outlined in Section 14A: Discontinuation: Involuntary Withdrawal or where clinical assessment determines the need for a dosage change.
2. In urgent circumstances to avoid interruption of MMT, the community methadone physician may choose to continue prescribing methadone for a patient who becomes incarcerated for a maximum period of 2 weeks.
3. The community methadone physician is not obligated to continue prescribing methadone for a patient who becomes incarcerated if the requirement for patient safety cannot be met to the satisfaction of the community physician.

17. Special Situations: MMT in Adolescents

Patients under 18 years of age may be considered for MMT, however abstinence-based treatment and/or opioid substitution tapering should also be considered for adolescents, particularly those with a shorter duration of opioid dependence. Caution must be exercised when considering MMT in an adolescent patient.

Standards

1. The Initiating Physician must consider abstinence-based treatment and/or opioid substitution tapering for withdrawal purposes for patients under 18 years of age.
2. The Initiating Physician must consider MMT for patients under 18 years of age only after a thorough assessment and discussion about all appropriate and available treatment options.
3. The Initiating Physician must ensure there has been a discussion with patients under 18 years of age (and other family members where appropriate, and with the consent of the adolescent if required) about the potential issues with methadone including side effects, risks and difficulty withdrawing and tapering off of methadone.
4. The Initiating Physician must consult with another MMT provider prior to initiating MMT in a patient under 18 years of age.

18. Special Situations: Pregnancy

This section outlines how to manage a pregnancy in an MMT patient.

Pregnant opioid-dependent women are at increased risk of obstetrical and medical complications, including prematurity and low birth weight leading to higher rates of infant morbidity and mortality. The benefits of MMT during pregnancy include improved prenatal care and social stability. Methadone crosses the placenta but has not been found to be teratogenic. Neonatal abstinence syndrome (NAS) is commonly associated with methadone exposure during pregnancy and other opioid agonists or partial agonists. Pregnant opioid dependent patients are considered high risk pregnancies and should be managed by physicians with appropriate expertise.

Pregnancy increases methadone metabolism in many patients and higher doses and/or split doses are often required. In order to maintain stability, methadone dosing will need to be adjusted throughout pregnancy and in the postpartum period.

All women of child bearing age on MMT are to be given appropriate advice about contraception and the risks and benefits of becoming pregnant while on MMT.

Standards

1. The Initiating or Maintaining Physician must offer MMT to pregnant opioid dependant patients on a priority basis.
2. The MMT physician will refer their pregnant MMT patient for obstetrical care as soon as pregnancy is confirmed.
3. All physicians caring for an MMT patient must communicate and collaborate with the obstetrical physician and hospital staff regarding the use of MMT during pregnancy, the plan for labour and delivery, and remain available for consultation and assistance as required.

Guidelines

1. Opioid dependant patients on MMT who become pregnant shall be encouraged to continue MMT during their pregnancy.
2. Methadone will not provide adequate pain relief during labour and additional analgesia should be considered. Regular methadone dosage should be continued and not considered as part of the pain management plan.
3. Physician providing obstetrical care should be encouraged to obtain temporary, patient-specific exemptions to prescribe methadone well in advance of patient admission.
4. MMT physicians should encourage breastfeeding during MMT (unless otherwise contraindicated), as methadone levels are low in breast milk and MMT reduces the symptoms of Neonatal Abstinence Syndrome (NAS).
5. Plans should be made well in advance for continuation of MMT during in-hospital perinatal care.
6. Physicians should consider split doses in the third trimester for patients who experience early withdrawal due to changes in their metabolism of methadone.
7. Postpartum maternal methadone requirements usually drop. The dose may need to be decreased by 5 to 10 mg weekly until a new stable dose is reached. Following the reduction in dose, split doses may no longer be required.
8. The MMT physician may need more frequent contact with the patient during the immediate postpartum period. This may include face-to-face visits, telephone or email contact.

19. Special Situations: Concurrent Diseases

In general, priority should be given to patients where the risks of ongoing illicit drug use by the individual are substantial. Concurrent medical conditions that may be considered to elevate risk include HIV, Hepatitis C or serious psychiatric illnesses.

The role of MMT in preventing infection with HIV is well-documented. HIV positive patients with an Opioid Dependence Disorder benefit from enhanced social, psychological and physiological stability during MMT. Their overall MMT and HIV treatment and compliance is enhanced.

Standards

1. Risks to the individual, society and public health must be evaluated when considering priority access to MMT.

Guidelines

1. Some medications used for the treatment of HIV/AIDS can affect serum methadone levels. Consultation with a knowledgeable physician or pharmacist is recommended. Adjustments to methadone dosage should follow the standards and guidelines in the “Dosages: Initiation Phase” and “Dosages: Maintenance Phase” sections.
2. Daily observed anti-retroviral treatment can be linked to daily witnessed ingestion of methadone and can assist in the patient’s compliance with a potentially difficult treatment regimen.

Appendix A.

Alberta Methadone Maintenance Treatment Standards and Guidelines Advisory Committee – Terms of Reference and Membership

May 29, 2012

1. Purpose

To provide advice and recommendations to the CPSA on updates and changes to the Standards and Guidelines for Methadone Maintenance Treatment in Alberta.

2. Scope

The Advisory Committee will provide counsel and advice in updating and revising the Standards and Guidelines for Methadone Maintenance Therapy in Alberta (published in 2005).

The Committee will advise the CPSA on the following:

- a) Strengths and challenges of the current Standards and Guidelines
- b) Changes in treatment and demand for services (since 2005) that need to be addressed in the revised Standards and Guidelines
- c) How changes to the Standards and Guidelines could result in increased consistency and access to safe clinical methadone maintenance treatment management
- d) How changes to the Standards and Guidelines could result in improved patient care, patient health and social outcomes
- e) What should be considered a “standard of practice” and what should be considered “best practice guideline”
- f) Quality of evidence and research gathered
- g) Providing feedback on the revised Standards and Guidelines
- h) The impact of the Standards and Guidelines on service demand levels

- i) MMT Standards and Guidelines from other jurisdictions

3. Membership

While the meetings of the Advisory Committee will be held in Edmonton, membership will consist of individuals from Northern and Southern Alberta, including representation from outside of the province's two major cities. Committee membership is comprised of the following individuals:

Barry Andres, Alberta Health Services
Colleen Babiuk-Ilkiw, Towards Optimized Practice
Dr. Ian Forster, Lifemark Health Institute
Shao Lee, Alberta College of Pharmacists
Dr. Ron Lim, Alberta Health Services Opioid Dependency Program
Dr. Richard Martin, Grande Prairie family physician
Dr. Mat Rose, Boyle McCauley Health Clinic
Wayne Spychka, Alberta Health
Doug Stich, Towards Optimized Practice
Dr. Michael Trew, Alberta Health Services
Dr. Hakique Virani, Metro City Medical Clinic

The CPSA was represented by:

Ed Jess, Director, Physician Prescribing Practices
Dr. Susan Ulan, Senior Medical Advisor,
Physician Prescribing Practices
Dr. Janet Wright, Assistant Registrar

4. Term

The Advisory Committee commenced in May 2012 and met many times in Edmonton. The revised Standards & Guidelines were first presented to Council in 2013 and distributed for public consultation in September to November 2013. The Standards and Guidelines received final approval from Council in December 2013, and were published in 2014.

Appendix B.

Important Information about Methadone Maintenance Treatment for all Physicians

The goal of MMT is to provide safe, effective and consistent treatment for individuals with opioid dependence. MMT is one component of a comprehensive treatment program for an opioid dependent patient.

Methadone is an oral long-acting synthetic opioid which is effective in treating both opioid dependence and for analgesic purposes. It is rapidly absorbed with a long half-life with the potential for accumulation which can lead to sedation, respiratory depression and death. This risk is greater when methadone is combined with alcohol, sedatives or other opioids. It is an important medication but it must be used cautiously and titrated individually for each patient.

For these reasons, there are requirements that physicians must meet before receiving authorization from Health Canada to prescribe methadone. To prescribe methadone for opioid dependence or for analgesia, physicians must be exempted under Section 56 of the Controlled Drugs and Substances Act which requires the approval of the College of Physicians & Surgeons of Alberta (CPSA).

For information on the CPSA Methadone Program and application process and requirements, please see the CPSA website at www.cpsa.ab.ca.

Other Important Information about Methadone:

- Risk of methadone overdose is highest in the early initiation stage
- A single dose of methadone may be fatal in an opioid naive individual
- Methadone can prolong the QTc interval and must be used cautiously in patients who are at risk of developing arrhythmias
- Methadone is metabolized by the cytochrome P450 system and physicians must be aware of potential drug interactions with methadone
- Physicians must access Netcare and/or Triplicate Prescription Program data to assist with patient care
- Random Urine Toxicology Testing is an integral part of routine MMT
- Missed doses must be managed carefully as tolerance to methadone may be rapidly lost and can result in unexpected overdose
- Open and ongoing communication between the physician, pharmacist and other treatment providers is essential to reduce the risk of harm

Appendix C.

Drug Interactions with Methadone

The following appendix outlines how methadone interacts with a variety of prescription medications. It is important to note that new prescription drugs are introduced frequently, and as a result, this may not be a comprehensive list of prescription medications that interact with methadone.

If a physician is unsure of the potential interaction between methadone and other medications, contact a pharmacist.

Anti-Infective	Increased Methadone Effect	Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
Antibacterials			Azithromycin Bedaquiline Ciprofloxacin Clarithromycin Erythromycin		
	Fusidic Acid		Gatifloxacin Gemifloxacin Levofloxacin		Only a concern with systemic formulations (No interaction with topical/ophthalmic formulations)
			Moxifloxacin Norfloxacin Ofloxacin Spirafloxacin Telavancin Telithromycin	Linezolid	
Antifungals	Fluconazole Itraconazole Ketoconazole Posaconazole Voriconazole		Itraconazole Ketoconazole Posaconazole		

Antihistamine		Increased Methadone Effect	Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
				Astemizole		
				Terfenadine		
		Cimetidine				
Antineoplastic					Procarbazine	
				Eribulin/Halaven		
		Lapatinib		Lapatinib		Inhibition of CYP 3A4 mediated metabolism of methadone AND additive QT interval prolongation effects
		Nilotinib		Nilotinib		
				Pazopanib		
				Sunitinib		
				Sorafenib		
				Crizotinib		
				Dasatinib	Dasatinib	
			Dabrafenib			Seek alternative drug therapy. If concomitant use can not be avoided, monitor closely for diminished therapeutic effects of methadone
		Thiotepa				Increases palisade concentrations of methadone
				Toremifene		
				Vandetanib		
				Vemurafenib		
Antiparkinson						
	Dopamine Agonists			Apomorphine		
				Arsenic Trioxide		
				Amantadine		
	Monoamine Oxidase Inhibitors	Rasagiline		Rasagiline		Combining this MAO-1 with methadone is contraindicated
					Selegiline	
Benign Prostatic Hyperplasia						
	Alpha-1 Blockers			Alfuzosin		

Gastrointestinal		Increased Methadone Effect	Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
	Anorexiant				Lorcaserin	
	Antacids	Cimetidine				Case report of severe respiratory depression with combined use (may not be clinically significant). May be used concurrently in some cases.
				Famotidine		
	Antiemetics			Granisetron		
				Ondansetron		
				Dolasetron		
				Droperidol		
		Meclizine				Additive CNS depressant / respiratory depression effects
	Prokinetics			Cisapride		
				Domperidone		
Neurological						
	Anticonvulsants		Carbamazepine			
			Fosphenytoin			
				Felbamate		
		Perampanel				May potentiate impaired cognitive and motor effects
	Migraine				Almotriptan	
Psychiatric						
	Antidepressants			Amitriptyline	Duloxetine	
				Amoxapine	Selegiline	
				Citalopram	Isocarboxazid	
				Ecitalopram		
				Imipramine	Phenelzine	
				Nortriptyline		
				Protriptyline		
		Desipramine		Desipramine		
			Desvenlafaxine			No action required. Monitor patient
		Doxepin		Doxepin		
		Fluvoxamine				
				Fluoxetine		
		Clomipramine		Clomipramine		Increased risk of constipation and urinary retention

Psychiatric, cont'd		Increased Methadone Effect	Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
				Sertraline		
	Tranlycypromine					Enhances the adverse/toxic effects of methadone
	Trimipramine			Trazodone Trimipramine		
					Tryptophan	
Antipsychotics				Asenapine Haloperidol Iloperidone		
	Loxapine					Additive CNS depressant effect
				Mesoridazine Paliperidone Pimozide		Use in combination with methadone contraindicated
			Risperidone			Use in combination with methadone contraindicated
				Quetiapine Clozapine Ziprasidone		Signs and symptoms of opioid withdrawal may be observed with concomitant use of risperidone
Barbituates	Amobarbital					Enhances the adverse/toxic effects of other CNS depressants but is often clinically appropriate. It is important to recognize that the risk of unwanted effects may increase with use.
	Butabarbital					Enhances the adverse/toxic effects of other CNS depressants but is often clinically appropriate. It is important to recognize that the risk of unwanted effects may increase with use.
	Methohexital					Increases risk of respiratory depression
	Phenobarbital					Increases risk of respiratory depression
Benzodiazepenes	Diazepam					Enhances the adverse/toxic effects of methadone
Phenothiazines	Fluphenazine					May enhance the hypotensive effect of methadone
	Perphenazine					Additive sedative and respiratory depressant effects
	Prochlorperazine					
	Promazine					
	Promethazine					
				Thioridazine		
	Trifluoperazine					Enhances the hypotensive effect of methadone

