Principles for the Provision of Opioid Dependence Treatment
By Manitoba Pharmacists

Updated September 2016
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Part One:
Summary of Methadone for Harm Reduction and Pain

Common Concentration

a. **Harm Reduction:** Methadose™ (methadone HCl) is a commercially available oral liquid concentrate indicated for substitution treatment in opioid drug dependence in adults by Health Canada. It comes in a concentration of 10 mg/ml.

The following products are to be used when patients are being treated for opioid dependency:

<table>
<thead>
<tr>
<th>Product</th>
<th>DIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadose™ 10mg/ml oral liquid</td>
<td>2394596</td>
</tr>
<tr>
<td>Methadose™ Sugar Free 10mg/ml oral liquid</td>
<td>2394618</td>
</tr>
</tbody>
</table>

This change took effect as of October 16, 2014. The use of compounded methadone stock solution will be discontinued on the effective date of the next Manitoba Health Formulary Bulletin update in mid-January 2015. This transition period of approximately three months will allow for part fills of existing prescriptions to be filled using the old pseudoPIN of compounded methadone stock solution. Please see **Appendix A** for the information sent to pharmacists from Manitoba Health, Healthy Living and Seniors regarding the changes in methadone reimbursement procedure.

If dispensing the dye-free, sugar-free, unflavoured Methadose™, the methadone dose **must** be diluted with a suitable crystalline diluent in a sufficient quantity (qs) to 60 to 100mL final volume for witnessed dose ingestion by the pharmacist.

If dispensing the red, cherry-flavoured Methadose™, the dose may be ingested without dilution for witnessed dosing by the pharmacist. However, the cherry-flavoured formulation may be diluted if deemed necessary by the pharmacist or prescriber.

b. **Analgesia:** Metadol® is a commercially available product indicated for pain management by Health Canada. The same transition period as stated above for methadone for harm reduction will occur for methadone for analgesia. Please see **Appendix A** for the information sent to pharmacists from Manitoba Health, Healthy Living and Seniors regarding the changes in methadone reimbursement procedure for Metadol® and Methadose™ for pain management.

Common Care Plan

a. **Harm Reduction:** For harm reduction, the methadone prescriber, patient and pharmacist will enter into a common written care plan with the rights, obligations, conditions and consequences agreed upon.

Knowledgeable

Pharmacists must be knowledgeable in all aspects of methadone use when involved in care with methadone. Section 18 of the Pharmaceutical Regulation states that a member may only engage in the aspects of pharmacy practice that he or she has the requisite knowledge, skill and judgment to provide or perform and that are appropriate to his or her area of practice.
a. *Harm Reduction:* For harm reduction, the expectation is that the pharmacist will be knowledgeable in the use of methadone for opioid dependence treatment. The expectation is that there will be at least one pharmacist at each pharmacy with specialized training in harm reduction and if that is not possible (i.e. first 6 months), in the interim there will be a “trained” pharmacist functioning as a mentor at another location. The pharmacist with specialized training at a pharmacy is responsible for training all pharmacists who will be dispensing methadone. For further information on the accepted training program, please see the section on “Education and Training”.

b. *Analgesia:* Where methadone is used for pain, the expectation is that the pharmacist will be knowledgeable in the use of methadone for analgesia. Specialized training should be considered for use of methadone in pain in a similar manner to methadone used for harm reduction.

References

Pharmacists must have onsite or readily available references and treatment guidelines when involved in harm reduction and/or analgesia. Recommended references include the College of Physicians and Surgeons of Manitoba’s [Manitoba Methadone and Buprenorphine Maintenance recommended practice](https://www.cmaj.org/content/early/2016/08/09/cmaj.160817), the [Center for Addictions and Mental Health Methadone Maintenance: A Pharmacist’s Guide to Treatment](https://www.camh.net/services/clinical-practice/chapter-methadone-maintenance).

a. *Harm Reduction:* Minimum requirements onsite include the CPhM and CPSM guidelines and/or standards and a reference similar to that offered by CAMH;

b. *Analgesia:* Minimum requirements onsite include the CPhM and CPSM guidelines and/or standards and a reference similar to that offered by CPSO.

Deliveries

a. *Harm Reduction:* Deliveries (by persons other than a pharmacist) are not acceptable; with the understanding that there may be exceptions as determined in consultation with the methadone prescriber and the agreement of the sponsoring harm reduction program. The witnessing of ingestion cannot be delegated by a pharmacist and therefore delivery and witnessing needs to be done by a pharmacist (with the exception of deferring to a methadone prescriber at an established harm reduction program or another pharmacist). If in the professional judgement of the pharmacist and prescriber that delivery is necessary, individual case review, justification and documentation are required.

b. *Analgesia:* Deliveries may be undertaken with the same precautions afforded narcotics of a similar nature and can be accepted by an agent (if appropriate).

Witnessed Ingestion

a. *Harm Reduction:* When methadone is used for harm reduction, witnessed doses (non-carries) must be observed, logged with date and time in a patient specific, patient identified and confidential manner.

b. *Analgesia:* Not applicable.
Delegation

a. **Harm Reduction:** The act of witnessing the ingestion of methadone for methadone maintenance treatment (MMT) cannot be delegated by a pharmacist, with the exception of deferring to a methadone prescriber at an established harm reduction program or another pharmacist.

b. **Analgesia:** Not applicable.

Policy and Procedures Manual

A site specific Policy and Procedures Manual should be readily available onsite when methadone is dispensed for harm reduction and/or management of pain.

Labelling

All patient labels will be compliant with the provisions of *The Pharmaceutical Act* and Regulations;

a. **Harm Reduction:** For methadone maintenance therapy, the label needs to indicate the date of ingestion and the total dosage (mg) in the bottle with a notation that the dosage was made up to a set volume (if applicable). Methadone doses that have been pre-measured into individual patient dose bottles/containers must be clearly labelled with the patient name, dosage, and initials of the pharmacist who checked the measured doses.

b. **Pain:** Labelling needs to be completed as per a regular prescription.

Private Area

a. **Harm Reduction:** For harm reduction, a confidential area in the pharmacy for counselling and observation of ingestion is required.

b. **Pain:** An area suitable for confidential counselling is required by the CPhM Standards and Practice Direction in all pharmacies for all prescription and non-prescription medication.

Equipment

It is recommended that all devices used for methadone preparation be used only for methadone.

Tamper Proof Seals

It is strongly recommended that each individual methadone dose delivered offsite (i.e. to an institution) be sealed with a tamper-proof seal.

Carries

It is recommended that bottles/containers for carries are returned to the pharmacy and accounted for prior to issuing further carries to prevent diversion. These bottles are not to be reused but disposed of in an appropriate manner.
Part Two: Introduction to Opioid Dependence Treatment and Methadone

Introduction

These guidelines provide an overview of the pharmacist’s role in opioid dependence treatment in Manitoba. Two of the available medications available for opioid dependence treatment include methadone (brand name: Methadose™) and buprenorphine/naloxone in a 4:1 ratio (brand name: Suboxone®). Methadone and buprenorphine-naloxone can bring normal functioning back to an individual since they are opioids that cause little to no euphoric effects. Additionally, these medications have a long half-life to enable suppression of the withdrawal symptoms and cravings of opioid addiction that often contribute to relapse. The choice of therapy between these two options will depend on a number of factors including (but not limited to):

- The degree of opioid dependence and tolerance experienced by the patient,
- An evaluation of the patient’s risk of harm from the chosen therapy including the risk of non-compliance,
- The patient’s concomitant health conditions and comorbidities,
- The potential for significant drug interactions with other concomitant therapies,
- The patient’s ability to access the specialized services and expertise of an opioid dependence program,
- The patient’s response to therapy,
- The patient’s ability to afford the chosen therapy, and
- The patient’s lifestyle and social history.

These guidelines will focus more closely on methadone maintenance treatment (MMT), but more information on buprenorphine/naloxone can be found further on in this document.

There are an increasing number of methadone patients as well as methadone dispensing pharmacies in Manitoba. MMT in Manitoba began in 1970 with the treatment of one heroin addict. In 2007, the number of patients receiving MMT in Manitoba was nearly 500. It was estimated that there were approximately 1,200 methadone patients in Manitoba in 2014. The provision of methadone in practice can be both rewarding and challenging. These guidelines are intended to provide a standard framework for successfully integrating this important program into practice.

Harm Reduction Philosophy

The Manitoba methadone maintenance treatment program is based on a harm reduction philosophy. Harm reduction attempts to decrease the harmful consequences of illicit drug use to the individual, family, community and society. The goals of the program are to reduce illicit opioid use, needle sharing, criminal activity and mortality associated with addiction. The intent of a methadone maintenance program is that the patient should function like they are in abstinence while on the program.

Methadone is an important therapeutic tool in the treatment of opioid addiction. It has been shown to be more effective than placebo in decreasing illicit opioid use and imprisonment. Many people stabilized on methadone can return to work or school and become contributing members of society. A portion of these patients may eventually be tapered off the program.

Overview of MMT

Until 2007, methadone was the only substance approved in Canada for the long term (>180 days) treatment of opioid dependence. Buprenorphine, a partial µ-opioid receptor agonist, can also be used in the treatment of opioid addiction. Pharmacists are expected to be knowledgeable about either product prior to dispensing. More information on buprenorphine/naloxone can be found further on in this document.
Methadone is an oral substitute for heroin and other opioid narcotics. It prevents withdrawal symptoms and reduces cravings. Oral methadone does not induce euphoria in stabilized patients and it blocks the euphoric response to other opioids. Methadone’s long half-life allows it to be dosed once daily for MMT. Since methadone is dispensed from a licensed pharmacy, it is from a safe source and of known dose and purity.

Methadone is also affordable. It is covered by most third party payers, including Manitoba Pharmacare and the Non-Insured Health Benefits program. While some patients may pay up to several hundred dollars a day for illicit drugs, prescription methadone can cost significantly less.

There are many benefits to MMT, however some people feel it is inconvenient to have to drink a witnessed dose at the pharmacy on a regular basis. Although this may be cumbersome for some patients, it can help them establish a routine which is considered part of their rehabilitation.

Unfortunately, there continues to be much stigma associated with methadone maintenance and many people do not understand how methadone works. Pharmacists can play an important role in educating the general public and other health care professionals on MMT.

**Criterion for Admission to MMT Program**

Prior to admission to an MMT program, patients should be informed of all other treatment options for their opioid dependence so they are able to make an informed decision.

Opioid dependence is a psychological disorder that is defined in DSM IV as 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 opioid withdrawal syndrome.
   b) The same (or related) opioid 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 doctors 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).

It should be noted that tolerance and withdrawal on their own do not constitute opioid dependence. For example, a cancer patient that is on morphine for pain control will likely develop tolerance to morphine and require higher doses. If this patient’s morphine is abruptly stopped he/she would experience withdrawal symptoms. Substance dependence requires the behavioral component(s) to be present in order for the diagnosis to be made.
When considering a patient for MMT, the methadone prescriber will ensure the patient has a significant history of opioid use/abuse. This is usually confirmed with a positive urine drug screen and/or other appropriate collateral information. Typically the patient will have greater than a one year history of opioid use and have failed abstinence treatment or have a small likelihood of benefit from non-methadone treatment. Prior failure on MMT does not preclude someone from restarting the program. The prescriber will discuss the commitment required for the program and the expectations that he/she has of the patient. The patient will be required to make an informed decision in order to participate in the program. It is a good idea to have a 3-way (prescriber-patient-pharmacist) agreement that specifically lays out the expectations each party has of the program. Some pharmacies prefer to use a 2-way agreement (pharmacist-patient). A sample agreement has been provided in the Appendix B.