Psychiatric, cont'd		Increased Methadone Effect	Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
		Thiethylperazine	Dabrafenib			Additive sedative and respiratory depressant effects
		Thioridazine				Additive sedative and respiratory depressant effects
		Chlorpromazine		Chlorpromazine		Enhances the hypotensive effect of methadone
	Sedatives / Hypnotics			Chloral Hydrate		
		Fospropofol				Additive sedative and cardiorespiratory effects (reduction in dose of one or both drugs may be necessary)
Opioids						
	Opioid Antagonists/ Partial Agonists		Buprenorphine			May result in precipitation of withdrawal symptoms
		Tapentadol				Increase in CNS and respiratory depression
			Butorphanol			May result in precipitation of withdrawal symptoms
			Naltrexone			May result in precipitation of withdrawal symptoms
			Nalbuphine			May result in precipitation of withdrawal symptoms
			Pentazocine			May result in precipitation of withdrawal symptoms
			Dezocine			May result in precipitation of withdrawal symptoms
		Fentanyl				
Urologic						
	Anticholinergics (for incontinence)			Solifenacin		
Abortifacient						
		Mifepristone		Mifepristone		
Herbal Drugs						
		Cat's Claw	St. John's Wort			
		Chamomile				
Food						
		Grapefruit Juice				Monitor for the increased effect of methadone
		Ethanol				Avoid the concomitant use of alcohol and methadone. Advise patients to avoid this combination, due to potential CNS depressant effects
Respiratory						
				Formoterol		
				Salmeterol		

Increased Methadone Effect		Decreased Methadone Effect	QTc Prolongation	Serotonin Syndrome	Comments about Interaction
Other			Octreotide Galantamine Pasireotide Vilanterol Tetrabenazine		
	Cyclobenzaprine		Perflutren Lipid Microsphere		CNS agent, monoamine depletor Enhances the adverse/toxic effect of methadone. Risk for constipation and urinary retention
		Dexamethasone	Tizanidine		Dexamethasone is a CYP 3A4 inducer, therefore consider alternative steroid
MS Therapies	Sphingosine 1-Phosphate (S1P) Receptor Modulators		Fingolimod		

Comments:

1. PADIS has compiled this list of medications based on the current research and resources available (see reference list). No list is all inclusive and it is conceivable a medication which interacts with methadone or causes QTc prolongation may not appear on the list.
2. The cytochrome P450 system plays an important role in drug interactions involving methadone. Methadone is an inhibitor of CYP 2D6 and a substrate of CYP 3A4, 5, 7, and CYP 2B6. Consequently inhibitors of CYP 3A4, 5, or 7 will result in elevated methadone levels.
3. Management of potential drug interactions requires clinical judgement with consideration of drug and patient specific factors. In some cases, no specific action may be required, while in other cases close monitoring and/or changes in drug therapy might be warranted when an interaction is noted.
4. Practitioners wanting more information on the nature of these drug interactions are encouraged to call PADIS at 1-800-332-1414.

Appendix D.

Key Indicators of Stability and Instability

Indicators of Stability

The patient's level of stability and evaluation of the benefits of MMT are based on improvements in all areas of a patient's life.

The following are some of the indicators of patient stability. These indicators should be considered when:

- planning a transfer of care from the Initiating Physician to a Maintaining Physician
- a patient has requested carries and/or a non-crystalline suspension of methadone
- a patient is considering a voluntary withdrawal from methadone

It is important to note that in many cases, while a patient's dose can be stable and effective, the patient themselves may never be considered truly stable.

Methadone Dosage and Use of Other Substances Indicators

- Reported suppression or elimination of opioid withdrawal symptoms
- Reported reduction or elimination of craving for opioids
- Reported and documented absence of over-sedation or euphoria on current dosage
- Reported evidence of the reduction or elimination in the number of injection drug-use events
- Demonstrated awareness of resources to obtain clean injection apparatus and knowledgeable in proper cleaning and non-sharing of equipment
- Demonstrated knowledge of the serious health consequences of CNS depressant use when combined with methadone
- Reported management of methadone related side effects

- Evidence of unadulterated urine samples that are absent of proscribed substances
- Demonstrated personal and social stability
- Reported sense of well-being
- Reported active avoidance of situations that are recognized triggers for relapse
- Abstinent social support systems identified and in place
- Demonstrated efforts to achieve positive lifestyle changes
- Positive supportive information from treatment team members
- Demonstrated mechanisms in place for the safety and storage of carries

Medical and Psychiatric Issue Indicators

- Documented stabilization of acute medical conditions
- Established attendance for ongoing health care for chronic conditions
- Demonstrated improvement in overall health status
- Noted improved dental health and hygiene
- Stable medical and mental health status
- No reports of accidental overdose
- The patient has an ongoing relationship with a primary care provider who has knowledge of or is the prescriber of the methadone

Basic Necessities Indicators

- Provisions made for food, clothing, housing and safety needs and financial assistance if necessary
- Demonstrated management of basic personal care activities
- Relatively stable and secure living conditions

- Receipt of prenatal care
- Documented established childcare resources
- Transportation resources available
- Documented stable source of income
- Demonstrated involvement in productive activity: school, employment, volunteering
- Reported involvement in healthy and safe leisure activities

Relationship Indicators

- Documented regular attendance for medication, UTT, counseling and medical appointments
- Documented follow up with appropriate resources as per patient assessment and agreed upon treatment goals
- Reported positive interactions with treatment team members
- Reported maintenance of positive support systems

- Reported absence of major conflict within family support system
- Reported resolution of, or ongoing efforts to resolve, legal problems
- Evidence of no illegal activities

Indicators of Instability

- Positive UTTs
- Fraudulent urine specimen
- Missed appointments or DWIs
- Multiple doctoring
- Unstable and insecure living arrangements and social environment
- Unstable dosing pattern
- Pattern of missed doses
- Evidence of unstable medical psychiatric and social instability

Appendix E.

Diagnostic Criteria for Substance Dependence

*Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders IV, Text Revision, Copyright 2000, American Psychiatric Association.**

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:

- a. The need for markedly increased amounts of the substance to achieve intoxication or the desired effect
- b. Markedly diminished effect with continued use of the same amount of the substance

2. Withdrawal, as manifested by either of the following:

- a. The characteristic withdrawal syndrome for the substance
- b. The same (or a closely related) substance is taken to relieve (or avoid) withdrawal symptoms

3. The substance is often taken in larger amounts or over a longer period than was intended.

4. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
5. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple physicians or driving long distances), use the substance (e.g., chain smoking), or recover from its effects.
6. Important social, occupational or recreational activities are given up or reduced because of substance use.
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was worsened by alcohol consumption).

Specify if:

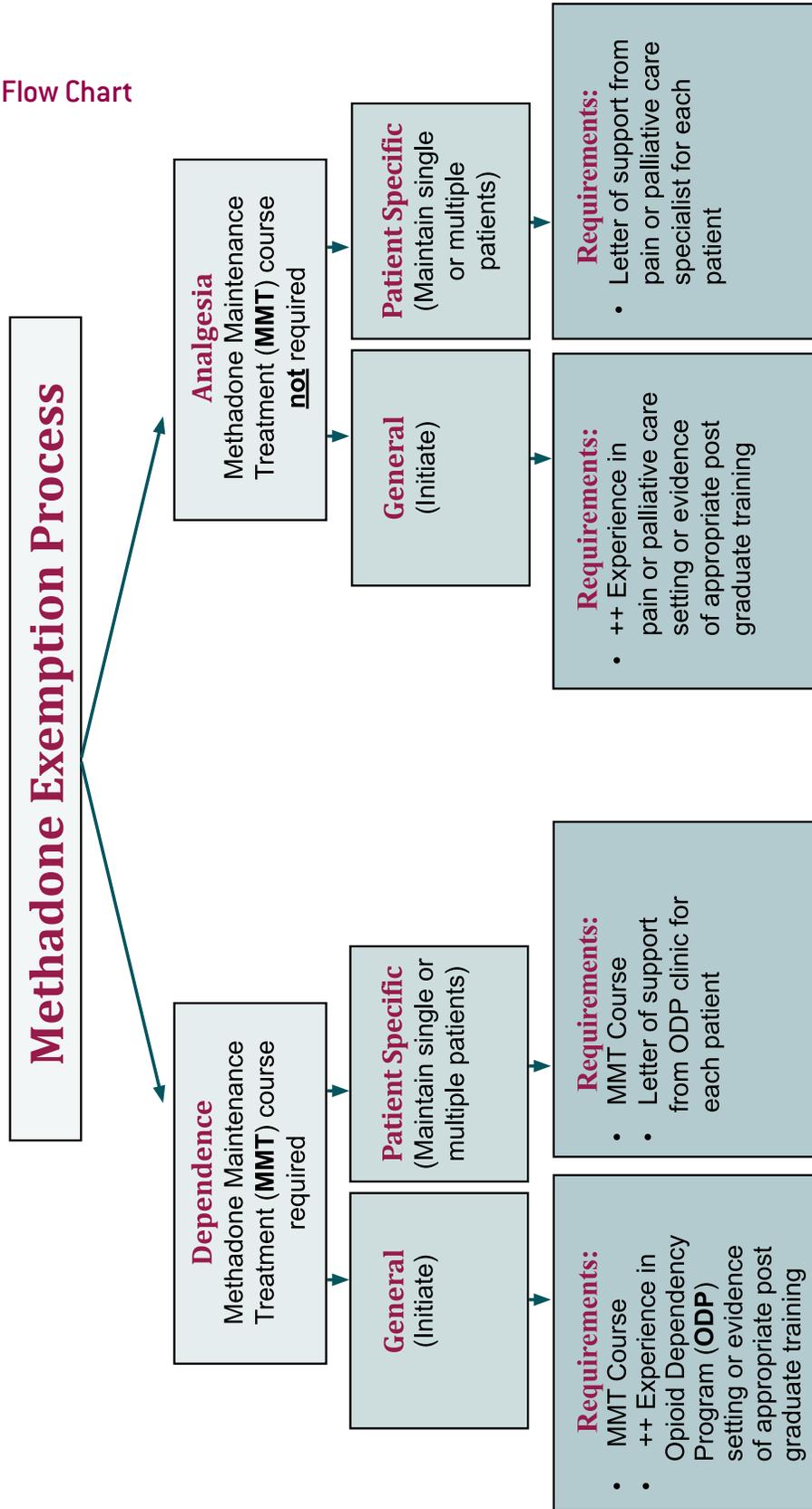
With Physiological Dependence: evidence of tolerance or withdrawal (e.g., either item 1 or 2 is present).

Without Physiological Dependence: no evidence of tolerance or withdrawal (e.g., neither item 1 nor 2 is present).

**Please note that in May 2013, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, DSM-V, was published. The section Substance Use Disorders now combines substance abuse and substance dependence into a single disorder measured on a continuum from mild to severe. Each specific substance is addressed as a separate use disorder (e.g. opioid use disorder). For more information on the revised chapter of "Substance Use Disorder", please see the following link: <http://www.dsm5.org/Documents/Substance%20Use%20Disorder%20Fact%20Sheet.pdf>*

Appendix F.

Methadone Exemption Flow Chart



Appendix G.

Health Canada Methadone Exemption Application Form, pg 1 of 3



Health
Canada

Santé
Canada

Methadone Exemption Application Application pour une exemption



College of
Physicians
& Surgeons
of Alberta

1. Physician Information/Information du médecin

Surname/Nom:		Given Name/Prenom:	
License Number/Numéro de licence:			
Specialty/ Spécialité:			
Post Graduate Training/ Formation professionnelle:			
Primary Practice Address/ Adresse du lieu d'exercice:	Institution:		
	Street/Rue:		
	City/Ville:		
	Province:		
	Postal Code/Code postal:		
Telephone Number/Numéro de Téléphone:	Fax Number/ Numéro de Fax:		
E-mail Address/ Courriel:			
Mailing Address (if different from above) Adressé de correspondance (si Différente)			
Language/Langue	English <input type="checkbox"/>	Français <input type="checkbox"/>	

2. Exemption

Indication:	Dependency/ Dépendance <input type="checkbox"/>	Analgesia/Analgésie <input type="checkbox"/>
Additional Information/Informations complémentaires:	General/ Général <input type="checkbox"/> (Initiation/ lancement)	Patient Specific/ pour patient(e) seulement <input type="checkbox"/> (Maintenance/ entretien) If patient specific, name of patient(s)/ nom du/de la patient(e):

3. Qualifications and Experience/ Qualifications et Expérience

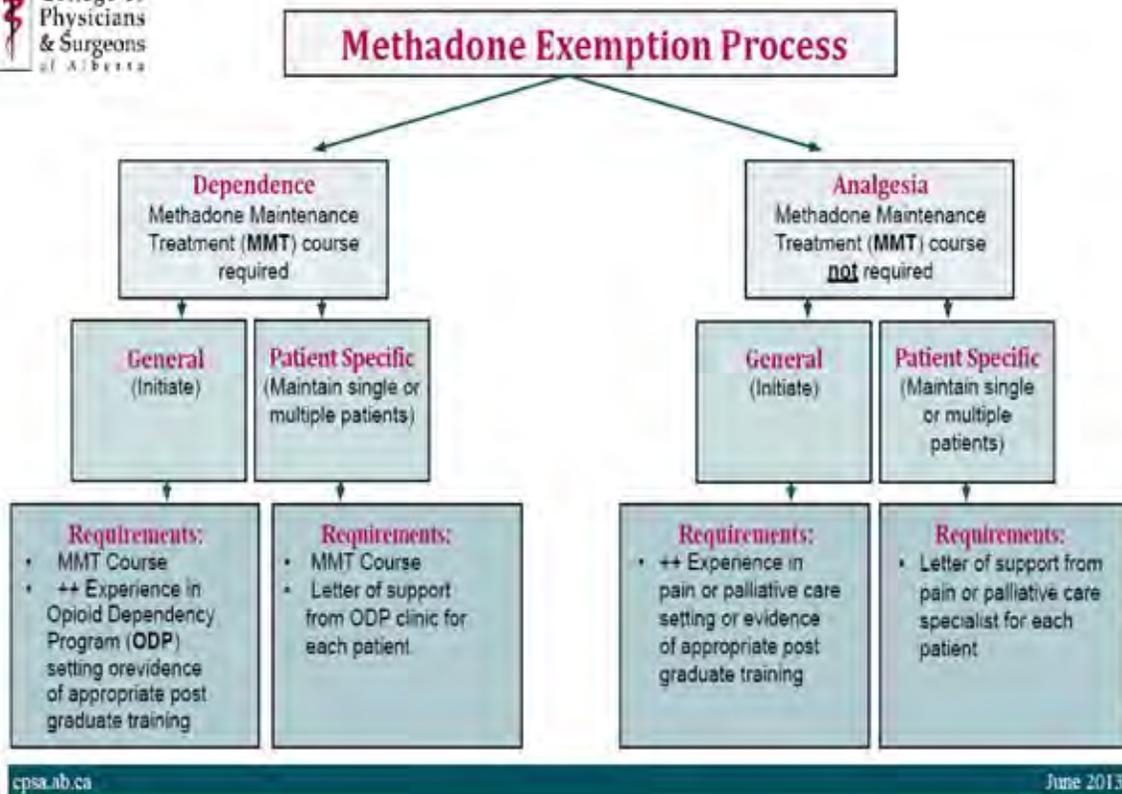
Describe qualifications and experience with methadone (courses, seminars, conferences, etc)/ Décrire qualifications et expérience avec la methadone (cours, séminars, conférences, etc.):

Type of practice/Type de pratique:

Solo/ seul

Group/ en groupe

4. College of Physicians & Surgeons of Alberta Requirements for Prescribing Methadone



*** Information required must be submitted before consideration can be given to your application***

4. Declaration

By, this and under the condition that the released information is treated confidentially, I request the College of Physicians and Surgeons of Alberta (CPSA) recommend to the Office of Controlled Substances, Health Canada, that I be exempted from the application of subsection 5(1) of the Controlled Drugs and Substances Act with respect to methadone.

Par la présente, et sous la condition que l'information publiée est traitée de façon confidentielle, je demande au Collège des médecins et chirurgiens de l'Alberta (AFPC) de recommander au Bureau des substances contrôlées, Santé Canada, que je sois exempté de l'application du paragraphe 5 (1) de la Loi réglementant certaines drogues et autres relativement à la méthadone.

Signature:		Date:	

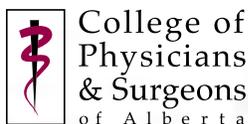
Please send the application to the address below/ Veuillez faire parvenir la demande à l'adresse ci-dessous :

Methadone Program
College of Physicians & Surgeons of Alberta
2700 - 10020 100 Street NW, Edmonton AB T5J 0N3
Phone (780) 969-4944
Fax (780) 420-0651

A copy of the application may be faxed to (780) 420-0651 or emailed to/ Une copie de la demande peut être envoyée par télécopieur au (780) 420-0651 ou par courriel à MethadoneInfo@cpsa.ab.ca

Appendix H.

Application for Temporary Methadone Exemption to Prescribe Methadone in a Hospital or Correctional Facility



College of
Physicians
& Surgeons
of Alberta

Application for Temporary Methadone Exemption to Prescribe Methadone in a Hospital or Correctional Facility

TO:

National Compliance and Exemption Division
Health Canada Office of Controlled Substances
150 Tunney's Pasture Driveway
Tunney's Pasture, AL 0300B
Ottawa ON K1A 0K9

Phone: 1-866-358-0453

FAX: 613-952-8576

Email: exemption@hc-sc.gc.ca

In Alberta, the temporary exemption is valid for a maximum of 60 days and includes an authorization to prescribe methadone at the patient's current dose. Any change in the methadone dose must have the approval of a physician with a general methadone exemption. Physicians with temporary exemptions are not permitted to initiate patients on methadone.

Physician's Full Name:	
Physician's License #:	
Physician's Phone #:	
Name and Address of Hospital or Correctional Facility:	
Patient's Full Name:	_____
	Male <input type="checkbox"/> or Female <input type="checkbox"/>
Methadone Indication:	Dependence <input type="checkbox"/> or Analgesia <input type="checkbox"/>
Methadone Dose:	
Date requesting physician wrote prescription: (Not the date the prescription is to start, unless they are the same)	
Pharmacy Phone #:	
Name of Person calling/faxing/e-mailing:	
Verbal Authorization from Health Canada Given to: (for Health Canada purposes)	
Date Verbal Authorization Given:	
Time Verbal Authorization Given: (for Health Canada purposes)	

Appendix I.

Methadone Dosing Initiation Chart

Methadone Dosing – Initiation

Patient Factors	Initial Dose	Dose Increase	Frequency
Low Risk of Methadone Toxicity	30 mg or Less	10 mg	No more than every 3 days during early and late stabilization
Moderate Risk of Methadone Toxicity	20 mg or less	10 mg	No more than every 4 days during early and late stabilization
High Risk of Methadone Toxicity	10 mg or less	5 mg or less	No more than every 5 days during early and late stabilization

Appendix J.

Methadone Missed Doses Chart

Methadone – Missed Doses*

Number of Missed Doses	Action	Dose Change
1 Day Missed	Consider review of dose and prescription.	<p>May resume same methadone dose</p> <p>During initiation or early stabilization:</p> <ul style="list-style-type: none"> • For low risk of methadone toxicity: methadone dose must be maintained for at least 3 days at the same dose • For moderate risk, dose maintained for 4 days at the same does • For patients at high risk, dose maintained for 5 days at the same dose
2 Consecutive Days Missed	Cancel remainder of the prescriptions and write new prescription	Methadone dose decrease by at least 25%
2 Out of 7 Days Missed	Reassess by initiating physician on a priority basis	Consider methadone decrease by at least 25%
3 Days Missed	Cancel prescription and patient must be reassessed by the initiating physician	Methadone dose decrease by at least 50%

**Communication with the initiating physician must occur for all missed doses, regardless of the cause.*

Appendix K.

Sample Triplicate Prescription and Dispensing Schedule – Methadone Initiation

Methadone prescriptions are written on the physician's personalized triplicate prescription and must clearly specify all of the following:

- Start/end dates
- Methadone dose in a form that reduces its risk of diversion
- Days of the week requiring daily witnessed ingestion (DWI)
- Carried doses with days specified
- Instructions on missed doses and special instructions

THIS METHADONE DISPENSING SCHEDULE FORMS PART OF THE TRIPLICATE PRESCRIPTION NUMBER

11227101

THAT REPLACES ALL PREVIOUS METHADONE PRESCRIPTIONS

Patient Name: Test Test
 Pharmacy: Downtown Prescription Centre Phone: 7804292988 Fax: 7804292982

Rx: Methadone solution mixed with a crystalline juice such as Tang®. For methadone maintenance.
Pharmacist please note: This prescription is limited by the dispensing dates, for which first and last dates are clearly indicated. The total amount prescribed is provided to allow timely reporting to the CPISA TPP. The actual amount dispensed may be less due to, for example, missed doses. Report all missed or vomited doses, or any concerns, to the prescribing physician/Methadone Maintenance Treatment Program.
****A dose should never be provided if the patient is intoxicated.****
****Under no circumstances should a dose be provided beyond the last date for which a "daily dose" is indicated.****
 Metro City Medical Clinic (Phone 780-429-3991; Fax 780-429-3988)

Methadone Dose (mg)	First date dose	Last date dose	Total (mg)
20	2014/02/01	2014/02/04	80
30	2014/02/05	2014/02/08	120
Total dose (mg):			200

All doses are daily witnessed ingestion except the following Carried Doses:
****NO CARRIES****
 Prescriber Signature: 
 Prescriber Name: Hakiq Virani

ALBERTA TRIPLICATE PRESCRIPTION FORM
 Void after three days. Take both copies to pharmacy of choice. PLEASE PRINT

HEALTH CARE NUMBER: 515151-011211 DATE ISSUED: 14.02.01
 TEST O. TEST
 MALE DATE OF BIRTH: 80.08.28
 NO FIXED ADDRESS
 EDMONTON AB.

ONLY ONE DRUG/DOSAGE PER FORM NO REFILLS PERMITTED

METHADONE IN JUICE
 - 200 - TWO HUNDRED -

IN JUICE PER SCHEDULE FOR METHADONE MAINTENANCE

My Subscription: 
 DR. HAKIQ VIRANI 11318
 10419 102 AVE NW
 EDMONTON AB T5J 0B4
 780-429-3991 11227101
 PHARMACY USE ONLY

DATE DISPENSED:

5395381

Appendix L.

Sample Triplicate Prescription and Dispensing Schedule – Methadone Maintenance

THIS METHADONE DISPENSING SCHEDULE FORMS PART OF THE TRIPPLICATE PRESCRIPTION NUMBER

10961202

THAT REPLACES ALL PREVIOUS METHADONE PRESCRIPTIONS

Patient Name: Test Test

Pharmacy: Medicine Shoppe #225

Phone: 7804771192

Fax: 7804775127

Rx: Methadone solution mixed with a crystalline juice such as Tang®. For methadone maintenance

Pharmacist please note: This prescription is limited by the dispensing dates, for which first and last dates are clearly indicated. The total amount prescribed is provided to allow timely reporting to the CPSA TPP. The actual amount dispensed may be less due to, for example, missed doses.

Report all missed or vomited doses, or any concerns, to the prescribing physician/Methadone Maintenance Treatment Program.

A dose should never be provided if the patient is intoxicated.

Under no circumstances should a dose be provided beyond the last date for which a "daily dose" is indicated.

Metro City Medical Clinic (Phone 780-429-3931; Fax 780-429-3988)

Methadone Dose (mg)	First date dose	Last date dose	Total (mg)
85	2014/06/01	2014/06/28	2380
Total dose (mg):			2380

ALBERTA TRIPPLICATE PRESCRIPTION FORM

Void after three days.
Take both copies to pharmacy of choice.
PLEASE PRINT

HEALTH CARE NUMBER: 55555-01121 | DATE ISSUED: 14.06.01

TEST O. TEST

MALE FEMALE | DATE OF BIRTH: 80.08.28

123 NICEPLACE, DOORS ROAD
EDMONTON AB.

ONLY ONE DRUG/DOSAGE PER FORM NO REFILLS PERMITTED

METHADONE IN JUICE
-2380 - TWO THOUSAND, THREE HUNDRED EIGHTY

IN JUICE PER SCHEDULE FOR METHADONE MAINTENANCE

No Substitution:  11318

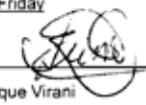
DR. HAKIQE VIRANI
10419 102 AVE NW
EDMONTON AB T5L 0B4
780-429-3991

11227102

PHARMACY USE ONLY

DATE PRESCRIBED: [SAMPLE Rx]

All doses are daily witnessed ingestion except the following Carried Doses:
Monday, Wednesday, Friday

Prescriber Signature: 

Prescriber Name: Hakiq Virani

5395383

Appendix M.