Overview of Methadone for Analgesia

Methadone was originally developed in 1941 by IG Farbenindustrie in Germany. It was marketed in the United States by Eli Lilly as an analgesic by the name of Dolophine®. While methadone is a very effective analgesic, it is important to note that methadone dosed once daily is non-analgesic in a patient stabilized on MMT. Since the analgesic effects of methadone do not last as long as its suppression of opioid withdrawal, it typically needs to be administered every 8 hours for pain control.

Pharmacology of Methadone

Methadone is a synthetic opioid that acts as an agonist at the mu-opioid receptor. This action is similar to morphine and heroin, however, it is structurally unrelated.

Absorption: Methadone has high oral bioavailability (79% range 35-100) and is quickly absorbed (30 minutes +/- 15 minutes). Peak plasma levels of methadone can occur between 1 and 7.5 hours post oral dose (average peak occurs between 2.5 and 4 hours).

Distribution: Methadone is lipophilic and highly protein bound. It has a free fraction of 13% however there is significant inter-patient variability. Its volume of distribution is 4L/kg (range 2-13 L/kg).

Metabolism: Methadone has a half-life of 35 ± 12 hours. Methadone is primarily metabolized by CYP P450 3A4 and to a lesser extent by 1A2, 2B6, 2C8, 2C9, 2C19, and 2D6. It is also a weak inhibitor of 2D6. Methadone’s major metabolite is 2-ethylidene-1,5-dimethyl-3,3 diphenylpyrrolidine (EDDP) which is inactive. It has 2 active metabolites that are produced in very small amounts and are not clinically significant.

Excretion: Methadone undergoes urinary and fecal excretion. Urinary excretion of methadone increases as the magnitude of the dose increases. Methadone’s major metabolite EDDP is also eliminated both in the urine and feces.

Methadone’s long half-life allows it to be dosed once daily for MMT. It should be noted that methadone takes 3 to 7 days to reach steady state; for a methadone naïve adult a daily dose as low as 40 mg can be lethal by day 3. Single doses as low as 30 mg have known to be fatal in children.
Tolerance to methadone is lost very quickly and after 3 days of missed doses, the patient must not be given their current maintenance dose. True tolerance to methadone is rarely achieved therefore most people can be maintained on the same maintenance dose for years without requiring an increase.

Cross tolerance of other opioids to methadone is incomplete and erratic. One cannot accurately predict a patient’s methadone maintenance dose based on other opioid use nor should tolerance to methadone be assumed when initiating a new patient on methadone.

Adverse Effects

Much of methadone’s side effect profile is similar to other opioids. Please see the Methadose™ or Metadol® product monograph for more information.

| Frequently observed but improve with time | Drowsiness, nausea, weight gain, nervousness, appetite changes |
| Frequently observed and persistent | Constipation, sweating, sleep disturbances, changes in sexual desire/function, dry mouth |
| Infrequently observed | Vomiting, dizziness, flushing, unsteadiness, itching, myalgias, arthralgias, abdominal cramping, swelling of the feet and ankles, QTc interval prolongation (usually only occurs at higher doses), dental problems |

Drug Interactions

Methadone is primarily metabolized by CYP P450 3A4. (It is also metabolized to a lesser extent by CYP 1A2, 2B6, 2C8, 2C9, 2C19 and 2D6.) It is also a weak inhibitor of 2D6. Most interactions will be a result of induction or inhibition of CYP 3A4. Generally these interactions can be managed by monitoring for signs of toxicity or withdrawal and adjusting the dose accordingly. The sequence of witnessed dosing of the drugs is key to evaluating the significance of the interaction. When a patient is stabilized on a drug that affects liver metabolism and methadone is introduced, the interaction may not be observed unless the drug is discontinued. In a patient on a stable MMT dose, careful consideration and monitoring is required on initiation or discontinuation of a medication known to interact with methadone.

Drugs with additive effects

Extreme caution should be taken when drugs with additive adverse effects are prescribed, particularly those that can cause central nervous system or respiratory depression. In most methadone related deaths, concurrent use of sedatives such as benzodiazepines and alcohol were found to have contributed to the cause of death.

Opioid antagonists and partial agonists

Drugs that are opioid antagonists or partial agonists should be avoided in patients stabilized on methadone as they can precipitate withdrawal. Examples of these drugs are buprenorphine, pentazocine, butorphanol, nalbuphine, and naltrexone.

QTc Interval Prolongation

Methadone at higher doses can prolong the QT interval and concomitant use of other QT interval prolonging agents should be avoided.
Table 1: Drug Interactions with Methadone

<table>
<thead>
<tr>
<th>Drugs that may increase methadone level</th>
<th>Drugs that may decrease methadone levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Amiodarone</td>
<td>• Fluvoxamine</td>
</tr>
<tr>
<td>• Cimetidine</td>
<td>• Grapefruit juice</td>
</tr>
<tr>
<td>• Ciprofloxacin</td>
<td>• Itraconazole</td>
</tr>
<tr>
<td>• Clarithromycin</td>
<td>• Ketoconazole</td>
</tr>
<tr>
<td>• Diazepam</td>
<td>• Nefazodone</td>
</tr>
<tr>
<td>• Echinacea</td>
<td>• Paroxetine</td>
</tr>
<tr>
<td>• Erythromycin</td>
<td>• Sertraline</td>
</tr>
<tr>
<td>• Ethanol (acute ingestion)</td>
<td>• Voriconazole</td>
</tr>
<tr>
<td>• Fluconazole</td>
<td>• Urinary alkalinizers</td>
</tr>
<tr>
<td>• Ethanol (chronic ingestion)</td>
<td>• Other P450 inhibitors</td>
</tr>
<tr>
<td>• Fluvoxamine</td>
<td>• Phenobarbital</td>
</tr>
<tr>
<td>• Grapefruit juice</td>
<td>• Phenytoin</td>
</tr>
<tr>
<td>• Itraconazole</td>
<td>• Primidone</td>
</tr>
<tr>
<td>• Ketoconazole</td>
<td>• Rifampin</td>
</tr>
<tr>
<td>• Nefazodone</td>
<td>• Risperidone</td>
</tr>
<tr>
<td>• Paroxetine</td>
<td>• Ritonavir</td>
</tr>
<tr>
<td>• Sertraline</td>
<td>• Saquinavir</td>
</tr>
<tr>
<td>• Voriconazole</td>
<td>• St. John’s wort</td>
</tr>
<tr>
<td>• Urinary alkalinizers</td>
<td>• Urinary acidifiers</td>
</tr>
<tr>
<td>• Other P450 inhibitors</td>
<td>• Other P450 inducers</td>
</tr>
</tbody>
</table>

The above table does not include all possible drug interactions. The table is meant as a guide and does not preclude the use of sound clinical judgment.
Part Three: Methadone Overview

Methadone Dosing

MMT can be divided into 3 phases: the initial or early stabilization phase, the late stabilization phase and the maintenance phase. The initial stabilization phase has been reported to be the most common phase for death from methadone maintenance treatment. This is generally due to an overestimation of tolerance and an underestimation of methadone accumulation. As mentioned earlier, cross tolerance to methadone from other opioids is incomplete and unpredictable. “Dose Equivalency” reference tables should not be used to convert opioid intake to methadone for addiction.

Early Stabilization Phase (0-2 weeks):

This phase encompasses the first 2 weeks of the program. During this phase patients will be initiated on methadone and gradually titrated upward. The starting dose of methadone is 10-30 mg/day. The lower end of the dosing range (10-20 mg/day) should be used for those patients at higher risk of toxicity (elderly, on a drug that inhibits methadone metabolism, concomitant use of sedating medications).

The methadone dose can be increased by 5-10 mg every 3-4 days as required to suppress opioid cravings and alleviate withdrawal symptoms. It is very important not to increase the dose too quickly as the drug is accumulating for 5 days. The key is to “start low and go slow!” The pharmacist should ensure that the patient is aware of signs of toxicity and what to do about them. During this period the patient will have all their doses supervised unless the pharmacy or clinic is closed. The pharmacist should be aware that the patient may continue using their drug of choice during this period as methadone will not yet be at a maintenance dose and will wear off before their next dose.

Late Stabilization Phase (2-6 weeks):

This phase encompasses weeks two to six of the program. During this phase the patient’s dose will be optimized and the use of other opioids should be decreased. Dose adjustments of 5-10 mg every 5 to 7 days are made depending on severity, onset and duration of withdrawal symptoms. Most patients will be on 50-80 mg of methadone during this phase. The patient will still have all doses supervised (unless pharmacy/clinic closed) during this period.

Maintenance Phase (6 weeks +):

This phase encompasses the time period after the initial six weeks. By this time the patient should be on or close to their maintenance dose. The use of other opioids should be largely eliminated and the patient should not be experiencing withdrawal effects for the full 24 hour period. When a patient is receiving their optimal methadone dose they will not have withdrawal symptoms, opioid cravings will be reduced, euphoria from opioid use will be blocked and the patient will not have any psychomotor or intellectual impairment.

The usual maintenance for methadone is between 50-120 mg/day although doses upwards of 200 mg may be required in some patients. Pharmacists should be aware that potential QT interval changes can begin to manifest in doses above 100mg. Professional judgment must be used to evaluate patients who are using other medications that can also prolong the QTc interval.

If dose adjustment is required during this phase it is usually between 5-10 mg/day every 5 to 14 days. Dosage adjustment may be required if the patient subjectively complains of withdrawal symptoms, if cravings become
intense or if they relapse to opioid use. Patients should be cautioned to avoid driving or operating heavy machinery for several hours after dose increases until their body adjusts to the higher dose.

*Extended Methadone Maintenance*

This phase is only for long term stable patients. These patients have been socially rehabilitated and the intent of the extended program is to allow for more flexibility. Patients on this program meet the following criteria:

A. Two consecutive years of biopsychosocial stability in a methadone maintenance program.
   - Employment or other socially productive activity
   - Absence of criminality
   - Absence of drug and alcohol abuse
B. Reliability and honesty in keeping appointments and interactions with clinic staff.
C. Ability to safely store medications.

These patients are seen less frequently by their methadone prescriber, once every 1 to 3 months. The patients must have a negative urine drug screen on every visit or they will be reverted back to the standard program. The methadone is dispensed every 2 weeks or monthly and a witnessed dose must be taken at the time of dispensing under supervision of a pharmacist. Tablets may be given as an alternative to liquid methadone, and must be indicated by the prescriber.

*Urine Drug Screens*

The utility of urine drug screening is twofold. The prescriber will use the test to confirm that the patient *is not* taking illicit drugs and also to confirm that the patient *is* taking methadone.

If a patient tests positive for illicit substances it may indicate lifestyle instability. Patients will most likely lose carry privileges if they produce a “dirty” or positive urine sample for street drugs. If your patient has been prescribed narcotics or benzodiazepines from another practitioner offer to call the methadone clinic/prescriber on their behalf so that he/she is not penalized for producing a positive urine sample.