Methadone Maintenance Treatment Agreement – Sample

This is an agreement for methadone maintenance treatment between

_____ and _____
(patient/client) (physician/clinic)

1. I understand that the methadone maintenance doctor will perform an assessment and medical examination, will establish the diagnosis of an Opioid Dependence Disorder, and will prescribe methadone if it is considered appropriate and safe for me.
2. I agree to take methadone under medical direction, to assist me in dealing with my opioid dependence. I have tried or considered other treatment options. I understand that methadone is generally a long-term treatment.
3. I understand that I will become physically dependent on methadone and will experience withdrawal symptoms if I suddenly stop taking it.
4. I understand that methadone may cause drowsiness especially when starting treatment or when I receive increases in my dose. As a result, this may impair my ability in operating motor vehicles.
5. I am aware that the methadone maintenance treatment team may consist of several professionals including doctors, pharmacists, nurses, counsellors, social workers and support staff, who will be in close communication with each other to assure safety in my care.
6. For safety reasons, the methadone doctor will contact my doctor in order to ensure that each is fully aware of the treatment being provided by the other.
7. I recognize that counselling and other addiction assessments are available to assist me in dealing with the psychological and social difficulties that can accompany problems of opioid dependence.
8. I understand that when on methadone, taking other narcotics (e.g. Tylenol #1, 2, 3, 4, codeine, morphine, oxycodone, hydromorphone, fentanyl) and/or other substances, especially alcohol and benzodiazepines (Ativan, Lectopam, Restoril, Rivotril, Serax, Valium, Xanax) could be dangerous, especially if taken in excess. These drugs may interact with methadone and cause overdose, coma, or even death.
9. I agree that when I see another doctor or dentist, I will inform them that I am taking methadone. I agree to provide copies of any prescriptions obtained by me for medical reasons to be reviewed by the methadone maintenance doctor. The treatment team, if necessary, may do follow up with the prescription doctor. I understand that in certain cases, the methadone prescribing doctor might not feel comfortable with prescribing methadone to me in combination with other medications that I have been prescribed.
10. I understand that initially I will be required to consume methadone daily under the direct observation of a pharmacist or other qualified health care professional. Even after carry privileges have been granted (see #11), I will still be required intermittently to drink a dose of my methadone under direct pharmacy or health care supervision.
11. I am aware that I may be granted a limited number of take-home carries of methadone once I have demonstrated sufficiently that I am no longer continuing to use illicit and/or other non-prescribed drugs and have made obvious positive and stable lifestyle changes. Carries may also be considered for specific reasons such as work/school. Carry privileges may not be provided if I miss clinic or medical appointments, not provide urine samples for toxicology testing when requested, misuse or divert my carries, as examples.
12. I realize that methadone can be fatal to others and will keep many methadone in my possession secure.

13. I understand that I must satisfy the doctor prescribing methadone for me that I have made all necessary arrangements to ensure the safety of myself and others, where carries are involved. This may include transporting and storing carries in a locked box or other secure container.
14. I realize that if I use my carries inappropriately, further carries will be suspended.
15. I understand that missed doses will be recorded on my file and will result in actions to ensure my safety. These may include a reduction or suspension of my dosage until I am reassessed.
16. I understand that the College of Physicians and Surgeons of Alberta (CPSA), Triplicate Prescription Program (TPP) monitors methadone prescriptions, and as such my prescription information will be recorded. This may involve the occasional review of my file by an external reviewer to ensure that my medical treatment is delivered in a safe manner. None of the information on my file will be given to anyone outside this review process.
17. I understand that all clinical information on my file is confidential and will not be released to anyone without my written consent, except where staff believes there is a medical emergency and intervention is required by clinical staff and/or other persons.
18. I agree to attend ongoing medical examinations, urine drug testing, other laboratory testing, and counselling appointments when required.
19. A witnessed collection may be required in the following examples: an invalid sample based on its temperature, results or repeated missed appointments for the required urine drug testing.
20. I agree to behave in a respectful manner towards all treatment team members and other patients/clients.
21. I understand that any violence, threats of violence, verbal abuse or disruptive behaviour, or diversion of my methadone, will not be tolerated and could result in my termination from treatment.
22. I understand that my dose may be decreased and then stopped if it is determined that I am not benefitting from methadone maintenance treatment. Involuntary withdrawal from methadone may be more rapid if it is medically indicated for my safety or the safety of others.
23. I understand that it is my responsibility to be aware that my prescription is coming due and take the appropriate steps (e.g. make an appointment to see my doctor) to get it filled.

The undersigned fully understands the conditions of this agreement, agrees to the provisions in full and has received a copy of this document.

Patient/client signature

Witness signature

Date

Date

Addendum to Methadone Maintenance Treatment Agreement

I understand that the pharmacist and other staff at the pharmacy are a part of the treatment team.

I will ensure my behaviour is always respectful and honest towards this important part of the team, and I will not engage in any activities in or around the pharmacy that may have a negative impact on the pharmacy, its staff, clients or customers.

Patient signature

Pharmacy representative signature

Date

Pharmacy representative name and title

Appendix N.

Alberta College of Pharmacists Three-Way Agreement

Alberta College of Pharmacists: Prescriber-Pharmacy-Patient Three-Way Agreement for MMT*

Your prescriber prescribed methadone maintenance treatment for your opioid dependence disorder. Our pharmacy will provide the services for methadone maintenance treatment.

Methadone is a medication that is generally taken long-term and will require your commitment and responsibility to take the drug only as prescribed. A pharmacist will determine if it is safe for you to take your daily dose and then watch you as you ingest the dose. Observation of daily doses will continue until your doctor considers that you may be ready to try

take-home doses. Some patients may never be considered for take-home doses if their personal safety and the safety of the community are of concern.

Your doctor or program service providers and pharmacist will work together to support you. They may consult each other, your family doctor (as applicable), or other members of your treatment team if issues and concerns arise as you progress with your treatment. You are also welcome to consult your doctor or pharmacist as needed if you have concerns about your condition or your treatment.

This agreement is between:

Your pharmacy and its staff

Your prescriber

You, our patient

This agreement outlines responsibilities and obligations of each party to ensure a mutual understanding and awareness of the expectations involved in our collaboration. The entire agreement is detailed in the following pages.

Your pharmacy agrees to provide you with:

- Professional, non-judgmental services that recognize your rights to respect and personal dignity.
- Access to trained professionals who are competent in methadone maintenance therapy to answer your questions and concerns about your treatment(s).
- Professional expertise, skills, and knowledge about your treatment that will always have your best health interests in mind for decisions that are made.
- Privacy and confidentiality with your private and health information. Your private information will only be shared with your consent or if we are required by law.
- Ongoing monitoring of your response and progress with methadone while you remain under the pharmacy's care.

Your doctor agrees to provide you with the following:

- Professional, non-judgmental, services that recognize your rights to respect and personal dignity.
- Professional expertise, skills, and knowledge about your treatment that will always have your best health interests in mind for decisions that are made.
- Regularly scheduled appointments offered at a frequency that is deemed necessary for your personal health and safety and that is based on your progress and needs while on methadone treatment.
- Ongoing monitoring of your response and progress with methadone while you remain in his or her care.
- Privacy and confidentiality with your private and health information. Your private information will only be shared with your consent or if required by law.

As the patient on the methadone treatment, I agree to:

1. Take methadone as treatment for my opioid dependence. I will take it as prescribed by my doctor. I will let my doctor and/or pharmacist know if I am

experiencing any withdrawal effects or any side effects from the treatment.

2. Keep my appointments with my doctor. I know that my doses of methadone will only be prescribed if my doctor can monitor my response and progress. I know that my appointments are especially important in the initiation phase of therapy until I am stabilized on methadone because the first few weeks of therapy is a time when patients can be harmed by therapy. If I do not keep my appointments, my doctor may no longer be able to prescribe the drug to me.
3. Keep my regular daily meeting with my pharmacy to receive my daily methadone dose. I will make every effort to be punctual and reliable and I will call the pharmacy if I am going to be late. If I am not compliant with my daily doses, I am aware that my methadone treatment may have to stop as it can pose a danger to me to have inconsistent dosing with methadone.
4. Bring and show my photo ID each time I visit my pharmacy for my daily dose.
5. The pharmacy calling my doctor they have any concerns about my safety on the treatment(s).
6. The pharmacy calling my doctor if a dose is missed, lost, stolen, and/or partially administered.
7. Call the local police, as well as my pharmacist and my doctor, if I lose a dose or if a dose in my possession is stolen, as the drug may be dangerous to the community.
8. Inform any other doctor, dentist, or pharmacy that I am on methadone treatment. I will also inform my pharmacy and methadone maintenance doctor of any other medication that I am prescribed as I realize that some treatments may interact with methadone and cause harm to me. My methadone doctor may be more aware of this issue than a doctor not trained in this specialized treatment.
9. Keep both my doctor and pharmacist informed of all the drugs (prescription and non-prescription) that I am taking, including natural health products and vitamins.
10. Take urine tests or other tests required to monitor progress and safety on methadone treatment as directed by my doctor or pharmacist.
11. Be polite and respectful while on the premises of the pharmacy. I agree that I will not be disruptive, violent, abusive, or threaten or cause harm to anyone or to any property. I acknowledge that bad behaviour may result in the termination of my services from the pharmacy. Also, some offences may be brought to the attention

of law enforcement as determined by provincial and federal legislation.

As the patient on the methadone treatment, I am aware that:

1. The pharmacy will not provide me with my daily methadone dose if I arrive intoxicated or with other symptoms where taking the methadone dose may be harmful to me.
2. Methadone may cause drowsiness, especially at the initiation of therapy and when doses are adjusted. I agree not to drive or operate machinery that requires my alertness when I am being initiated on therapy (typically the first two weeks) or when I am having doses adjusted or if I am having treatment effects that are making me sleepy and not alert.
3. Taking narcotics, sleeping pills, alcohol, or other sedating substances may interact with methadone to cause overdose, coma, or even death. I will not take other medications unless prescribed by either my methadone or pain doctor or my family doctor (if different).

Through this agreement, I have been made aware that in Alberta, the laws that govern physicians and pharmacists require that the Triplicate Prescription Program is used to monitor methadone and other narcotic prescriptions. This information will be recorded. This may involve occasional review of my file by an external reviewer working within the regulatory colleges of physicians or pharmacists to view my health files or the pharmacy's prescription files. I am aware this is a legal requirement that my prescriber and pharmacist do not control that is part of the regular auditing and inspection process of their respective governing bodies. I understand that my personal health information may be shared in such circumstances as required by law.

Patient signature

Pharmacy representative signature

Date

Prescriber signature

Date

**Alberta College of Pharmacists Medication-Assisted Treatment for Opioid Dependence: Guidelines for Pharmacists and Pharmacy Technicians (2013)*

Appendix O.

Initial Patient Assessment Form – Sample

Name: _____

Age: _____

Date: _____

Expectations of/Goals for MMT – Why treatment? _____

Drug of choice: _____

Second drug of choice: _____

Addiction history: [c = current (past three months); p = past]

Include all: opioids, alcohol, benzodiazepines, cocaine, amphetamines, prescription stimulants, hallucinogens, solvents, tobacco, cannabis, steroids

Substance/first use	Route/progression/typical amount/frequency	Last use
	c	
	p	
	c	
	p	
	c	
	p	

How drug use started: _____

How opioid use started: _____

Length of opioid addiction: _____

Drug attitudes

What patient likes about opioid use: _____

What patient dislikes about opioid use: _____

Perceived control over drug use: yes ____ no ____

Triggers: _____

Drug behaviour

Needle injections a day: current ____ at peak use ____

Needle source: _____

Opioid source: current _____ at peak use _____

Opioid prescriptions: current _____
past _____

Money spent on drugs: current _____ at peak use _____

Source of money for drugs: current _____ at peak use _____

Typical day (time getting, using, recovering from drugs)

current _____

past _____

Risk behaviours (needle sharing, crime, driving, safe sex, sex work):

current _____

past _____

DSM Criteria

Need for increasing dose over time: yes ____ no ____

Used more than planned: yes ____ no ____

Drug overdoses: yes ____ no ____

Hospital admissions or other significant health consequences resulting from drug related illness: yes ____ no ____

Presence of withdrawal symptoms (dysphoria, insomnia, myalgia, lacrimation/rhinorrhea, sweating, piloerection, papillary dilation, nausea/vomiting/diarrhea): _____

Addiction treatment

Attempts to cut down or stop: yes ____ no ____

How tried to cut down or stop: _____

Past treatment of addiction (detox, structured treatment program, methadone, NA/AA): _____

Plans for treatment of other current drug problems: _____

Longest period in full remission: _____

Factors involved in relapse: _____

Effects of drug use on life

Family: _____

Friends: _____

Crime: _____

Housing: _____

School: _____

Job: _____

Physical health: _____

Mental health: _____

History of behaviour addiction (gambling, internet, exercise, shopping, sex, work, eating): _____

Immunization (HAV, HBV) _____ Date _____

Current medications (prescribed, OTC, herbal, contraception, allergies): _____

Current MDs: _____

Current medical problems (including HIV, HCV, psychiatric): _____

Past history (admissions): _____

Past transfusions: _____

History of abuse: _____

Family history (addiction, psychiatric, ischemic heart disease, hypertension, stroke, diabetes, cancer, respiratory (emphysema/COPD), neurologic (Parkinson's), liver)

Father: _____

Mother: _____

Sister(s): _____

Brother(s): _____

In women

G: _____ P: _____ TA: _____ Miscarriage: _____ Adopted out: _____

First day of LMP: _____

Menstrual cycle characteristics: _____

Current contraception method: _____

Social history

Financial: _____

Employment: _____

Education: _____

Drug plan: _____

Relationship: _____

Family: _____

Children: _____

Housing: _____

Legal: _____

Sexual: _____

Review of systems allergies

Skin: tattoos, piercing

Neuro: vision, weakness, headache, paresthesia

ENT

CVS: edema, chest pain, palpitations

Resp: SOB, cough, smoking

GI: pain, swelling, constipation

MSK: arthralgia, myalgia

GU: hematuria, retention, LMP, birth control

Psych: depression, sleep, suicidal ideation, anxiety

Fatigue: _____

Weight: _____

Appetite: _____

Pain: _____

Mood: _____

Smoking: _____ PPD: _____ Pack years _____

Examination

BP: _____

Weight: _____

Height: _____

BMI: _____

Pulse: _____

General appearance: _____

Skin: tattoos _____ piercings _____

Spiders/palmar erythema, jaundice: _____

Track marks: _____

Eyes: pupil size _____

ENT: _____

Teeth: _____

Thyroid: _____

Adenopathy: _____

Neuro: _____

Chest: _____

CVS: _____

peripheral edema: _____

Abdomen: _____ Ascites: _____ Liver: _____ Spleen: _____

GU: _____ Testes: _____

MSK: _____ Dupuytren's: _____

Psych: _____ Depression: _____

Plan

- Discuss methadone benefits and drawbacks.
- Methadone - start date and dose: _____
- Initial blood work (CBC, Lytes, AST, ALT, GGT, TBili, ALP, Cr, BUN, Albumin, INR, PTT, FBG, Lipids: TC, TG, LDL, HDL, TSH)

- Pre-test counseling for HIV, Hep BsAg, Hep CAbs, VDRL/RPR +/-bHCG
- Contract signed
- Urine Toxicology Test
- Sign release of info for past records
- TPP/Netcare profile obtained
- Psychosocial support plan

Physician signature: _____ Date: _____

*** The information presented in this appendix was drawn from the College of Physicians and Surgeons of Nova Scotia: Methadone Maintenance Handbook: May 2012.*

Appendix P.

Methadone Maintenance Clinical Note – Sample

Name: _____

Date: _____

Current Methadone Dose: _____ mg

Number of Take-home

Doses: _____

Missed doses: Yes _____ No _____

Psychological Issues Update:

Mood: Normal – Other _____

Sleep: Normal – Insomnia

Anxiety: Absent – Present

Energy: Normal – Other _____

Suicidal Ideation: Absent – Present – NA

Supervised UDS: O/E:

Methadone: _____

Cocaine: _____

Opiates: _____

Benzodiazepines: _____

Oxycodone: _____

Creatinine: Normal/Abnormal _____

Interpretation of UDS _____

O/E:

Appearance: Alert – Intoxicated

Behaviour: Normal – Abnormal

Gait: Normal – Abnormal

Speech: Normal – Abnormal

Eye contact: Normal – Abnormal

Patient stated drug/alcohol use & route

Since last visit:

Opiates: Yes _____ No _____

Cocaine: Yes _____ No _____

Benzodiazepines: Yes _____ No _____

Alcohol: Yes _____ No _____

Other problematic drug use: Yes _____ No _____

Reported methadone sedation: Yes _____ No _____

Reported methadone withdrawal: Yes _____ No _____

Take-home dose safety issues discussed: Yes ___ No ___

Take-home dose locked up in a box: ___ No ___ – NA

Safe with take-home dose: Yes _____ No _____

Stable housing: Yes _____ No _____

Stable employment/social support: Yes _____ No _____

Reviewed dangers of methadone diversion:
Yes ___ No ___ – NA

Clinically stable: Yes _____ No _____

Opioid Cravings:

None – Mild – Moderate – Severe

Opioid Withdrawal:

None – Mild – Moderate – Severe

Opiate Withdrawal Symptoms:

None – Insomnia – Anxiety – Dysphoria – Nausea
– Diarrhea – Hot flashes – Irritability – Myalgia –
Restlessness – Rhinorrhea – Sneezing – Sweats –
Yawning – Pupil dilated – Malaise – Abdominal Cramping
– Piloerection

Timing of Withdrawal from Last Dose: _____

Counselling/Clinical Notes: _____

Plan:

Rx: Methadone ___ mg po od from _____ to _____

Take-home doses: M T W T F S S
for _____ week(s) RTC _____ day/week

Appendix Q.

Take-Home Dose Agreement – Sample

Things you are expected to do when you are allowed to get take-home methadone

Methadone is a strong drug, and when people are allowed to take it home from the clinic or pharmacy, they have to be very careful with it. People could get sick or die if you don't follow the rules for take-home methadone. Here are some things you should know:

- A single dose of methadone can kill someone who is not used to taking it
- A single dose of methadone can kill someone who is taking another drug
- Children often die if they take methadone when they are not supposed to

You have to sign your name on this page before your doctor can give you take-home methadone. When you sign your name, it means that you know you are expected to do the things below. If you don't understand these things, ask your doctor to explain them to you. If you still don't understand these things, you should not sign your name.

1. You are expected to store your take-home doses in a locked box, in a location where it won't be stolen or accidentally taken by another person. You are expected to show this locked box to your doctor if you are asked to.
2. You are expected to swallow your dose of methadone only on the day(s) they are prescribed. You are expected to take a full dose once every 24 hours. You should not take it more often or less often.
3. You are expected to swallow the methadone dose in

front of the pharmacist on the day that you pick up your take-home doses.

4. You are expected to return all your used methadone bottles to the pharmacist before you get your next take-home doses.
5. You will not give, lend, or sell your take-home doses to anyone else. You know that selling methadone is against the law and that it is dangerous for other people.
6. You know that take-home doses are a privilege and not a right. You know that your doctor can stop giving you take-home doses if he or she thinks that is the right thing to do.
7. If your health stays the same and you do what you are supposed to with your take-home doses, they will be continued and you will be given more doses to take home once every two weeks.
8. The clinic does not have to replace your take-home doses if they are lost, spilled, thrown up or stolen. Stolen take-home doses should be reported to the local police department.
9. You know that your doctor, the pharmacist or the clinic staff can tell you at any time that you have to bring in all your full and empty take-home methadone bottles for them to check. If you don't bring in your bottles when they tell you to, they can stop giving you take-home doses or make you leave the program. They might also call the police.
10. You are expected to let the clinic know if your address or phone number changes.

Signatures

Patient Name

Patient signature

Date

Witness Name

Witness signature

Date

Appendix R.

Tapering Readiness Questions – Sample

When a patient indicates that he or she would like to leave treatment, a number of questions should be asked to determine if the person is ready to taper from methadone. Physicians should consider asking the patient the following questions:

1. Have you been abstaining from illegal drugs, such as cocaine and non-prescribed opioids and benzodiazepines?
2. Do you think you are able to cope with difficult situations without using drugs?
3. Are you employed or in school?
4. Are you staying away from people who use drugs and illegal activities?
5. Have you gotten rid of your “works”/“outfit”?
6. Are you living in a neighbourhood that doesn't have a lot of drug use, and are you comfortable there?
7. Are you living in a stable family relationship?
8. Do you have non-drug-using friends that you spend time with?
9. Do you have friends or family who would be helpful during a taper?

10. Have you been participating in counselling that has been helpful?
11. Does your counsellor think you are ready to taper?
12. Do you think you would ask for help when you were feeling bad during a taper?
13. Have you been on methadone for a long time (> 1 year)?
14. Are you in good mental and physical health?
15. Do you want to get off methadone?

The more questions the patient can honestly answer in the affirmative, the greater the likelihood that he or she is ready to taper from methadone. Consider that each negative response represents an area that probably needs work to increase the odds of a successful taper.*

**Adapted from “Tapering Readiness Inventory” from Treatment of Opiate Addiction with Methadone: A Counselor Manual, U.S. Department of Health and Human Services (DHHS) SMA94-2061. Reproduced in S. Brummett, R. Dumontet, L. Wermuth, M. Gold, J.L. Sorensen, S. Batki, R. Dennis & R. Heaphy (1986), Methadone Maintenance to Abstinence: The Tapering Network Project Manual, University of California, San Francisco. Methadone Maintenance: A Counsellor’s Guide to Treatment, 242*

Appendix S.

Opioid Withdrawal and Tolerance

MMT Physicians must be familiar with the clinical features of opioid withdrawal.

Opioid Withdrawal

Opioid withdrawal peaks at 2-3 days after the last use. Physical symptoms largely resolve by 5-10 days, although psychological symptoms can continue for weeks or months.

Serious complications of withdrawal include miscarriage, premature labour, suicide, and overdose or relapse due to loss of tolerance.

Opioid Withdrawal Signs and Symptoms		
Physical Symptoms	Psychological Symptoms	Physical Signs
Myalgia	Restlessness	Lacrimation
Abdominal cramps	Dysphoria	Rhinorrhea
Nausea	Insomnia	Dilated pupils
Chills	Anxiety	Abdominal
Hot flashes	Irritability	tenderness
Electric or uncomfortable feeling	Fatigue	Vomiting
Yawning	Drug craving (the insomnia and anxiety may be severe and distressing)	Diarrhea
		Sweating
		Chills
		Piloerection
		Tachycardia
		Hypertension

The patient on inadequate doses of methadone will describe a characteristic set of symptoms. The symptoms appear a certain number of hours after the methadone dose, although there may be some variation with the patient's activity level and other factors. The onset of symptoms is delayed with each dose increase.

Alternative explanations should be sought if the patient:

- gives an inconsistent history of withdrawal symptoms;
- has one isolated symptom (such as insomnia or nausea);
- advises the onset of symptoms is not related to the time of the dose; or
- has been taking a stable dose and suddenly complains of withdrawal (see below).

A dose might be considered acceptable if the patient sleeps comfortably at night and only has mild withdrawal symptoms on awakening, which are tolerable to the patient.

Conditions Commonly Confused with Withdrawal

The clinician should determine why the patient continues to report withdrawal symptoms despite dosage adjustment. Common reasons for ongoing withdrawal include:

- medication use that speeds methadone metabolism (such as phenytoin, chronic alcohol use)
- opioid use
- diverting doses

Physicians should consider a medication review with the pharmacist. The following conditions cause symptoms that are confused with withdrawal:

Pseudonormalization should be suspected if the patient regularly complains some weeks after a dose increase that it is no longer 'working.' Patients who are mildly intoxicated on opioids feel more enthusiastic and energetic. As they develop tolerance, they may feel they need a dose increase to recreate this effect, which they view as both desirable and normal.

Insomnia is often the dominant symptom of opioid withdrawal. Other causes should be ruled out if the patient reports insomnia that isn't accompanied by other withdrawal symptoms and is not relieved by a dose increase. Depression, anxiety, and use of alcohol and cocaine are common causes of insomnia in this population. A careful sleep history will identify day-night reversal, daytime napping and other causes of night-time insomnia. Careful instruction in sleep hygiene should be undertaken. Medication should be used only when the patient is on a stable dose of methadone and sleep hygiene counselling has failed. Trazodone or other non-benzodiazepine hypnotics are the treatments of choice.

Sedation and Withdrawal Symptoms: Occasionally patients report sedation several hours after dosing, with withdrawal symptoms and insomnia at night. The sedation may simply represent the onset of sleep following a night of insomnia due to withdrawal. The methadone dose might be too high, causing excessive sleep during the day and inadequate sleep at night. The patient may have day-night reversal, independent of the methadone dose.

Other conditions: Patients may be anticipating that an increase in their dose will manage symptoms that have little to do with withdrawal. Common examples include depression, anxiety, irritable bowel syndrome, and some

forms of chronic pain. The physician should identify these symptoms, explain to the patient the limitations of MMT, and assist the patient in finding an appropriate management strategy.

Diagnostic Criteria for Opioid Withdrawal

A. Either of the following:

- 1) cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer)
- 2) administration of an opioid antagonist after a period of opioid use

B. Three (or more) of the following: developing within minutes to several days after Criterion A:

- 1) dysphoric mood
- 2) nausea or vomiting
- 3) muscle aches
- 4) lacrimation or rhinorrhea
- 5) papillary dilation, piloerection or sweating
- 6) diarrhea
- 7) yawning
- 8) fever
- 9) insomnia

C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Medical Treatment of Acute Opioid Withdrawal

Buprenorphine

If you have the authority/approval to prescribe buprenorphine, its tapering is substantially more effective than clonidine and other non-opioid treatments in reducing opioid withdrawal symptoms and retaining patients in treatment.