To confirm that the patient has been taking methadone, the prescriber will look for a positive methadone result on the drug screen. If the prescriber suspects that the sample has been tampered with and the patient is diverting his/her methadone, then it is prudent to perform additional testing for the methadone metabolite.

*Tapering off Methadone*

Occasionally a patient will request or be forced to taper off the methadone program. This can be for a variety of reasons and pharmacists should take this opportunity to discuss the patient’s treatment with them. A pharmacist can play an important role in helping patients manage side effects, etc. The pharmacist should counsel the patient on the risk of relapse of opioid use and encourage the patient to have prevention strategies in place. The rate of taper is usually 5-10% of the current dose every one to two weeks. Once the patient reaches 20 mg/day the taper should be slower as withdrawal effects become more pronounced. Many patients can only tolerate decreases of 1 to 2 mg every one to two weeks at this point. Patients should be monitored for signs of withdrawal and the taper should be reversed or held if cravings become too intense.

*Split Dosing*

Methadone prescribing may authorize “split doses” for various reasons. A very small proportion of patients may metabolize methadone rapidly and some patients may be better able to tolerate the side effects of the methadone if their dose is divided. The metabolism of methadone changes in pregnant women and some may require split doses during the latter half of their pregnancy.
Authorized split doses for patients who must have every dose witnessed require the patient to attend the pharmacy in the morning for a portion of their dose and again in the evening for the remainder. Pharmacists may not dispense a carry of the remainder of the patient’s daily dose unless specifically directed to do so by the prescriber in writing. If a patient requests or appears to require split dosing contact the prescriber for authorization.

Pregnancy

MMT is generally considered the standard of care for pregnant women with an opioid addiction. Opioid use disorder is dangerous for the fetus and is associated with increased risk of low birth weight, prematurity, neonatal withdrawal and sudden infant death syndrome. Opioid addiction affects fetal health primarily through effects of variable opioid withdrawal which is associated with fetal compromise and stillbirth. Conversely, MMT is associated with increased birth weight, decreased infant mortality and increased gestational age.

The goal of MMT is to use the dose of methadone that will keep the patient comfortable and abstinent from illicit opioids. The patient should be maintained on methadone for the duration of her pregnancy and for several months post-partum. As metabolism changes during pregnancy the patient should be monitored for sudden increased requirements of methadone (10-20 mg) or the need to split the dosing. Pharmacists can play an important role in determining when the patient needs a dosing change as they will follow the patient on a daily basis. Adjustment of the dose post-partum will likely be required. Pharmacists can also guide the patient in making health lifestyle changes during this period and recommending additional resources to the patient when appropriate/necessary.

Pregnant women should not miss a dose of methadone. The withdrawal symptoms associated with missing a dose may cause fetal distress. If the woman is feeling nauseous recommend that she sip the methadone slowly as this may prevent emesis of the dose. In some situations, it may be advisable to have the women remain in the pharmacy until the dose is absorbed. If emesis occurs during this period, then you can accurately assess what portion of the dose should be replaced. The prescriber should be contacted immediately and a replacement dose ordered.

Methadone crosses the placental barrier and, therefore, the newborn should be monitored closely for signs of neonatal abstinence syndrome and treated with medical care.

Breast Feeding

Methadone is considered compatible with breast feeding according the American Pediatric Society. However, since methadone is present in the breast milk it is important that the patient and their prescriber discuss the risks and benefits of breastfeeding while being maintained on methadone. It is important to note that methadone in the breast milk will not necessarily prevent symptoms of neonatal abstinence syndrome.

Incarceration

The provision of methadone in correctional facilities provides for continuation of the harm reduction philosophy. An important goal is to prevent transmission of blood borne pathogens such as HIV and HCV. Injection drug use is known to be high among inmate populations and therefore it is believed that MMT can help prevent the spread of HIV and HCV. The National Task Force on HIV, AIDS, and Injection Drug Use recommended the following:

- Continuation of methadone in patients previously stabilized on methadone prior to incarceration.
- Make MMT available to those inmates who are in opioid withdrawal.
- Evaluate the need for MMT prior to release and ensure transfer to an appropriate community program upon release.
If your pharmacy is providing methadone to a correctional facility you must ensure that the patients are receiving the correct dose. If the patient has been stabilized on methadone prior to incarceration you must contact the dispensing pharmacy to verify the date, time and dose of the last drink. If a patient has been diverting his/her methadone, giving the usual prescribed dose in the correctional facility can result in sedation or death. Methadone should be dispensed with a tamper proof seal prior to being delivered to the correctional facility.

Treatment of Acute Pain

Methadone is non-analgesic in a person stabilized on MMT. A common misconception among health care professionals is that if a person is on methadone then they do not need to be treated for their pain. Unfortunately, due to the stigma associated with drug addiction many of these patients are managed inappropriately when they present with acute pain. As many of these patients will have a history of drug seeking behavior, the problems in assessing and treating pain in somebody who is methadone maintained are at least threefold:

1. The objective assessment of a subjective phenomenon (pain).
2. The question whether the pain presentation of the patient suffering from opiate dependence is in fact “drug seeking” or a genuine request for relief of real pain.
3. The appropriate dose of opiate or other analgesics or adjuncts in a methadone maintained patient.

The first and second problems are best dealt with by a thorough and objective assessment of the presenting illness and its correlated pain. This is a matter of clinical judgement and includes making one’s best estimate as to the appropriate treatment for similar causes of pain in other patients.

For mild to moderate pain, recommend the use of NSAIDs and acetaminophen as first line therapy. These should be prescribed in the usual dosages and frequency.

For more severe pain, patients should be initiated on opioid analgesics (morphine, oxycodone, hydromorphone, or codeine) in doses similar to those used for other people with similar pain. Monitor the patient’s pain level and adjust the dosing accordingly. Patients stabilized on MMT (greater than 3 months) will likely require higher doses (10-50%) and more frequent dosing of short acting opioids. The patient should be maintained on their usual MMT dose while being treated for acute pain. Ideally discussion should occur between any practitioner prescribing a new opioid for these patients and the methadone prescriber. In addition, the pharmacist should consider notifying the methadone prescriber if a patient receives a new prescription for a benzodiazepine or opioid from another practitioner.

Pentazocine, nalbuphine, and buprenorphine are partial opiate antagonists and should not be administered to MMT patients as they will cause severe opiate withdrawal.

Overdose

Methadone overdose is a medical emergency as is any other opioid overdose. Methadone overdose is characterized by extreme sedation, stupor or coma, respiratory depression, bradycardia and hypotension. Naloxone, an opioid antagonist, is used to treat methadone overdose. The difficulty in treating a methadone overdose is the exceptionally long half life of methadone. A naloxone infusion should be considered over repeated bolus dosing. Naloxone should be administered for a minimum of 24 hours (up to several days) followed by at least 12 hours of monitoring after the infusion is stopped. Naloxone competitively inhibits methadone at the opioid receptor thus the infusion is required until sufficient time has passed that the patient’s own metabolism has cleared the methadone out of his/her system. Care should be taken to titrate the naloxone slowly so as not to precipitate severe withdrawal in the patient.
Diversion

Diversion of take home doses of methadone can have fatal consequences if taken by a person naïve to methadone. In most cases, methadone is diverted to friends and family who are experiencing opioid withdrawal but are not on the program, or sold for profit. It is also taken by some people for the psychoactive effects that can occur at doses higher than a person’s tolerance.

Some tactics for preventing/minimizing diversion include:

- Having the patients return their empty carry bottles to the pharmacy. The bottles should be counted to ensure all the bottles are returned and none have been given away.
- Requiring the patient to present their remaining take-home doses to the pharmacy at random intervals.
- Educating the patient on the dangers of taking methadone if you have not developed a tolerance to it.
- Requiring the patients to present their lock box prior to dispensing take home doses for the first time. Storage in a locked box will prevent accidental ingestion by someone who may think it is simply juice (especially children).
- Methadone must always be dispensed directly to the person. “Friends” are not allowed to pick up someone else’s methadone.
- Maintaining a sight line on the patient at all times when they are given their methadone to be ingested. Some patients may try to “pocket” their dose, or spit it into another container.

Chronic Viral Infections and MMT

Methadone is important from both an individual and public perspective with respect to HIV/AIDS and hepatitis C. As discussed earlier, methadone is a harm reduction strategy aimed at reducing the spread of diseases (including HIV/AIDS and hepatitis C) through needle sharing and prostitution. For the individual, methadone can help stabilize the patient and thus increase compliance with AIDS medications. Many AIDS medications interact with methadone but these interactions can generally be managed by monitoring for side effects and adjusting the dose accordingly. It is especially important to closely monitor patients when their medication or dose changes or is discontinued. The pharmacist can play an important role in encouraging compliance with these medications on a regular basis. Helping this patient population manage side effects is equally important and can have a huge impact on quality of life.

Recommended Readings

Pharmacists must have onsite or readily available references and treatment guidelines. Minimum requirements include the College of Pharmacists of Manitoba Principles for the Provision of Opioid Dependence Treatment by Manitoba Pharmacists and the College of Physicians and Surgeons of Manitoba Recommended Practices “Manitoba Methadone and Buprenorphine Maintenance” document. A list of additional resources can be found on the Centre for Addiction and Mental Health website at http://www.camh.ca/en/education/about/services/camh_library/Documents/RLGmethadone.pdf

Other recommended readings include:

**Part Four:**
Implementing Opioid Dependence Treatment in Pharmacy Practice

**Methadone**

**Including Methadone Maintenance Treatment (MMT) in your Pharmacy Practice**

A patient’s success with opioid dependence treatment can be linked to the interactions they have with their health care providers. All members of the health care team should monitor the patients’ progress and recommend changes to their care as needed. Pharmacists must have a clear understanding of the goals of the program and a willingness to participate fully with other members of the health care team in order to contribute to their patients’ success. Pharmacists are in a unique position as they will see the patient more than any other member of the treatment team. These daily interactions allow the pharmacist to monitor their patients’ progress and identify actual and potential drug related problems.

**Community considerations and workflow**

By including methadone in your pharmacy practice you are providing an important service to your patients and your community. You might choose to provide methadone to a small number of patients, perhaps beginning with those who are already patients of your pharmacy. A confidential area in the pharmacy for counselling and observation of ingestion is required.

If you decide to make methadone a part of your practice, the community may notice the increased visibility of opioid addicts in the area. There are a number of steps you can take to proactively address and alleviate the community’s concerns:

- Establish solid working relationships with the practitioners/clinics who prescribe methadone for your patients. Ensure they realize you will be an active participant in your patient’s care, and that you will be communicating frequently with the prescriber if the patient is having difficulty on the program.
- Consider meeting with the community police office to let them know that you will be involved in the methadone program. Ensure that they realize that there are benefits to the community in helping opioid addicted patients obtain methadone maintenance treatment.
- Ensure that your patients realize their responsibility to the community. Although their primary concern will be obtaining methadone on a regular basis, they must be informed that the program can only operate effectively if they respect the surrounding businesses and homes as well as other patients. This can be enhanced by ensuring agreements highlight behavior both inside and outside the pharmacy.
- Ensure that drinking cups used for methadone dispensing do not leave the pharmacy. Monitor the area outside your pharmacy to ensure it is clean and free of drinking cups and methadone carry bottles.

If methadone becomes a major focus of your practice, careful planning and diligence will be required to avoid patient line-ups and patient loitering. Line-ups are not acceptable to the surrounding neighborhood and can focus undue attention to the program. Strategies to reduce line-ups of patients outside your pharmacy include:

- Establish a regular opening time, and stick to it. Do not open the pharmacy a few minutes early because you happen to be in early. If patients begin to arrive early, let them know that they must not loiter in front of the pharmacy before opening.
- Ensure that your waiting area is large enough to accommodate the number of clients you have.
- Consider establishing “appointments” for your patients on methadone. For example, you may want to schedule half of your patients to attend the pharmacy in the morning and the other half to attend in the afternoon.
Policy and Procedure Manual

A site specific Policy and Procedures Manual should be readily available onsite when methadone is dispensed for harm reduction and management of pain.

Education and Training

Pharmacists must be knowledgeable in all pertinent aspects of methadone use when involved in care with methadone in order to prevent errors and close calls. Section 18 of the Pharmaceutical Regulation states that a member may only engage in the aspects of pharmacy practice that he or she has the requisite knowledge, skill and judgment to provide or perform and that are appropriate to his or her area of practice. At least one pharmacist must be extensively knowledgeable at each pharmacy that provides methadone and the expectation is that the opioid dependence treatment course listed below will be successfully completed within 6 months of initiating care. Successful completion of this course would demonstrate compliance with Section 18 of the Regulation with respect to MMT. An exception to this rule would be for a pharmacy that must provide methadone for continuation of care. In this situation the pharmacy would have a 6 month grace period to allow a pharmacist to take the required course. In the interim any pharmacy dispensing methadone waiting for specialized training must have a “trained/knowledgeable” pharmacist functioning as a mentor who may be at another pharmacy. Contact CPhM for assistance in finding a mentor.

The new Opioid Replacement Therapy 101: An introduction to clinical practice joint training program replaces the Principles for the Provision of Opioid Dependence Treatment by Manitoba Pharmacists Certificate Program as the required specialized opioid dependence treatment training for pharmacists dispensing methadone. The CPhM, in partnership with the College of Physicians and Surgeons of Manitoba (CPSM) and the College of Registered Nurses of Manitoba (CRNM), is excited to launch this new multi-disciplinary training course for care providers who wish to become involved in treating those with opioid use disorder. This collaborative approach will enrich discussions during the training process. It will ensure that all physicians, nurse practitioners and pharmacists successfully complete training with the same high standard of knowledge and insight into the collaborative approach to treatment that serves this complex patient population best. Training together will hopefully translate into stronger and more frequent interdisciplinary collaboration in clinical practice. The two day course is packed with practical knowledge and skill building exercises, including opportunities to practice interviewing patients with opioid use disorder in a supportive environment. Please see the CPhM website for more information on the Opioid Replacement Therapy 101 course including future offer dates, pre-requisites, and registration details.

Those who previously completed the Principles for the Provision of Opioid Dependence Treatment by Manitoba Pharmacists Certificate Program are encouraged to complete the new, updated program, but it is not required.

Please contact the CPhM office if you are wondering if a similar course would meet the training requirement for providing opioid dependence treatment in your practice.

Pharmacist - Practitioner Communication

The methadone prescriber/patient/pharmacist will enter into a common care plan with the rights, obligations, conditions and consequences agreed upon.

Pharmacists who participate in the methadone maintenance program interact with most of their patients on a daily basis. Even those patients with carry privileges see their dispensing pharmacist more often than any other health professional, including their physician or methadone prescriber.
In order to ensure that the prescriber is making therapeutic decisions based on reliable information from and about the patient, you must inform the prescriber if you have concerns about the patient’s progress or success with the program. Contacting the prescriber regarding your concerns is essential for patient care.

There are several situations that should be reported to the prescriber /clinic. The following are examples of reportable situations:

- If a patient exhibits unusual behavior
- If a patient has not picked up their daily dose
- If a patient refuses all or a portion of their daily dose
- If a patient appears to be impaired or intoxicated when they arrive at the pharmacy
- If a patient has filled a prescription for opioids, or other mood-altering medications that have not been previously approved by the methadone prescriber
- If a patient vomits dose after witnessed dosing
- Failure to provide a lock box
- Breach of treatment agreement

It is good practice to document these communications with the prescriber. This can be done either in an electronic record or on the hard copy of the prescription.

**Methadone Exemption for Prescribers**

In order to prescribe methadone, an exemption must be obtained from the Office of Controlled Substances, Health Canada. A prescriber may have an exemption for methadone for addiction, methadone for analgesia or both when appropriate.

In Manitoba, prescribers who wish to prescribe methadone for addiction must take a methadone training course and they must work several shifts under supervision in a methadone clinic. The applications are then reviewed by the Registrar of the appropriate college who may make additional recommendations.

It is the responsibility of the dispensing pharmacist to verify that the methadone prescriber has the appropriate exemption. This information can be obtained by contacting the the Bureau of Drug Surveillance in Ottawa at 1-866-358-0453. As well, prescriber lists including prescribers with methadone and/or buprenorphine/naloxone exemptions are now available on the secure member portal of the CPhM website. Pharmacists will no longer need to contact the College office by phone for this information but can log in and access this information anytime. The lists are for access by pharmacists only. They are to be used solely for referencing a prescriber’s license number and/or exemption status and are not for distribution. The names of methadone or buprenorphine/naloxone prescribers or any other information contained in these lists cannot be provided to patients or anyone else requesting this information.

The lists from the College of Physicians and Surgeons of Manitoba are updated monthly, and changes to the methadone and buprenorphine/naloxone prescriber list will be updated throughout the month as additions or deletions occur. Pharmacists may access the prescriber lists by logging in to their Member homepage with their unique user name and password, scrolling down to the “My Documents” section, and clicking on the Prescriber Lists.

If a prescriber exemption is not included in the lists, please confirm his/her exemption status by contacting the appropriate licencing body:

- College of Physicians and Surgeons of Manitoba at (204) 774-4344 or toll free (in Manitoba) at (877) 774-4344
- College of Registered Nurses of Manitoba (204) 774-3477.

Information on Temporary Exemptions in hospital can be found under the section, “Temporary Exemptions”.
M3P Prescription Program

Methadone is covered by the M3P program and must be written on the duplicate prescription form. These prescription pads are personalized and numerically recorded for the prescriber. Prescribers cannot exchange pads or write on a form that is not their own.

The prescription must contain the following information:

- The daily dose must be written both numerically and alphabetically.
- The total dose must be written both numerically and alphabetically.
  - A prescription that is written that clearly indicates the daily dose of milligrams (or milliliters) of methadone to be dispensed and that clearly indicates the start and end date on which the methadone is to be dispensed would satisfy the total dose requirement. The prescription written this way is clear and does not pose any patient safety concerns. If needed, the pharmacist can add the total dose as this information does not interfere with the therapeutic intention of the prescriber.
- The first and last day must be clearly stated. No doses are to be given beyond the last day even if the patient missed a day and technically has a dose left.
- The doses to be witnessed and those to be carried must be clearly indicated either on the prescription or on an accompanying pharmacy agreement.

Where there is any discrepancy or doubt about a methadone prescription, the pharmacist should verify the prescription with the prescriber.

Any changes to a patient’s previously stable dose requires a new prescription. A change in the witnessed dosing dates or number of carries can be taken verbally or by fax.

Faxing M3P Prescriptions for Methadone or Buprenorphine/Naloxone

Prescriptions for methadone or buprenorphine/naloxone may be transmitted via facsimile only for the purpose of a methadone/buprenorphine maintenance program. Faxed prescriptions for methadone or buprenorphine/naloxone for opioid dependency must be written on an original M3P form with a note attached to clearly indicate the daily dosage. A sample template can be found in Appendix C that may be used for faxing prescriptions, including M3P prescriptions for methadone and buprenorphine/naloxone. This form can be used by prescribers when faxing prescriptions to a pharmacy.

It is the pharmacist’s responsibility to verify the origin of transmission, the authenticity of the prescription, and if not known to the pharmacist, the signature of the prescriber. Faxed prescriptions for methadone or buprenorphine/naloxone may be accepted from another province as long as the above requirements are met.

The pharmacy must keep the faxed M3P prescription and faxed written documentation together for a minimum of 5 years (electronic or hardcopy). The original prescription no longer needs to be sent to the pharmacy in these situations.

In rare emergency situations, a pharmacist may be asked to accept duplicate prescription forms by fax on an interim basis for methadone for analgesia. In these emergency situations, the pharmacist is required to assess each and every situation using professional judgment in direct consultation with the prescriber.

- If an emergency faxed duplicate is warranted, obtain written documentation from the prescriber, including:
  - The methadone prescriber’s signature,
  - The request for fax transmission of a M3P prescription,
A brief description of the emergency situation, and
- Guarantee of delivery of the original duplicate prescription to the pharmacy on a stated reasonable date.

A sample document can be found in Appendix D that may be used to document why a facsimile of a M3P prescription has been accepted. This document can be sent to the prescriber to fill in, sign and return to the pharmacy.

**New Patient on Opioid Dependence Treatment**

Upon receiving a new patient on methadone or buprenorphine-naloxone, pharmacists are required to confirm that the prescription is written by a valid prescriber with the appropriate exemption. The pharmacist must screen and assess the appropriateness of the treatment at the dose prescribed.

Pharmacists should review the store hours, the dispensing and dosing process, the obligations of the patient and the pharmacy, the mutual expectations including expectations for conduct and behaviour within the pharmacy, the procedure for handling missed, spoiled, lost/stolen, or vomited doses, and counselling regarding the therapy including pertinent clinical details related to safety and efficacy. This preliminary discussion is best documented by signing a two-way agreement between the pharmacy and the patient to acknowledge the mutual agreement and understanding of key elements involved in the provision of the medication. Pharmacies with highly collaborative practices may also consider a three-way agreement between the prescriber, pharmacy, and patient.\(^i\)

**Methadone Dispensing**

All methadone prescriptions for patients being treated for opioid dependence must be dispensed using the commercially available methadone 10 mg/ml products. Pharmacists may no longer dispense compounded methadone (as of mid-January 2015) since a commercially available product has been introduced. Please see the Manitoba Health, Healthy Living and Seniors Methadone Reimbursement Procedure and Questions and Answers in Appendix A or contact Manitoba Health for updated information.

**Dispensing Methadose™**

Methadose™ is available in two dosage forms: a 10 mg/ml red, cherry-flavoured oral concentrate, and a 10 mg/ml dye-free, sugar-free, unflavoured oral concentrate.

The cherry-flavoured formulation is a hypertonic concentrate containing sucrose 40%, and therefore does not lend itself to injection. It can be dispensed without further dilution, however, pharmacists/prescribers may dilute this formulation at their clinical discretion.\(^i\)

The clear, dye-free formulation is not hypertonic; therefore, in Manitoba, pharmacists are required to dilute this product to a final volume of approximately 60 ml to 100 ml with a coloured, flavoured vehicle such as grape flavoured Kool-Aid™ or orange Tang™. Dilution with a crystalline liquid is required to minimize the risk of abuse and/or diversion by injection.