Protocol:

- Initial dose – similar to maintenance protocol (4-8 mg/day)
- Increase dose by 2-4 mg daily until therapeutic dose achieved (usual range 8-16 mg)

- Inpatients: Reduce dose by 2 mg every 1–3 days
- Outpatients: reduce dose by 2 mg every week
- Use adjuvant medications as necessary, e.g. antidiarrheals and anti-inflammatories (see below)

Clonidine

Outpatients:

- Clonidine 0.1 mg PO bid to tid
- May increase to 0.2 mg bid to tid after first day;
- Continue bid to tid for 3–5 days then PRN for 3–5 more days.

Inpatients:

- Check BP prior to each dose;
- Hold if BP < 90/60 or marked postural drop;
- May increase to 0.3 mg bid to tid.

Adjuvant medications:

- NSAID or acetaminophen for myalgia;
- Loperamide for diarrhea;
- Gravol or other antinauseant;
- Trazodone 50–100 mg HS for insomnia.

Precautions:

- Do not prescribe clonidine if BP < 90/60, patient pregnant, on antihypertensives or has heart disease.
- Warn patients about postural symptoms and drowsiness. Postural symptoms are dose-related, so be cautious with higher doses.
- Warn about mixing with opioids, or having prolonged hot bath (both can cause hypotension).
- Don't prescribe for longer than 2 weeks (rebound hypertension).
- Warn patients they're at risk for overdose if they relapse to their usual dose; always combine clonidine protocol with a documented treatment plan.

Tolerance

Tolerance is said to occur when higher doses are required over time to achieve the same effect, and the same dose has less effect over time. Tolerance to the psychoactive effects of opioids develops within days, and is lost within days.

***The information presented in this appendix was drawn from the College of Physicians and Surgeons of Ontario: Methadone Maintenance Treatment Program Standards and Clinical Guidelines: February 2011.*

Appendix T.

Admission and Discharge Form – Submitted to CPSA

Methadone Patient/Client Admission and Discharge

To be provided to CPSA within 2 business days of admission/discharge dates

Date: _____

Attention: Janet Wright
Triplicate Prescription Program
College of Physicians & Surgeons of Alberta
Phone: 780-412-2680 or 1-800-320-8624
Fax: 780-429-1981 [confidential fax machine]

From: Contact name: _____

Contact number: _____

The following methadone maintenance patient/client has been admitted or discharged from MMT:

Patient name: _____

Healthcare number: _____

Date of birth: _____

Gender: Male / Female

Admission date to MMT: _____

Discharge date (last recorded ingestion date): _____

Formal discharge date: _____

Profile required: _____

Has informed consent been obtained from the patient? _____ Yes _____ No

Has the patient signed a treatment agreement? _____ Yes _____ No

Appendix U.

CPSA Standards of Practice – Informed Consent



Ethics, Integrity and Professionalism

Informed Consent Standard 28

Reissued: January 7, 2014¹

Standards of Practice of the College of Physicians & Surgeons of Alberta are the minimum standards of professional behavior and ethical conduct expected of all physicians registered in Alberta. Standards of Practice are enforceable under the *Health Professions Act* and will be referenced in the management of complaints and in discipline hearings. The College of Physicians & Surgeons of Alberta also provides **Advice to the Profession** to support the implementation of the Standards of Practice.

- (1) A physician is responsible for ensuring that consent, which may be implied or may be expressed orally or in writing, is obtained from a patient before performing an examination or treatment or before disclosing the patient's personal health information, except where permitted by law to act without consent. A physician must:
 - (a) be aware of authoritative advice on informed consent, such as that of the Canadian Medical Protective Association, before establishing a policy on consent procedures in his or her medical practice,
 - (b) consider the risks to the patient, the potential for pain and discomfort, and the invasiveness of the procedure when deciding on the type of consent required,
 - (c) if relying on implied consent, be certain that the actions of the patient would be interpreted by others as having implied permission for the physician's actions,
 - (d) ensure that written consent is obtained before performing a surgical operation, and
 - (e) consider the knowledge and expertise of trainees and staff if delegating the consent procedure.
- (2) A physician must determine a patient's capacity to give consent in accordance with *Assessing the Mental Capacity of a Patient, Standard 9*.
- (3) A physician who obtains consent from a substitute decision maker on behalf of a patient must comply with applicable laws.
- (4) A physician must respect the right of a patient to withdraw consent at any time.
- (5) In obtaining full and informed consent for disclosure of personal health information or for procedures of higher risk of harm for the patient, a physician must discuss, at a minimum:
 - (a) the exact nature and the anticipated benefits of the proposed examination, treatment or release of personal health information,
 - (b) reasonable and accepted alternative examinations or treatments that are generally available,
 - (c) the natural history of the medical condition at issue,
 - (d) consequences of not undertaking the examination or treatment or disclosing personal health information,

Terms used in the Standards of Practice:

- *Physician* means any person who is registered or who is required to be registered as a member of this College. The College regulates physicians, surgeons and osteopaths.
- *Must* refers to a mandatory requirement.
- *May* means that the physician may exercise reasonable discretion.
- *Patient* includes, where applicable, the patient's legal guardian or substitute decision maker.

- (e) the common and significant risks of the examination or treatment or disclosure and alternatives,
 - (f) serious risks, even if unlikely,
 - (g) special risks, that although uncommon, may have particular relevance to the patient, and
 - (h) any questions the patient may have.
- (6) A physician who obtains consent from a patient for participation in research must also comply with direction and advice from an approved research ethics board.

¹Replaces *Informed Consent*, Standard 27 issued January 1, 2010 (standard number change only)

Terms used in the Standards of Practice:

- *Physician* means any person who is registered or who is required to be registered as a member of this College. The College regulates physicians, surgeons and osteopaths.
- *Must* refers to a mandatory requirement.
- *May* means that the physician may exercise reasonable discretion.
- *Parent* includes, where applicable, the patient's legal guardian or substitute decision maker.

Appendix V.

CPSA Standards of Practice – Supervision of Restricted Activities



College of
Physicians
& Surgeons
of Alberta

Collaboration and Communication

Supervision of Restricted Activities Standard 4

Issued: January 1, 2010

Standards of Practice of the College of Physicians & Surgeons of Alberta are the minimum standards of professional behavior and ethical conduct expected of all physicians registered in Alberta. Standards of Practice are enforceable under the *Health Professions Act* and will be referenced in the management of complaints and in discipline hearings. The College of Physicians & Surgeons of Alberta also provides **Advice to the Profession** to support the implementation of the Standards of Practice.

- (1) A physician may supervise another person performing a restricted activity, as defined in section 2 of Schedule 7.1 of the *Government Organization Act*, if the physician:
 - (a) is authorized and competent to perform that restricted activity, and
 - (b) is satisfied with the knowledge, skill and judgment of the supervised person performing the restricted activity.
- (2) A physician may supervise a student performing a restricted activity, as defined in section 2 of Schedule 7.1 of the *Government Organization Act*, if the physician has confirmed that the supervised person is a student enrolled in a professional health services training program.
- (3) Notwithstanding subsection (1) and (2), a physician must not supervise a person in performing a restricted activity if that person:
 - (a) would be in violation of section 46 of the *Health Professions Act*, regarding Mandatory Registration or
 - (b) is registered with a healthcare profession in Alberta but is not authorized by that profession's regulatory authority to perform that restricted activity.
- (4) A physician may supervise a regulated healthcare professional, an unregulated worker or a student performing a restricted activity only if the physician is satisfied that:
 - (a) it is safe and appropriate for the supervised person to perform the restricted activity on the particular patient,
 - (b) the equipment and resources available to perform the restricted activity are safe and appropriate, and
 - (c) the patient provides informed consent to the procedure being performed under supervision unless consent is not possible because of emergency.
- (5) A physician who supervises a person performing a restricted activity must remain readily available for consultation during the performance of the restricted activity.

Terms used in the Standards of Practice:

- *Physician* means any person who is registered or who is required to be registered as a member of this College. The College regulates physicians, surgeons and osteopaths.
- *MAY* refers to a mandatory requirement.
- *MAY* means that the physician may exercise reasonable discretion.
- *Patient* includes, where applicable, the patient's legal guardian or substitute decisionmaker.

Appendix W.

Emergency Department Management of Methadone Overdose

Copyright [C] Centre for Addiction and Mental Health (CAMH), *Methadone Maintenance Treatment: A Physician's Guide* (Toronto: CAMH, 2007). This appendix may be reproduced freely for use by physicians and treatment staff, but must be reproduced in its entirety.

Patient: _____

Physician: _____

Poison Centre Phone #: _____

Physician Phone #: _____

Relevant details (to be completed by methadone provider):

- Usual methadone dose
- Dose of the suspected overdose (if known)
- Concurrent alcohol, benzodiazepine or other drug use
- Medications
- Relevant medical/psychiatric history
- Circumstances of the overdose (intentional or accidental):

Clinical Features of methadone overdose:

Methadone acts for at least 24 hours, much longer than other opioids. Symptoms begin up to 10 hours after the overdose. Early symptoms include nodding off, drowsiness, slurred speech and emotional lability. Respiratory depression occurs later.

ED protocol for managing suspected methadone overdose

Monitoring:

- Check frequently for vital signs, respiratory rate and O₂ sat
- Hold a brief conversation to assess alertness.
- ECG and cardiac monitoring to check for prolonged QT interval and ventricular arrhythmias (methadone can cause torsades de pointes).

Medical Management with intubation or naloxone

Naloxone is a safe treatment in patients who are not physically dependent on opioids (e.g., patients not in methadone therapy who took methadone recreationally). For methadone- or opioid dependent patients, intubation avoids risks of naloxone-induced withdrawal. Intubation is necessary if:

- RR < 12; hypercapnia; persistent desaturation despite supplemental oxygen

- Patient fails to respond to naloxone within 2 min
- Naloxone precautions:
- Ventricular dysrhythmias and cardiac arrest can occur with naloxone-induced withdrawal, especially if patients are withdrawing from other substances.
 - Patients in naloxone-induced withdrawal may become agitated and leave against medical advice.
 - Naloxone can induce emesis.

Above risks are avoided with intubation.

Naloxone dosing

- If the patient has severe respiratory depression, give 2.0 mg naloxone IV.
- If there is minimal respiratory depression, give 0.01 mg/kg weight to avoid precipitating withdrawal.
- If there is no response after the initial dose, repeat naloxone 2–4 mg every 2–3 min.
- If there is no response after 10–20 mg naloxone, search for other causes for the coma.
- If the patient responds to naloxone, infuse at 2/3 of the effective dose per hour.
- Give a bolus of 1/2 the effective dose 15–20 min after starting infusion.
- Titrate dose to avoid withdrawal, while maintaining adequate non-assisted respirations.

Recommended ED observation periods

- Observe for at least 10 hours post-overdose.
- Discharge if patient is completely asymptomatic during that time.
- If patient becomes symptomatic at any time during the 10 hours, monitor for at least 24 hours post-overdose.

- If patient is intubated or on naloxone, continue intubation/naloxone for at least 24 hours post-overdose.
- Monitor for at least 6 hours after naloxone or intubation is discontinued.

Departure AMA: If the physician feels the patient is not safe to leave, the following Alberta Health Services (AHS) Admission Certificate should be completed:

Alberta Government **Admission Certificate (Form 1)**
Mental Health Act Section 2

I _____ of _____
(print name of physician) (address)

certify that I personally examined _____
(print name of person examined)

of _____ on _____ at _____
(home address) (date) (time)

at _____
(place of examination)

Note:
All three criteria must be met.

In my opinion the person examined is

(a) suffering from mental disorder,
(b) likely to cause harm to the person or others or to suffer substantial mental or physical deterioration or serious physical impairment, and
(c) unsuitable for admission to a facility other than as a formal patient.

Note:
Both (a) and (b) must be completed.

I have formed my opinion

(a) on the following facts observed by me:

(b) on the following facts communicated to me by others:

Place an "X" in the box if conveyance is required. The person is not in a facility and is to be conveyed for examination to _____
(name of facility)

at _____
(address of facility)

_____ (date of issue) _____ (time of issue)

_____ (printed name of physician) _____ (signature of physician)

Note: Section 1(g) of the Act reads:

(g) "mental disorder" means a substantial disorder of thought, mood, perception, orientation or memory that grossly impairs

(i) judgment, (ii) behaviour, (iii) capacity to recognize reality, or (iv) ability to meet the ordinary demands of life.

MH1977 (2013/09)

Discharge instructions: Tell patient not to take any methadone, alcohol or sedating drugs until seen by methadone physician the next day. Have a family member or support person observe overnight, and call an ambulance if the patient appears more drowsy, is difficult to arouse or snores much more loudly than usual.