The clear, dye-free concentrate may be preferred for patients who have dye allergies, who prefer a sugar-free option, or for those who prefer an alternate flavor to cherry.
**Diluting Methadose™**

Diluted Methadose™ must be prepared by staff who are competent in the processes and use of equipment to dispense the diluted solution.

The dye-free, sugar-free, unflavoured oral concentrate must be diluted to a total volume of approximately 60 to 100 ml with a suitable crystalline diluent such as grape Kool-Aid™ or orange Tang™ to mask the bitter taste of methadone and to discourage diversion. **Dilution of the unflavored oral concentrate with water is not acceptable.**

Although dilution is not required for the cherry-flavoured formulation, there may be situations where dilution should be considered—for example, when dispensing small volumes where surface adhesion of the concentrate to the dispensing device or bottle may result in inaccurate or variable dose delivery, where risk of potential abuse and/or diversion is suspected, or when dispensing carries.

After witnessing the ingestion of the Methadose™ cherry-flavoured oral concentrate, given the concentrated solution of 10mg/ml, the pharmacist must provide water to rinse the dispensing device i.e. cup, to rinse any residual medication and must witness ingestion of the water and engage the patient in a short conversation to ensure that the entire dose has been ingested to reduce the risk of diversion by cheeking.\textsuperscript{vii}

Ensure that equipment or devices used for dispensing and dilution meet standards for accuracy of measuring devices. Measuring devices used in the dispensing of methadone must be accurately measured using a calibrated device that will minimize the error rate to no greater than 0.1 ml. Graduated cylinders are not recommended. Distinctly label equipment and devices used to measure Methadose™ and use these devices exclusively to dispense methadone where possible. Keep this equipment in a designated area to avoid mix-ups.

The stability and sterility of Methadose™ diluted with a crystalline drink such as Kool-Aid™, Tang™, or Crystal Light™ is unknown as published studies are not available. Dispensing guidelines within many provincial jurisdictions have identified the duration of stability of methadone in various diluents from a collection of past literature (see Table 2); however, available literature does not address the issue of sterility, which includes the likelihood of bacterial growth in the prepared solution stored under refrigerated or unrefrigerated conditions. The information in Table 2 is provided as best existing guidance to allow you to use professional judgment when assigning best-before dates to diluted Methadose™.\textsuperscript{i}

Pharmacists are required to use best judgment to assign the beyond-use date for diluted products. All diluted Methadose™ products must be refrigerated and carries are permitted a maximum expiry date of 14 days from the date of dilution. The dispensing staff must assign dates based on the earliest expiry of the ingredients used or 14 days refrigerated, whichever comes first. Dilution with fruit juices may require a shorter dating as an opened juice bottle may have a best before date that is earlier than 14 days.

Formulations prepared in juices should have an expiry that does not exceed the shelf-life of the juice under the conditions of storage recommended upon opening the bottle. In general, dispensing methadone in fruit juices or diluents not identified below or within a product monograph is discouraged due to the lack of sufficient evidence for stability and sterility upon extended storage of the mixture, especially beyond immediate ingestion upon dilution.

To avoid the potential for mix-ups during dosing, and to optimize the stability and sterility of dispensed carries, diluted Methadose™ should not be prepared far in advance.

Note: Published guidance on the stability of methadone solutions is reported in many provincial guidelines based on a study from the early 1990s. However, there is a need for more updated testing to acknowledge both the stability and sterility of prepared products under various compounding conditions.
Table 2: Methadone stability in various diluents for carries\textsuperscript{ix}

<table>
<thead>
<tr>
<th>Diluent</th>
<th>Stability at room temperature (20\textdegree{} to 25\textdegree{} C)</th>
<th>Stability at refrigerated temperature (5\textdegree{} C)</th>
<th>Period of acceptable sterility for oral consumption under refrigeration (i.e., bacterial or pathogenic growth)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grape flavoured Kool-Aid</td>
<td>17 days</td>
<td>55 days</td>
<td>• Unknown for dilution with Methadose • 14 days for diluted Metadol preparations</td>
</tr>
<tr>
<td>Orange flavoured Tang</td>
<td>11 days</td>
<td>49 days</td>
<td>• Unknown for dilution with Methadose • 14 days for diluted Metadol preparations</td>
</tr>
<tr>
<td>Allen’s Apple Juice</td>
<td>9 days</td>
<td>47 days</td>
<td>• Unknown for dilution with Methadose • 7 days for diluted Metadol preparations</td>
</tr>
<tr>
<td>Grape flavoured Crystal Light</td>
<td>8 days</td>
<td>34 days</td>
<td>• Unknown for dilution with Methadose • 14 days for diluted Metadol preparation</td>
</tr>
<tr>
<td>Grape flavoured Crystal Light with 0.1% sodium benzoate</td>
<td>29 days</td>
<td>Not available</td>
<td>• Unknown for dilution with Methadose</td>
</tr>
</tbody>
</table>

Storage

An unopened bottle of Methadose™ has a shelf life of approximately four years from the date of manufacture. The expiry date will appear on the bottle. Once opened, it can be stored at room temperature (15-30\textdegree{}C) for six months. Diluted preparations must be refrigerated.\textsuperscript{ix}

Pharmacy Storage and Security

The primary goal when selecting a storage container or site for storage of methadone solution is the prevention of mistaken consumption. If methadone solution or concentrate is stored in the refrigerator of the pharmacy it is essential to ensure that all staff beverages be stored elsewhere. The containers used to store methadone should be distinctive and recognizable. Pharmacists should avoid using similar containers to store other liquids in the dispensary. Avoid using containers that have other uses, such as distilled water bottles and beverage bottles.

There is no evidence of an increased risk of theft or robbery in pharmacies that dispense methadone. As in all pharmacies, adequate security systems must be in place to minimize the possibility of theft.

Labelling of Prescription Bottles

All patient labels will be compliant with the provisions of The Pharmaceutical Act and Regulations. For methadone maintenance therapy, the label needs to indicate the date of ingestion and the total dosage (mg) in the bottle with a notation that the dosage was made up to a set volume (if applicable). For example, the sig on a label may read “Drink the contents of this bottle containing 85mg of methadone mixed in Tang to a total volume of 60mL once daily (Nov. 1-Nov. 23)".

Methadone doses that have been pre-measured into individual patient dose bottles/containers must be clearly labelled with the patient name, dosage, and initials of the pharmacist who checked the measured doses. As well, please see further information on warning labels under “Take Home Doses (Carries)” on page 28.

Methadone Inventory Records

All of the requirements for recording purchases of narcotics must be met for methadone. Perpetual inventories are an effective means of tracking inventory levels by recording the volume of methadone solution received and dispensed. For pharmacies that dispense large amounts of methadone, reconciliation of methadone on-hand should be done more frequently (i.e. once monthly).
The Regulations of *The Controlled Drugs and Substances Act* require pharmacist to report loss or theft of controlled substances within 10 days of discovery of said loss.

**Billing**

Billing for methadone shall be submitted on the day of service provision. Methadose™ must be entered into DPIN as the total number of milliliters of Methadose™ dispensed. For example, 80mg of methadone would be billed as 8 mL (of Methadose™ 10mg/ml). If a patient is dispensed Methadose™ carries, the total quantity of Methadose received by the patient must be entered into DPIN along with the correct days supply, on the day of service provision. Missed doses of methadone must be reversed in the DPIN network before the end of the business day. Please see Appendix A for the Methadone Reimbursement Procedure from Provincial Drug Programs, Manitoba Health, Healthy Living and Seniors or contact Manitoba Health directly for updated information.

**MY, MZ, and Interaction Codes Caution**

Previously the software that generated the critical patient care codes in DPIN did not recognize the pseudo-DINS of compounded methadone. Therefore the DPIN would not generate critical patient care codes, MY (duplicate drug other pharmacy) or MZ (duplicate therapy other pharmacy) for prescriptions where compounded methadone oral solution was dispensed. As well, drug interactions for compounded methadone were not identified in DPIN and were not flagged. Now, with the commercial availability of methadone 10 mg/ml oral solution, relevant patient care codes and drug interactions should be generated by DPIN. Pharmacists are to review the critical patient care codes and drug interactions, decide on an appropriate action, and document the response in the appropriate place(s). Please note that pharmacists should still review a methadone patient’s DPIN record occasionally to ensure that there is no misuse of other mood-altering medications. Any concerns should be brought to the attention of the methadone prescriber, and if deemed appropriate, the prescriber of the mood-altering medication.

**Witnessed Ingestion**

The pharmacist is responsible for:
- Confirming the patient’s identity,
- Reviewing the patient’s profile for pertinent concerns,
- Assessing the patient for intoxication,
- Documenting the witnessed dose ingestion,
- Monitoring the patient post-ingestion for a duration based on individual patient circumstances, and
- Ongoing monitoring and troubleshooting.

**Positive Identification**

The pharmacist must take reasonable steps to positively identify the patient prior to dispensing methadone to the patient for the first time. It is recommended that the patient provide government issued photo identification. If the patient cannot provide the required identification, the prescriber may be contacted to assist in verifying the patient’s identity. Some pharmacies that have multiple pharmacists and/or use relief pharmacists keep a photo of the patient on file (with the patient’s permission) so that the patients do not have to provide photo identification each time they come in. Addressing the patient by their full name and stating their dose in a confidential manner is a good practice to ensure the correct person is receiving the correct dose.

**Daily Witnessed Ingestion**

When a patient is prescribed daily witnessed ingestion they must attend a pharmacy that is open every day of the week. In most cases, the directions on the prescription will indicate which doses are to be witnessed and
which doses are to be carried, however if the prescriber is unclear in his or her intentions, the pharmacist must assume daily witnessed ingestion and supervise every dose. The act of witnessing methadone ingestion by a pharmacist is not a function that may be delegated. In the event the pharmacy is not open 7 days a week, or is closed for holidays, the prescriber must authorize the pharmacist to provide carries for the days the pharmacy is closed, or make appropriate arrangements with another pharmacy. If this is the case, communication between the two pharmacies is paramount.

The pharmacist must assess the patient prior to providing him/her with methadone. Once the patient receives the methadone, the pharmacist must maintain a sight line with the methadone until the full dose is ingested to ensure that the dose is not diverted. After the patient drinks the methadone, a short conversation is required to ensure that the entire dose of methadone has been swallowed. Confirmation that the methadone is swallowed is necessary as some patients may try to keep the methadone in their mouth until they can spit it into a container. It may be helpful to have a policy that does not allow outside drinks to be present for the witnessed dose. If water is given to the patient in a cup, ensure that the empty cup is returned to the pharmacist.

After witnessing the ingestion of the Methadose™ cherry-flavoured oral concentrate, given the concentrated solution of 10mg/ml, the pharmacist must provide water to rinse the dispensing device i.e. cup, to rinse any residual medication and must witness ingestion of the water and engage the patient in a short conversation to ensure that the entire dose has been ingested to reduce the risk of diversion by cheeking.

**Intoxicated Patients**

Prior to dispensing methadone to a patient the pharmacist must assess the patient for signs of intoxication. These signs can include, but are not limited to, slurred speech, un-coordination, smelling of alcohol or other unusual behaviors. If you suspect that the patient is intoxicated the dose should be held until the patient is sober. The prescriber should be notified of the situation and the course of action discussed. In most methadone related deaths, concurrent use of sedatives such as alcohol or benzodiazepines were found to have contributed to the cause of death. Methadone withdrawal, while uncomfortable for the patient, is not life threatening but methadone given in combination with other intoxicating drugs can be fatal. If possible, explain to the patient that you are holding the dose to ensure his/her safety and clearly document your actions.

**Refusing methadone administration**

The decision to administer methadone to a patient should always be subject to your professional judgment. As discussed in the previous section, if you suspect that the patient is intoxicated, dosing should be refused until the situation has resolved. If the patient has missed more than 3 consecutive days of methadone doses, the dose must also be held. Please see section on “Missed Doses” on page 30 for further information.

**Documentation**

Pharmacies must maintain a log of witnessed and take home doses. This log should include the time of dosing of witnessed ingestions. This information is important for both pharmacists and prescribers in assessing patients. If the patient should vomit a dose, having the exact time of witnessed dosing is helpful in deciding on a replacement dose. For stores that are open 24 hours, this information will prevent intoxication/overdose resulting from witnessed dosing times that are too close together. The methadone log should also state the name of the patient, a picture (if possible), and the patient’s address or date of birth which can be used to verify their identity. It may be helpful to state the days they normally witness and carry on the log as well. If a patient is transferring from another pharmacy to your pharmacy it is important to know when the patient had their last witnessed ingestion and the amount of methadone received. This should be documented on the original prescription. Some pharmacies will have the patients sign for their witnessed ingestions and carries in the methadone log. This is an excellent tool for preventing and resolving discrepancies. A separate sheet should be maintained for each patient to prevent confusion and maintain privacy.
Guest Drinkers

Occasionally you may be asked to accept a patient on a temporary basis to be medicated at your pharmacy. This may be for a variety of reasons such as vacation or business travel. In these cases the patient can either not be provided with enough carries for the entire duration of travel or they are not stable enough to have carries for the entire duration of travel.

Pharmacists can dispense out-of-province prescriptions for methadone for dependence and/or buprenorphine-naloxone for dependence if they confirm the following:

- The prescription is authentic, current, and appropriate;
- For methadone prescriptions, that the prescriber has the appropriate exemption to prescribe methadone from the Office of Controlled Substances, Health Canada;
- For buprenorphine-naloxone prescriptions, that the out-of-province prescriber has authority to prescribe narcotics within their provincial jurisdiction, and meets the prescribing requirements for buprenorphine-naloxone within his/her province.

Please note that, as with other medications covered under the M3P program, pharmacists can fill prescriptions for methadone or buprenorphine/naloxone that are written on forms used in the province or territory where the practitioner resides. Prescriptions written by authorized practitioners in other provinces and territories need only meet the requirements in place in their jurisdiction for the prescription to be filled in Manitoba. Faxed prescriptions for methadone or buprenorphine/naloxone may be accepted from another province as long as the prescription is for the sole purposes of opioid dependence treatment and the facsimile includes a note from the prescriber clearly indicating the daily dosage.

Communication between the temporary and regular pharmacy is imperative at the beginning and ending of the dosing interval. This communication is required to prevent double dosing and/or missed dosing. Information on time and amount of last witnessed ingestion as well as any carries provided must be communicated between pharmacies. The “guest” is required to present identification to the temporary pharmacy prior to receiving any methadone to ensure positive identification. If there is a valid prescription at the regular pharmacy covering the period the patient will be at the temporary pharmacy, this prescription must be cancelled and the methadone prescriber must issue a new prescription for the temporary pharmacy. If/when the patient returns to the regular pharmacy, a new prescription is required.

Take Home Doses (Carries)

A “carry” refers to a dose of methadone (or buprenorphine-naloxone) that the patient is authorized to take home for self-administration. Take home medication or “carries” are given to stable patients to reduce disruption in and improve the quality of the patients’ daily life. These doses are consumed unsupervised at home. Carries are considered privileges and are given as a reward to stable patients. These patients must demonstrate to the prescriber that they are clinically stable and are able to store the methadone safely. Carries are not recommended for the initial 2 month period of MMT so the prescriber can adequately assess the patients.

The patient is the only person who can pick up his/her carries. These carries should be signed for by the patient in a methadone log. Typically, the patient will have a supervised dose on the day he/she picks up the carries. Under exceptional medical or social circumstances, and only with the authorization of the methadone prescriber, the pharmacist himself/herself may consider delivering the methadone to the patient to witness the
required dose and deliver the carries. Direct supervision of methadone ingestion by a pharmacist cannot be
delegated with the exception of deferring to a methadone prescriber at an established harm reduction program
or another pharmacist.

The number of carries each patient has is dependent on clinical stability, duration of time in the methadone
program and the ability to safely store the methadone. Patients will not receive carries during the first 2 months
of treatment with the exception of possibly a Sunday carry. After the initial 2 month stabilization period patients
may be granted up to 1 additional carry per month, to a maximum of 6 carries per week. Should the patient
become unstable while receiving carries the number of carries may be decreased. This can be for a variety of
reasons including missed appointments, positive urine drug screen, and/or unacceptable behavior in the
pharmacy or clinic.

Storage of Carries

Methadone can be harmful or fatal if taken by a child or an adult who is not tolerant of opioids. Accidental
poisoning can be prevented by the simple safeguards. Methadone must be dispensed from the pharmacy in
a bottle with childproof caps and stored in a lock box by the patient. Tackle boxes and small tool boxes with a
lock work well for this purpose. When initiating methadone carries, the pharmacist must request the patient
show them the lock box prior to the patient receiving his/her first carry, unless the pharmacist can confirm that
this has already been done by the prescribing clinic. This must be documented in the patient’s file. Patients
should be routinely counseled on the importance of safe and secure storage of methadone carries.

Patients should be advised to store carries diluted with juice or crystalline solution in the refrigerator to prevent
the juice/tang from going rancid.

Documentation for non-childproof caps

Should the patient request non-childproof caps this must be documented on their file and the pharmacist
should reinforce the importance of safe methadone storage and the patients responsibility in ensuring no other
persons have access to their methadone. As per section 81 of the Pharmaceutical Regulation, the patient must
declare in writing that they do not want childproof caps and it must be reasonable given the patients
circumstances.

Warning Labels

Counsel patients that methadone is very dangerous if consumed by anyone other than themselves. Methadone
is a hazardous substance when consumed by a child or adult who is not tolerant to opioids.

All methadone dispensed as carries must have an adequate warning label. The warning label must state that
the amount of drug contained could cause serious harm or toxicity if taken by someone other than the patient.
Some pharmacies insert a warning directly into the directions on the prescription label. There are commercially
available methadone warning labels or you can create auxiliary labels such as:

"Warning: Methadone can be fatal when taken in individuals for whom it is not prescribed."

"Warning: The contents of this bottle may cause harm or toxicity if taken by someone other than the
person whose name appears on the prescription label."

Destruction of Empty Methadone Bottles

The pharmacy is required to dispose of all bottles and containers used for methadone doses in a safe and
appropriate manner. Using a medication disposal company such as Stericycle is recommended. If the
pharmacy disposes of the bottles themselves, they must ensure that the patient information and most of the label is removed, and that medication is not remaining in the bottle.

**Vacation Supply**

A methadone prescriber may prescribe a larger than normal carry supply for a patient going on vacation. This supply can be for a maximum of 2 to 4 weeks. This extended supply is only given to patients who are stable and are deemed appropriate for a high number of carries (four to six carries, attending the pharmacy once to twice weekly). For non-stable patients the methadone prescriber may organize for them to “guest drink” at another pharmacy in the location they will be visiting. The pharmacy receiving the “guest” must ensure they have all pertinent information regarding the time and amount of the last dose. A new prescription is required by the interim pharmacy. Please see “Guest Drinkers” for more information.

**Counselling**

Counselling can provide patients with medication information, reinforce prior knowledge and dispel myths and misconceptions. In order to communicate effectively with patients, pharmacists need a strong knowledge base. Sufficient time and a private counselling area enable the pharmacist to maximize the benefits of counselling. A private counselling area is highly recommended in methadone dispensing as other patients will see the methadone being consumed and may inquire as to what the patients are drinking. This puts both the patient and the pharmacist in an uncomfortable position. The pharmacist must respect the patients’ rights to privacy and this type of situation can be avoided with a private counselling area.

Daily methadone dispensing provides the unique opportunity to have an on-going dialogue with your patients. It also requires innovative counselling as the basics will have been covered with the initial dispensing.

Pharmacists are required to have a short conversation with their patients each time they come in for a dose. Prior to dispensing the dose the pharmacist should assess the patient for signs of intoxication. This should be done simply by observing their mannerisms, speech, and appearance during a brief conversation. After the patient has ingested the methadone the pharmacist must have another short conversation to ensure the patient has swallowed the methadone. It is extremely difficult to talk without swallowing. These conversations provide pharmacists with the opportunity to emphasize the benefits of methadone treatments and provide support for the patient. By initiating dialogue you can have a positive impact on the patients’ treatment goals, compliance, management of adverse effects, and lifestyle choices. This can become a very rewarding part of your practice as you develop a trusting relationship with your patients.

**Replacement Doses**

Replacement of lost, stolen, or misplaced methadone “carries” cannot be provided. Only in an extraordinary circumstance can an exception be made. The pharmacist must assess the situation, evaluate the need for the replacement dose and contact the prescriber to discuss the situation. Direct communication with the prescriber is required and must result in a new prescription being written and received if replacement medication is to be dispensed.

**Vomited Doses**

When a patient reports that they vomited their dose, that dose should not automatically be replaced. In order for vomited doses to be replaced, emesis should be witnessed by the pharmacist or another health care professional. The prescriber should be contacted and provided with as much information as possible about the incident (time the dose was taken, time of vomiting, etc.). This is important in determining how much of the dose should be replaced if the prescriber chooses to do so. Methadone prescribers can authorize replacement doses by sending a written authorization to the pharmacy.
For patients who feel they might vomit their dose, recommend that they consume the methadone slowly in small sips. This can decrease the risk of vomiting. Have them remain in the pharmacy for 30 minutes post dose to ensure that the full dose is absorbed. If they do vomit their dose in this period then you will be in a better position to recommend a replacement dose to the methadone prescriber.

Methadone is rapidly absorbed after oral witnessed dosing. The following chart may be used as a guideline for replacing vomited doses.

<table>
<thead>
<tr>
<th>Time after Consumption of Dose</th>
<th>Replace</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 minutes</td>
<td>50-75%</td>
</tr>
<tr>
<td>15-30 minutes</td>
<td>25-50%</td>
</tr>
<tr>
<td>&gt;30 minutes</td>
<td>Do not replace</td>
</tr>
</tbody>
</table>

Pregnancy is a special circumstance and the vomited dose usually is replaced in the pregnant woman. Please see “Pregnancy” on page 16 for more information.

**Missed doses**

Methadone doses that are not consumed or picked up on the prescribed day are considered cancelled and must be reversed on DPIN before the end of the business day. If a patient misses their dispensing day they cannot receive the missed amount when they return to the pharmacy in the future.