** The information presented in this appendix was drawn from the College of Physicians and Surgeons of Ontario: Methadone Maintenance Treatment Program Standards and Clinical Guidelines: February 2011.

Appendix X.

Managing Potential Methadone Overdose

Reducing Risk of Toxicity During Initiation

Patient education

- The patient is to limit driving or use of machinery after a dose increase, particularly in the first few hours after dosing.
- The patient is to take the methadone dose in the morning, since the risk of overdose is increased at night.
- Whenever feasible (with the patient's consent), a family member or significant other should be educated about the symptoms of toxicity with instructions to go to the emergency department immediately at the first sign of toxicity. A patient information guide may be used for this purpose.

Explain the risks of diverted methadone

- A single dose of methadone can be fatal.
- Patients are responsible for the safe storage of their methadone.

Frequency of visits

- The MMT physician shall follow the frequency of visits as outlined in Standard 6.
- The MMT physician should inquire about sedation and other side effects.

Take-home doses

- No take-home doses shall be granted during the initiation phase.
- It is recommended that no take-home doses be given for the first three months unless necessary (undue hardship, pharmacy closed on Sunday) and the reason for this should be documented in the patient's chart.

Avoid prescribing any sedating drugs

- Includes benzodiazepines, non-benzodiazepine hypnotics, antipsychotics, antidepressants, and sedating antihistamines. Even moderate, therapeutic doses of these drugs may increase the risk of toxicity if they are initiated at the same time as methadone and the patient is not fully tolerant to their sedating effects.
- Patients should also be advised to avoid alcohol and over-the-counter sedating drugs.

Tapering High-dose benzodiazepine user

- Benzodiazepine abuse and dependence are common in this population.
- As with opioids, it is difficult to accurately judge a patient's benzodiazepine use and tolerance.
- Benzodiazepine tapering, while difficult on its own, can be very complicated and potentially unsafe when attempted with MMT initiation.

Intoxication or sedation

- At any stage of MMT, the pharmacist should be instructed to alert the MMT physician if the patient appears sedated or intoxicated.
- Intoxicated patients should not be medicated until assessed by their MMT physician.
- If signs of intoxication are observed after ingestion of methadone, the patient should be sent to the hospital by ambulance for assessment.

*** The information presented in this appendix was drawn from the College of Physicians and Surgeons of Ontario: Methadone Maintenance Treatment Program Standards and Clinical Guidelines: February 2011.*

Appendix Y.

Urine Toxicology Testing Techniques

Toxicology testing techniques are determined by the laboratory involved in providing this component of services in MMT based on the physician's order. Consultation with the toxicology personnel is important to determine the method and scope of their testing applications and will influence the specific drug testing orders by the physician. E.g. Immunoassay techniques may not screen effectively for synthetic narcotics such as Oxycodone or Meperidine and therefore the orders must specify these drugs.

Typical qualitative screening methods for specific drugs or medications are outlined below:

1. Enzyme Immunoassays
 - Amphetamines
 - Barbiturates
 - Benzodiazepines
 - Cannabinoid metabolites
 - Cocaine metabolite
 - Methadone
 - Methadone metabolite – on request
 - Opiates – may not detect synthetic opioids
2. Enzyme Oxidation
 - Ethanol

Confirmatory testing involves further testing subsequent of an original positive immunoassay result using another analytical method. This confirmatory testing verifies the immunoassay result and may provide differentiation within a drug class. Some examples of these confirmatory techniques are:

1. Gas Chromatography
e.g. Ethanol
2. Gas Chromatography/Mass Spectrometry or Liquid Chromatography/Mass Spectrometry
e.g. Amphetamine (amphetamine, methamphetamine, MDMA, etc)

Barbiturates (phenobarbital, secobarbital, amobarbital, etc)

Benzodiazepines (oxazepam, temazepam, etc)

Cannabinoid metabolites

Cocaine metabolites

Methadone and Metabolite

Opioids (codeine, morphine, oxycodone, 6-monoacetylmorphine, etc)

Opioids that metabolize to other prescribed opioids:

Some opioids metabolize into other prescribed opioids. These metabolites can be detected in UTT and, if not recognized as metabolites, may be misinterpreted as unsanctioned opioid use.

Opioid	Metabolite
Codeine	Morphine, hydrocodone
Morphine	Hydromorphone
Hydrocodone	Hydromorphone
Heroin	Morphine, [codeine contaminant]

Buprenorphine, fentanyl, hydromorphone, meperidine, methadone and oxycodone do not metabolize to other prescribed opioids.

Detection times:

Detection times are dependent on the rate of clearance of the substances measured. The times listed in the table below are approximate, and will depend on the specific testing materials used. With point-of-care testing, the detection times will be provided by the vendor. With hospital testing, it is recommended that the detection times be ascertained from the laboratory. It is important to recognize that some substances (barbiturates, benzodiazepines and cannabinoids) can be detected for weeks after last use.

Drug	Detection time
Amphetamines	2 days
Barbiturates	Short acting 1 day Long acting 2 to 3 weeks
Benzodiazepines	Therapeutic dose 3 or more days (depends on half-life of specific drug)
Cocaine	2 to 4 days
Opioids	2 to 3 days
Cannabinoids	Lighter smoker (1 joint) 2 to 3 days Moderate smoker (4 joints/week) 5 days Daily smoker 10 days Chronic smoker 4 weeks

False positive tests:

Many drugs can cross-react with immunoassay tests causing false positive results. When an unexpected UTT

result occurs, it is important to exclude the possibility of a false positive test. The following lists some substances that can cause false positive tests:

- THC: ketoprofen, naproxen, ibuprofen, sustiva, pantoprazole, promethazine, riboflavin, marinol, sativex, hemp seed oil
- Opioid: poppy seeds, chlorpromazine, rifampin, dextromethorphan, quinine, fluoroquinolones
- Methadone: quetiapine, methotrimeprazine
- Benzodiazepines: sertraline, oxaprozin, flurbiprofen, indomethacin, ketoprofen
- Amphetamine: Vicks Vapor nasal inhaler, ephedrine, pseudoephedrine, tyramine, ciprofloxacin, mefanamic acid, labetalol, methylphenidate, trazodone, desipramine, bupropion, propranolol, phenylephrine, mexilitine, selegiline, amantadine, rantidine, metronidazole, phenothiazines, some diet pills
- Cocaine: salicylates, fluconazole

Appendix Z.

Urine Toxicology Testing Collection Practice

UTT is clinically reliable when urine collection is directly observed. However, other measures can be taken to enhance the authenticity of the urine sample and consequently the test results. In most cases directly observing urine collection is not required.

Chain of custody is for legal matters and does not apply to MMT.

The primary care physician may not have direct lab services in concert with the clinical practice and therefore patients will have a choice of labs for this service. This document may be attached to the requisition for collection of urines to ensure the proper protocol is followed.

- Extra clothing such as coats and sweaters should be removed
- Parcels, bags and purses must not be taken into the collection area
- Patients should receive a pre-labelled urinalysis container prior to entering the collection area

- The patient must bring the sample directly to the collector and not place it in a pass-through-window
- No other urine samples should be accessible to the patient during the provision of the sample. ie: Specimen pass-through cabinet
- A minimum volume of 30 ml is required

Considerations:

- Hand washing facilities are made available to patient after provision of the sample
- Provide a dry collection area
- All sources of water should be disabled
- Bluing of toilet water
- Temperature check to be performed immediately after urine sample is obtained – using a temperature sensitive strip.
- Lab staff do not witness urine collection.

If there is concern about the integrity of the sample, please notify the ordering physician's office and indicate concerns on the requisition, providing all relevant details.

Appendix AA.

Resources

Clinical Resources

Alberta Health Services

<http://www.albertahealthservices.ca/>

Alberta Human Services

<http://humanservices.alberta.ca/programs-and-services.html>.

Alberta Methadone Clinics

http://www.cpsa.ab.ca/Services/Methadone_Program/Methadone_Program_Resources.aspx.

Alberta Supports

<http://www.programs.alberta.ca/Living/13765.aspx?N=770+13705>.

Buprenorphine Prescribing in Alberta

http://www.cpsa.ab.ca/Services/Physician_Prescribing_Practices/BuprenorphinePrescribing.aspx

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Link to documents: <http://nationalpaincentre.mcmaster.ca/opioid/>

Methadone Drug Interactions Information

Website(s): www.atforum.com and /or www.drug-interactions.com

Centre for Addiction and Mental Health

Phone: (416) 535-8501

Website: www.camh.net

My Health

<https://myhealth.alberta.ca/Pages/default.aspx>

Government Resources

Alberta Health

<http://www.health.alberta.ca/>

Alberta Justice and Solicitor General

<http://www.solgps.alberta.ca/pages/sitemap.aspx>

Health Canada Office of Controlled Substances

Phone: (613) 946-5139

Toll-free: 1-866-358-0453

Website: www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hecs-dgsesc/dscsp-psasc/index-eng.php

Professional Resources

Alberta College of Pharmacists

Phone: 780-990-0321

Toll-free: 1-877-227-3838

Fax: 780-990-0328

Email: acpinfo@pharmacists.ab.ca

Website: <https://pharmacists.ab.ca/nCollege/default.aspx>

Alberta College of Social Workers

<http://www.acsw.ab.ca/>

American Society for Addiction Medicine

Phone: 301-656-3920

Email: email@asam.org

Website: www.asam.org

College and Association of Registered Nurses of Alberta

<http://www.nurses.ab.ca/Carna/index.aspx>.

College of Physicians and Surgeons of Alberta

Phone: 780-423-4764

Fax: 780-420-0651

Alberta Physician Only Line: 1-800-320-8624

Website: <http://www.cpsa.ab.ca/Homepage.aspx>

Canadian Society for Addiction Medicine

Phone: 403-813-7217

Email: admin@csam.org

Website: www.csam.org

Appendix BB.

Glossary

Abuse, drug – Any use of an illegal drug, or the intentional self-administration of a medication for a non-medical purpose such as altering one’s state of consciousness, e.g., “getting high.” (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Addiction – A primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Agonist – Drugs that interact with receptor sites to cause the same effect that natural chemicals would cause at these sites. Karch, A, M. (2008). Focus on nursing in pharmacology. (4th ed.). Philadelphia: Wolters Kluwer/ Lippincott Williams & Wilkins.

Agonist – A substance that acts at a neuronal receptor to produce effects similar to those of a reference psychoactive substance, e.g. methadone is an agonist at the opioid receptors.

Antagonist – Drugs that combine with receptors that do not begin a change in cell function. When antagonists bind to receptors, agonists are prevented from binding and causing an action. Gutierrez, K. (2008). Pharmacotherapeutics: Clinical reasoning in primary care (2nd ed.). Saunders: St. Louis.

Antagonist – (Adopted Canadian Society of Addiction Medicine October 14, 1999) A substance that counteracts the effects of a reference psychoactive substance by inhibiting or reversing its effects at a neuronal receptor site, e.g. naltrexone acts as an antagonist at the opioid receptor.

Concurrent Disorders – (Adopted Canadian Society of Addiction Medicine October 14, 1999) The presence of one or more primary, physical and/or psychiatric disorders that have an interactive effect on the course of Substance Dependence and require specific diagnosis and treatment

in order to achieve stabilization and/or recovery.

Controlled Substance – There are many controlled substances listed under the Controlled Substance Act. These drugs are grouped under schedules. Below are examples of some of the better known drugs within each Schedule:

- Schedule I contains drugs made from the opium poppy such as heroin, codeine; drugs made from coca such as cocaine; and synthetically derived drugs such as methadone.
- Schedule II contains cannabis (marijuana) and its derivatives.
- Schedule III contains drugs such as amphetamines and lysergic acid diethylamide (LSD).
- Schedule IV contains drugs such as benzodiazepines and barbiturates.
- Schedule V and VI contain precursors required to produce controlled substances (National Association of Pharmacy Regulatory Authorities, 2002-2004).

Craving – (Adopted Canadian Society of Addiction Medicine October 14, 1999) A bio-psychological arousal and urge to return to addictive behaviour, characterized by a strong desire, pre-occupation and possible impulsivity.

Contingency Management – A type of treatment used in the mental health and substance abuse fields. Patients are rewarded (or less often, punished) for their behaviour; generally, adherence to or failure to adhere to program rules and regulations or their treatment plan.

Dependence, Physical – A state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Diversification – The intentional transfer of a controlled substance from legitimate distribution and dispensing channels. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Dose, stable – A “pharmacologically stable dose” is one that produces a fairly steady plasma level; it is established when the total daily dose is fixed for at least two weeks and:

- 1) frequency is scheduled and spread throughout the day, AND/OR
- 2) at least 70% of the prescribed opioid is controlled release.

Double-doctoring – Receiving a prescription for a narcotic, and then seeking and receiving another prescription or narcotic from a different practitioner without disclosing to that practitioner particulars of every prescription or narcotic obtained within the previous 30 days. [Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010]

Half-life – The time required for half of the total drug amount to be eliminated from the body. Generally after five half-lives, 97% of a drug will be eliminated. *Pharmacotherapeutics for Advanced Practice – A Practical Approach*, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006.