Pharmacists, emergency room physicians, private practice physicians and prescribers rely on DPIN to provide accurate and current information about a patient’s medication history. These professionals are making treatment decisions based on the DPIN patient record. Reversing doses that are not picked up as soon as possible ensures that DPIN is as accurate as possible.

Missed methadone doses may indicate a serious problem with the patient and the **prescriber/clinic should be notified about any missed doses**. The prescriber may require the patient to make up their missed witnessed dose on one of their regular “carry” days. **Patients who miss their methadone for 3 or more consecutive days should not be given a dose until they have been assessed by their methadone prescriber.** Due to the variability and unpredictable loss of tolerance to methadone the prescriber will need to be contacted for a new prescription at a lower dose. The following is a guideline for assessing appropriate doses.

1 or 2 days missed: Patient may be given their regular maintenance dose.

3 days missed: Patient’s dose should be cut by 50% or restarted at 30 mg or less if original dose was less than 60 mg. The patient can be titrated back up to their maintenance dose by no more than 10 mg per day. ix

4 or more days missed: Patient should be restarted at 30 mg or less and can be titrated up to their maintenance dose by 10 mg every 3 days or as otherwise directed by the prescriber. ix

**MMT in Hospital**

As the number of MMT patients increases so do the number of encounters with the hospital system. Methadone patients may be admitted for addiction related problems or for other medical or surgical issues. Regardless of the reason for the admission it is important that these patients receive the same standard of care as that of a non-methadone patient. Unfortunately, the stigma surrounding methadone exists not only in the lay public but also among health care professionals which can lead to the mismanagement of this patient population. The most common area for mismanagement is pain. Please refer to “Treatment of Acute Pain” for more information.
Continuation of Care

Upon admission of an MMT patient to the hospital, the patient’s pharmacy should be contacted to verify the date, time and dose of the last drink. If the patient has missed 3 or more days of methadone, then the attending physician should be notified and the dose adjusted accordingly. It is possible that a patient who is receiving multiple carries as an outpatient is not consuming their entire dose each week. In the interest of patient safety it may be prudent to offer these patients a dose reduction to prevent possible overdose with the witnessed dosing of their full maintenance dose. This should be done in a non-judgmental and non-confrontational manner. Alternatively, methadone may be given in split doses on the first 2 days and held if sedation is present. Upon discharge, the patient’s regular pharmacy should be contacted.

Temporary Exemptions

At times, patients receiving methadone for opioid dependency or pain may be admitted to hospital when there is no practitioner on staff authorized to prescribe methadone. If this occurs, attending practitioners responsible for the patient in hospital may obtain a temporary exemption from Health Canada to prescribe methadone for the patient already stabilized on methadone. The exemption is granted for the period of the patient’s hospitalization and expires on the earlier of the date on which the patient is discharged from the hospital or a maximum of 60 days. If the patient is hospitalized longer than two months, the authorization may be extended. It should also be noted that the temporary exemption is specific for that prescriber, patient and institution and the temporary exemption cannot be used to start methadone therapy in a methadone naïve patient. Prescribers with temporary exemptions to prescribe methadone for opioid dependence may do so at a patient’s current dose, or at a lower dose if clinically indicated. If the patient’s dose is changed, the regular prescriber must be contacted. A prescriber with a temporary exemption cannot write a prescription to be filled as an outpatient.

To obtain procedures for temporary exemption during hospital admission or for other inquiries, please contact the Methadone Program directly at: exemption@hc-sc.gc.ca

Telephone: (613) 946-5139 Toll free: 1-866-358-0453

The Office of Controlled Substances will typically grant the exemption the same day if contacted during business hours, or the next business day if contacted after hours. In the event that the exemption is being applied for after hours (evenings, weekends, holidays) the application approval should not be reason for delaying methadone treatment. The prescriber or pharmacist on the prescriber’s behalf should leave all the relevant information on the voicemail at the above number. The exemption is valid for 60 days or for the duration of the patient’s hospital stay, whichever is shorter. If the patient is hospitalized for longer than 60 days then a new exemption is required. The following information is required when calling/faxing for the exemption:

- Name of person calling
- Prescriber’s name
- Prescriber’s license number
- Name and address of the hospital including specific ward/unit
- Phone number where the prescriber can readily be reached
- Patient name and gender
- Indication for methadone (MMT or analgesia)
- Methadone dose
- Date methadone ordered to start in hospital
- Phone number of the hospital pharmacy

Provision of methadone within the hospital
If possible, it is recommended that the hospital supply the methadone directly from the inpatient pharmacy. This is preferable to using the “patient’s own medication” where the possibility of tampering exists. If not possible to provide methadone from the hospital, it is recommended to obtain the daily methadone doses directly from the pharmacy attended by the patient. The nursing staff should be made aware of the requirements for observing doses and that methadone should not be left at the patient’s bedside. Inserting explicit directions into the medication administration record for observing doses can be helpful.

Upon admission, communication with a patient’s pharmacy where methadone is usually received is vital to ensure double dosing does not occur. The patient’s pharmacy should also be contacted upon discharge. A new prescription will be required from the patient’s methadone prescriber.

**Initiating MMT in hospital**

MMT initiated in hospital must be done by a methadone prescriber experienced in addictions and with a valid full methadone exemption (not a temporary exemption). In the hospital setting, methadone may be titrated at a faster rate than that used in the community if the patient has adequate levels of monitoring. It is still important to remember that the drug is accumulating in the system for five days and that opioid cross tolerance is incomplete and unpredictable.

**Buprenorphine/Naloxone (Suboxone®)**

Buprenorphine/naloxone is an alternative option to methadone for addiction treatment within a community outpatient setting. Buprenorphine is available in combination with naloxone in a sublingual tablet form, marketed as *Suboxone®,* and is indicated for substitution treatment in opioid drug dependence in adults. Buprenorphine treatment provides an alternative, but is not a substitution to methadone maintenance treatment in Canada. ix

*Suboxone®* is available as a 2 mg and 8 mg sublingual tablet of buprenorphine in combination with naloxone in a 4:1 ratio. Naloxone is an opioid antagonist that can displace opioids from their receptors, leading to withdrawal symptoms; however, it is not absorbed orally and does not exert a pharmacologic response when administered sublingually. Ultimately, *Suboxone®* contains naloxone to deter use through the intravenous route.

Buprenorphine is a partial opioid agonist at the μ (mu) opioid receptor. It is associated with a reduced risk of death in overdose compared to full opioid agonists such as methadone because it has a ceiling effect and therefore a lower incidence of adverse effects such as respiratory depression. Respiratory depression can still occur if used in combination with other medications that cause respiratory depression. Because of the ceiling effect, many clinicians consider buprenorphine-naloxone to be a safer drug than methadone. However, buprenorphine’s ceiling effect may also result in limitations since its effectiveness plateaus once a certain serum level is reached. Higher doses or serum concentrations will not result in additional benefit. The main advantages of *Suboxone®* over methadone for medication-assisted treatment of opioid dependence are:

- It is safer in overdose;
- It is associated with an improved safety profile, including less sedation;
- Those dependent on more moderate doses of opioids may reach maintenance doses of *Suboxone®* more quickly during substitution therapy; and
- It is more portable than methadone solutions.

The main disadvantages for *Suboxone®* are:

- It is generally less effective in patients who have a tolerance to higher doses of opioids;
- There is a limited range for dose titration due to its ceiling effect;
- It may precipitate severe opioid withdrawal symptoms during the initiation phase or if a patient continues to use other opioids; and
- It is generally a more costly treatment on a dose-for-dose basis than methadone maintenance therapy.

The CPhM and the Methadone Intervention and Needle Exchange (MINE) Program at the Addictions Foundation of Manitoba (AFM), collaborated to create a one-page Suboxone® reference for pharmacists. The reference sheet outlines the differences between buprenorphine/naloxone and methadone, who can prescribe Suboxone® and precautionary measures for pharmacists. This short reference document is not meant to replace education on buprenorphine/naloxone and can be found in Appendix F.

Education

Section 18 of the Pharmaceutical Regulation states that a member may only engage in the aspects of pharmacy practice that he or she has the requisite knowledge, skill and judgment to provide or perform and that are appropriate to his or her area of practice. Pharmacists must be knowledgeable in all pertinent aspects of buprenorphine/naloxone use when involved in Suboxone® dispensing in order to prevent errors and close calls. Education is available for pharmacists with patients on Suboxone®. A free six hour professional development program covering the treatment of opiate dependent patients is available online at www.suboxone.ca. All pharmacists who have patients at their pharmacy on Suboxone® should complete this program.

Suboxone Exemptions for Practitioners

Health Canada grants federal exemptions to practitioners for methadone prescribing, with provincial supervision performed by the provincial regulatory authorities. Conversely, the criteria and requirements necessary to obtain an exemption to prescribe Suboxone® is determined by the provincial medical colleges. In Manitoba, it is necessary for the prescriber to hold a methadone exemption, take a 6 hour on-line Suboxone course, and apply to the appropriate college. It is the responsibility of the dispensing pharmacist to verify that the methadone prescriber has the appropriate exemption. Prescriber lists including prescribers with methadone and/or buprenorphine/naloxone exemptions are now available on the secure member portal of the CPhM website. Pharmacists will no longer need to contact the College office by phone for this information but can log in and access this information anytime. The lists are for access by pharmacists only. They are to be used solely for referencing a prescriber’s license number and/or exemption status and are not for distribution. The names of methadone or buprenorphine/naloxone prescribers or any other information contained in these lists cannot be provided to patients or anyone else requesting this information.

The lists from the College of Physicians and Surgeons of Manitoba are updated monthly, and changes to the methadone and buprenorphine/naloxone prescriber list will be updated throughout the month as additions or deletions occur. Pharmacists may access the prescriber lists by logging in to their Member homepage with their unique user name and password, scrolling down to the “My Documents” section, and clicking on the Prescriber Lists.

If a prescriber exemption is not included, please confirm his/her exemption status by contacting the appropriate licencing body:

- College of Physicians and Surgeons of Manitoba at (204) 774-4344 or toll free (in Manitoba) at (877) 774-4344
- College of Registered Nurses of Manitoba (204) 774-3477.

Dispensing Buprenorphine/Naloxone

Some things to remember when dispensing Suboxone®:
Dispense buprenorphine-naloxone carries in the original foil wrap as buprenorphine-naloxone is hygroscopic.
Dispense carries in a light-resistant bottle or vial.
Dispense carries in a child-resistant container. Only permit deviations from this standard at the patient’s request. Document the rationale within the patient’s records and include the patient’s acknowledgement and acceptance of this deviation. Provide adequate counselling regarding the potential dangers and toxicity to children and the public from inadvertent ingestion of doses intended for the patient.
Use an appropriate auxiliary label such as “Buprenorphine-naloxone may cause serious harm to someone other than the intended patient. Not to be used by anyone other than the patient for whom it was intended.” or “May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.”

Witnessing Suboxone® Dosing

A patient must have supervised daily dosing by a health care provider for a minimum of 2 months during initiation of Suboxone®. If you are witnessing an initial buprenorphine-naloxone dose, the prescriber must clearly communicate to you the timing of the initial buprenorphine-naloxone dose, since the patient is expected to be in opioid withdrawal at the time of initial dose administration. Additionally, the prescriber should provide parameters on the M3P prescription if additional dosing is to be permitted based on the patient’s response. Patients may need to be retained for several hours during first dose administration or following each dosage change. Witnessing a patient’s very first dose of buprenorphine-naloxone or dose change requires extensive knowledge beyond what is covered in these guidelines.