Harm Reduction – A continuum of services that represent a philosophical, pragmatic approach to providing care while minimizing the negative outcomes associated with substance use. The focus is goal oriented, humanistic and in keeping with a cost benefit awareness. [Pauly, Goldstone, McCall, Gold & Pyne, 2007]. Pauly, B., Goldstone, I., McCall, J., Gold, F., & Payne, S. [2007]. The ethical, legal and social context of harm reductions. *Canadian Nurse*, 103, 19–23.

Maintenance Therapy – Treatment of Substance Dependence by a prescription drug, to prevent withdrawal and reduce the harm associated with a particular method of administration, attendant dangers to health and/or social consequences, e.g. methadone for Opioid Dependence or nicotine replacement therapy (NRT) for tobacco.

Methadone Toxicity – When the level of methadone in the body exceeds the level that is determined safe.

Misuse, opioid – Use of an opioid in ways other than those intended by the prescribing physician (sometimes also called problematic opioid use). [Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010]

Narcotic – Any drug included in the “Schedule” under the Controlled Drugs and Substances Act: Narcotic Control Regulations. [Minister of Justice]

Opiate – A naturally-occurring or semi-synthetic compound derived from the opium poppy (papaver somnifer) [College of Physicians and Surgeons of Alberta, 2005].

Opioid – A compound having actions or properties similar to opiates. A broader term encompassing all opiates (such as heroin, morphine and codeine), as well as synthetic opiate-like compounds (such as methadone and fentanyl) [College of Physicians and Surgeons of Alberta, 2005]. A family of drugs that act by attaching to endogenous mu, kappa and delta receptors in the brain and share a common set of clinical effects, including analgesia, sedation, constipation, and respiratory depression. Note: Reference throughout this document to specific pharmaceutical products as examples does not imply endorsement of any of these products.

Pharmacodynamics – The set of processes by which drugs produce specific biochemical or physiological changes in the body-how the drug acts on the body. *Pharmacotherapeutics for Advanced Practice – A Practical Approach*, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006 [Arcangelo & Peterson, 2006].

Pharmacokinetics – Examining the absorption, distribution, metabolism and excretion of a drug, the onset of action, the half life, peak effect and duration of effects – how the body acts on the drug. Karch, A, M. (2008). *Focus on nursing in pharmacology*. (4th ed.). Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins.

Split doses – An alternative way of providing methadone to clients, consisting of two or more doses per day (so it is not ingested all at one time). It is used for clients who have demonstrated “rapid metabolism” of their once daily methadone dose (e.g. during third trimester of pregnancy) or are on medications that have been shown to induce rapid metabolism of methadone (i.e. certain HIV medications). A consultation with a experienced MMT provider should be considered in these circumstances. Split doses do not necessarily have to be equal; twice-daily observed ingestion may be necessary [College of Physicians and Surgeons of Alberta, 2005].

Stable daily dose – Optimal daily dose of methadone that will relieve withdrawal symptoms, block opioid-induced euphoria and reduce drug cravings without sedation or other significant side effects (College of Physicians and Surgeons Ontario, 2005).

Steady state – A constant mean concentration of a drug in the body, there are peaks and troughs in the drug level, but the fluctuations remain within a constant range Pharmacotherapeutics for Advanced Practice – A Practical Approach, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006. (Arcangelo & Peterson, 2006).

Substance – Any drug with pleasant psychoactive effects and addiction potential, including alcohol, illegal drugs, and prescription drugs. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Substance abuse – (American Psychiatric Association, 1994)

- A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12 month period:
 1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household).
 2. recurrent substance use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by substance use).
 3. recurrent substance-related legal problems (e.g. arrests for substance-related disorderly conduct)
 4. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g. arguments with spouse about consequences of intoxication, physical fights)

- B. The symptoms have never met the criteria of Substance Dependence for this class of substance.

Substance dependence – A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12 month period (American Psychiatric Association, 1994)

- A. Tolerance, as defined by either of the following:
 - i. a need for markedly increased amounts of the substance to achieve intoxication or desired effect; or
 - ii. markedly diminished effect with continued use of the same amount of the substance.
- B. Withdrawal, as manifested by either of the following:
 - i. the characteristic withdrawal syndrome for the substance; or
 - ii. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.
- C. The substance is often taken in larger amounts or over a longer period than was intended.
- D. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
- E. A great deal of time is spent in activities necessary to obtain the substance (e.g. visiting multiple doctors or driving long distances), use the substance (e.g. chain-smoking), or recover from its effects.
- F. Important social, occupational, or recreational activities are given up or reduced because of substance use.
- G. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g. current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

With physiological dependence: evidence of tolerance or withdrawal (i.e. either Item 1 or 2 is present).

Without physiological dependence: no evidence of tolerance or withdrawal (i.e. neither Item 1 nor 2 is present).

Substance misuse – The use of a psychoactive substance (drug or alcohol) for a purpose other than that for which it was intended, and that cause's physical, social, and psychological harm. The term is also used to represent the pattern of use: experimental, recreational and dependent (Rassool, 2002). Substance misuse and mental health: An Overview. Nursing Standard, 16, 46-52.

Substance tolerance – A neurological adaptation to the psychoactive effects of a substance; more of the drug is required to achieve the same effect. Tolerance develops quickly to the psychoactive effects of alcohol and opioids. Highly tolerant clients can behave almost normally after consuming opioid doses that would be fatal in non-tolerant clients (Kahan & Wilson, 2002). Tolerance to the psychoactive effects of opioids develops within days, and is lost within days (CPSO, 2005). A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010) Substance Use Disorders (Adopted Canadian Society of Addiction Medicine October 17, 2003) A category of two disorders, namely, Substance Abuse and Substance Dependence, as in DSM IV.

Substance withdrawal – Characteristic syndrome produced by abrupt cessation of a drug. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Tapering – A gradual decrease in a dose of a drug; could result in a lower daily dose or cessation of the drug. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Titration – A technique of adjusting a dose until a stable/optimal dose is reached; usually means gradually increasing the dose to allow the body to develop tolerance and minimize adverse effects. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Tolerance – A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Withdrawal – Characteristic syndrome produced by abrupt cessation of a drug. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

*** The information presented in this appendix was drawn and adapted from the College of Physicians and Surgeons of Ontario: Methadone Maintenance Treatment Program Standards and Clinical Guidelines: February 2011.*

Appendix CC.

Bibliography

1. American Psychiatric Association. (2000). Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association.
2. Bean, Philip, and Nemitz, Teresa (eds.), Drug Treatment: What Works? New York: Routledge, 2004, ISBN: 0-415-26817-6.
3. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. (2010). Hamilton, Ont.: Michael G. DeGroote National Pain Centre, McMaster University.
4. College of Clinical Pharmacology, 7 Jan. 2013. Web. 16 Jan. 2014. "P450 Drug Interaction Table." Indiana University. <http://medicine.iupui.edu/clinpharm/ddis/main-table/>.
5. College des Medecins du Quebec, Ordre des pharmaciens du Quebec (February 2000): The Use of Methadone in the Treatment of Opiate Addiction.
6. College of Physicians and Surgeons of British Columbia (December 2009): Methadone Maintenance Handbook.
7. College of Physicians and Surgeons of Newfoundland and Labrador: Guideline – Methadone Maintenance Treatment.
8. College of Physicians and Surgeons of Ontario (4th Edition; February 2011): Methadone Maintenance Treatment Program Standards and Clinical Guidelines.
9. College of Physicians and Surgeons of Nova Scotia (May 2012): Methadone Maintenance Treatment Handbook.
10. College of Physicians and Surgeons of Saskatchewan, Saskatchewan Health (June 2008): Saskatchewan Methadone Guidelines for the Treatment of Opioid Addiction.
11. "CredibleMeds :: Composite List - All QTDrugs." CredibleMeds. Azcert, 12 Dec. 2013. Web. 16 Jan. 2014. <http://crediblemeds.org/everyone/composite-list-all-qtodrugs/?rf=All>.
12. Curet LB, Dorato V, Wallerstedt C, Wilbourne P; Clinical Management of Methadone Dependence During Pregnancy, J. Perinat Neonat Nurs (2001) 14 (4):26-45.
13. Drug Interactions- Cytochrome P450 Drug Interaction Table www.drug-interactions.com
14. Drugs of Abuse Data Sheet www.dkml.com/dads.html
15. Ford, C., Halliday, K., Lawson, E., Browne, E. (2011): Guidance for the use of substitute prescribing in the treatment of opioid dependence in primary care, for the Royal College of General Practitioners
16. Health Canada, The Use of Opioids in the Management of Opioid Dependence (1992).
17. Health Canada: Best Practices Methadone Maintenance Treatment http://www.hc-sc.gc.ca/dhp-mps/substancontrol/exemptions/methadone/index_e.html
18. Health Canada: Best Practices: Concurrent Mental Health and Substance Use Disorders. It can be ordered either via email at publications@hc-sc.gc.ca or via telephone: (613) 954-5995.
19. Health Canada: Summary Report of the Workshop on Best Practices for Concurrent Mental Health and Substance Use Disorders
20. Henry-Edwards, S., Bell, J., Ritter, A.; Clinical Guidelines and Procedures for the Use of Methadone in the Maintenance Treatment of Opioid Dependence (August 2003) for the Commonwealth of Australia.

21. Johnson, K, Gerada C, Greenough A; Treatment of Neonatal Abstinence Syndrome; Arch Dis Child Fetal Neonatal Ed (2003); 88: F2-F5
22. Kakko, J., Heilig, M., & Sarman, I. (2008) Buprenorphine and methadone treatment of opiate dependence during pregnancy: comparison of fetal growth and neonatal outcomes in two consecutive case studies. *Drug & Alcohol Dependence*, 96, 69-78
23. Krantz M.J., Martin J., Stimmel B., Mehta D., Haigney M.C (2009 January 20); QTc Interval Screening in Methadone Treatment. *Ann Intern Med.* 150, 2009:387-395
24. Leavitt SB, Shinderman M, Maxwell S, Eap CB, Paris P, When "Enough" is not Enough: New Perspectives on Optimal Methadone Maintenance Dose, *The Mount Siani Journal of Medicine* Vol. 67 Nos. 5 & 6 (2000) 404-411
25. "Lexicomp Online Interactions." Lexicomp Online. Wolters Kluwer Health, n.d. Web. 16. Jan 2014. <http://online.lexi.com/lco/action/interact>
26. Luce J, Strike C. A Cross-Canada Scan of Methadone Maintenance Treatment Policy Developments. Ottawa, ON: Canadian Executive Council on Addictions; 2011.
27. McCarthy, J. J., Leanmon, M. H., Stenson, G., & Biles, L. A. (2008). Outcomes of neonates conceived on methadone maintenance therapy. *Journal of Substance Abuse Treatment*, 35, 202-206.
28. "Micromedex 2.0 Drug Interactions." Micromedex 2.0. Truven Health Analytics, n.d. Web. 16 Jan. 2014. <http://www.micromedexsolutions.com/micromedex2/librarian>
29. New Brunswick Addiction Services (July 2005): "Methadone Maintenance Treatment Guidelines".
30. New Zealand Ministry of Health; Practice Guidelines for Opioid Substitution Treatment in New Zealand 2008.
31. O'Brien, C. (2010). Addiction and dependence in DSM-V. *Addiction*, 106, 866-867.
32. Parker, James N and Parker, Philip M. (eds.), *Methadone: A Medical Dictionary, Bibliography, and Annotated Research Guide to Internet References*, San Diego: ICON Group International Inc., 2003, ISBN: 0-597-83716-3.
33. *Principles of Addiction Medicine* 3rd edition. (2003) Edited by Graham AW, Schultz TK, Mayo-Smith MF, Ries RK, and Wilford, BB. American Society of Addiction Medicine. Chevey Chase, Maryland.
34. Reist, D. (2010). *Methadone Maintenance Treatment in British Columbia, 1996-2008 Analysis and Recommendations*. Victoria, B.C.: Ministry of Healthy Living and Sport.
35. Seivewright, Nicholas, *Community Treatment of Drug Misuse: More than Methadone*, New York: Cambridge, 2000, ISBN: 0-521-66562-0.
36. *The Opioid Dependency Treatment (ODT) Subcommittee of the Addiction Task Group, (2004) A Framework for the Delivery of Opioid Dependency Treatment in Alberta* http://corp.aadac.com/content/corporate/services/odp_delivery_framework.pdf
37. Tober, Gillian, and Strang, John (eds.) *Methadone Matters: Evolving Community Methadone Treatment of Opiate Addiction*, Scarborough: Taylor and Francis Group, 2003, ISBN: 1-84184-365-2.
38. WHO (2009). *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence*.
39. Young, D. M. (2007). Management of opioid dependence in pregnancy: A review on the evidence. *International Journal of Mental Health and Addiction*, 5(3), 187-194.