The patient should take the initial buprenorphine/naloxone dose when they are in withdrawal. This is generally after 12 hours of having taken a short-acting opioid and 24 hours after the last dose of a long-acting opioid. If the patient was on methadone, it is recommended that the first dose of buprenorphine-naloxone be administered at least 24 hours after the last dose of methadone. (Note: methadone has a variable half-life in individuals. Clinicians generally use a range of three to five days from the last methadone dose before initiating the first buprenorphine-naloxone dose).

For witnessing of all Suboxone® doses, the contents of the packaging cup containing the buprenorphine-naloxone sublingual tablets are provided to the patient for dissolution under the tongue.

Advise patients not to swallow the tablets as they will not work this way. It may take from one to ten minutes for the tablet to dissolve under the tongue. If multiple tablets are required for the prescribed dose, it is preferable for the sublingual tablets to be administered simultaneously rather than dissolved consecutively under the tongue. Where necessary, pharmacists should use their discretion to determine if the patient is able to comply with the simultaneous administration of multiple tablets and to modify the administration instructions as necessary.

After the tablets are dissolved, ask the patient to lift up their tongue for observed confirmation that the tablets are no longer present.
Part Five:
Appendices
Appendix A:

Manitoba Health, Healthy Living and Seniors: Methadone Reimbursement Procedure and Questions and Answers

Information for Pharmacists

Methadone Reimbursement Procedure Provincial Drug Programs
Manitoba Health, Healthy Living and Seniors

Effective October 16, 2014

- The Provincial Drug Programs’ (PDP) Methadone Reimbursement Procedure (attached), which will become effective on October 16, 2014, will:
  - enhance patient safety by ensuring a more consistent and clear indicator in the patient’s Drug Programs Information Network (DPIN) history of the dose of methadone prescribed for and dispensed to the patient; and
  - ensure a consistent process for adjudication and reimbursement of methadone preparations by PDP through DPIN.

- This procedure aligns with methadone policies in other jurisdictions.

Methadone for Opioid Dependence:

- “Methadone powder in preparation of an oral solution”, PIN 909190, will no longer be eligible as benefit through PDP.

- Methadose* will be now be considered as an unrestricted Part 1 benefit for opioid dependence.

<table>
<thead>
<tr>
<th>Methadose* 10 mg/ml oral liquid</th>
<th>DIN 2394596</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadose* Sugar Free 10mg/ml oral liquid</td>
<td>DIN 2394618</td>
</tr>
</tbody>
</table>

- The PIN 909190 will be accessible until the effective date of the next Bulletin in mid-January 2015 for the purpose of filling part fills of existing prescriptions. As of that date, the PIN 909190 will be discontinued.

- Pharmacy operators must indicate the quantity of methadone dispensed as the total number of milliliters (ml) of Methadose* dispensed.
Pharmacy operators must specify in DPIN the total days supply of Methadose® provided to the patient.

If a patient is dispensed Methadose® carries, the total quantity of Methadose® received by the patient must be entered into DPIN along with the correct days supply. There should be a single entry into DPIN, and not separate entries on the same day.

**For example:** An M3P prescription is presented for methadone 2240 mg to be dispensed as 80 mg OD for 28 days. This can be entered as daily or weekly:

<table>
<thead>
<tr>
<th>Daily</th>
<th>Weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity Dispensed: 8 ml</td>
<td>Quantity dispensed: 56 ml</td>
</tr>
<tr>
<td>Day’s Supply: 1</td>
<td>Day’s Supply: 7</td>
</tr>
</tbody>
</table>

Pharmacy operators will be reimbursed the ingredient cost plus their usual and customary professional fee.

Pharmacy operators must record and keep a copy of the documentation in a retrievable manner, indicating how all calculations/billings were done, and tracking of all dosages dispensed.

Methadone compounded into a capsule formulation is not a benefit through PDP.

**Methadone for Pain Management:**

Metadol® will be considered as a Part 3 benefit for severe pain management for Palliative Care clients.

<table>
<thead>
<tr>
<th>Metadol® 1mg tablet</th>
<th>DIN 2247698</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metadol® 5mg tablet</td>
<td>DIN 2247699</td>
</tr>
<tr>
<td>Metadol® 10mg tablet</td>
<td>DIN 2247700</td>
</tr>
<tr>
<td>Metadol® 25mg tablet</td>
<td>DIN 2247701</td>
</tr>
</tbody>
</table>

Patients currently receiving other dosage forms of methadone will continue to receive benefit coverage until the effective date of the next Bulletin in mid-January 2015. After that date, no other forms of methadone will be covered.
- In order to avoid disruptions in treatment and/or ensure continuity of benefit coverage, it is imperative that pharmacists advise patients receiving methadone compounded into dosage forms other than a solution that they will be required to switch to an approved dosage form by the effective date of the next Bulletin in mid-January 2015.

- Manitoba Health may conduct audits of the accounts and records of the pharmacy owner relating to methadone claims submitted by the pharmacy owner, to determine compliance with the terms and conditions of this procedure.

*During the transition period between October 16, 2014 and the effective date of the next Bulletin in mid-January 2015:*

- It is recommended that new prescriptions for methadone be entered into DPIN using the new DINs and by the total number of ml of methadone dispensed. Existing prescriptions with part fills remaining can continue to be entered as they have previously been entered.

*As of the effective date of the next Bulletin in mid-January 2015:*

- All prescriptions, including remaining part fills, must be entered into DPIN using the new DINs and by the total number of ml of methadone product dispensed.

If you have any questions or concerns, please contact: PDPIfo&Audit@gov.mb.ca

Provincial Drug Programs  
300 Carlton St.  
Winnipeg MB R3B3M9  
Ph 204-786-8000 Fax 204-786-8634
METHADONE REIMBURSEMENT PROCEDURE

UPDATED (October 9, 2014)

QUESTIONS AND ANSWERS

Changes to The Specified Drugs Regulation of The Prescription Drugs Cost Assistance Act will indicate that Methadose® (for opioid dependence) and Metadol® (for pain management) will be covered benefits.

Will methadone capsules be covered under Part 3 Exception Drug Status (EDS)?

- Capsules compounded from methadone powder are not an eligible benefit through Provincial Drug Programs (PDP) and will not be covered under Part 3 EDS. This aligns Manitoba with other Canadian jurisdictions. Compounded methadone capsules are not benefits in Saskatchewan, Ontario, Quebec, Nova Scotia, PEI or Newfoundland and Labrador. British Columbia and New Brunswick require special authorization for methadone prepared in dosage forms other than the oral solution.

Will there be a transition period to accommodate the change in coverage? Will prescribers be informed of the policy in order to re-assess, re-write new prescriptions?

- This procedure will take effect as of October 16, 2014. A transition period of approximately three months until the effective date of the next Bulletin in mid-January 2015 will allow for: part fills of existing prescriptions to be filled (using the old pseudo PIN) and new prescriptions to be written and filled (using the new DINs). Those who prescribe methadone in Manitoba will be informed of the procedure.

Why is the quantity in DPIN being entered in Millilitres (ml) and not Milligrams (mg) of methadone?

- All Methadose prescriptions are to be entered in DPIN in millilitres. The entry in millilitres (ml) is consistent with the DPIN entry requirement for all other liquid formulations of products. The ml entry is consistent with the
• Pharmacy operators must specify in DPIN the total days supply of Methadose\textsuperscript{*} provided to the patient.

• If a patient is dispensed Methadose\textsuperscript{*} carries, the total quantity of Methadose\textsuperscript{*} received by the patient must be entered into DPIN along with the correct days supply. There should be a single entry into DPIN, and not separate entries on the same day.

  For example: An M3P prescription is presented for methadone 2240 mg to be dispensed as 80 mg OD for 28 days.
  This can be entered as daily or weekly:

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<th>Daily</th>
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</tbody>
</table>

• Pharmacy operators will be reimbursed the ingredient cost plus their usual and customary professional fee.

• Pharmacy operators must record and keep a copy of the documentation in a retrievable manner, indicating how all calculations/billings were done, and tracking of all dosages dispensed.

• Methadone compounded into a capsule formulation is not a benefit through PDP.

**Methadone for Pain Management:**

• Metadol\textsuperscript{*} will be considered as a Part 3 benefit for severe pain management for Palliative Care clients.

<table>
<thead>
<tr>
<th>Metadol\textsuperscript{*}</th>
<th>DIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1mg tablet</td>
<td>2247698</td>
</tr>
<tr>
<td>5mg tablet</td>
<td>2247699</td>
</tr>
<tr>
<td>10mg tablet</td>
<td>2247700</td>
</tr>
<tr>
<td>25mg tablet</td>
<td>2247701</td>
</tr>
</tbody>
</table>

• Patients currently receiving other dosage forms of methadone will continue to receive benefit coverage until the effective date of the next Bulletin in mid-January 2015. After that date, no other forms of methadone will be covered.
When we bill the Methadose 10mg/ml stock solution, do we submit the claim as a regular drug product or should we bill it as a compound?

- The practice of diluting Methadose with any diluent including crystalline solution is not compounding and is not eligible for reimbursement as an extemporaneous compound.

How am I paid for Methadose; what should my professional fee be?

- This procedure notes that pharmacists are to bill for the cost of the drug plus one professional fee. The professional fee would be at the same frequency as if you were dispensing the compounded methadone. If you have a fee structure for Methadose, whereby the fee may vary depending on the days supply provided, and charge these same fee(s) to a cash paying customer, this is acceptable.
- The pharmacy will not be reimbursed for the cost of the crystalline solution (Tang) that is used to prepare the methadone dose for the patient.

For NIHB clients, the only product on the current benefit list is the powder. Have you heard if they will add this new liquid as well?

- Manitoba Health understands that the NIHB drug plan will mimic what is done in each province. This has occurred in other provinces that have listed Methadose.

We get a lot of pain management people taking different doses - 1mg/ml, 5mg/ml 10mg/ml and 50mg/ml. How could they continue receiving their pain medication if only the 10mg/ml is covered?

- Methadose, like compounded methadone, will be listed on the Manitoba Formulary as an unrestricted Part 1 benefit.
- Methadose is manufactured in a 10 mg/ml strength to allow for easy conversion.
- The benefit status for Methadose and delisting of compounded methadone in Manitoba is consistent with actions undertaken in other Canadian jurisdictions.
How will the change affect patients?

- Some patients will note differences in the dispensing of Methadose versus compounded methadone solution, including:

  Colour change: Methadose is available as a colourless (flavourless) or red colour (cherry) formulation. Depending on the formulation of Methadose that is dispensed and the diluent added, there may or may not be a change in the colour of the final dose dispensed to the patient.

  Different taste: Methadose is available as flavourless or cherry-flavoured formulations. Depending on the formulation dispensed, the final methadone dose may or may not have a different flavour.

  Volume: The final volume dispensed may be different.

  Viscosity: Methadose may impact the viscosity or consistency of the final product dispensed to patients. Patients may perceive this change as being slightly thicker or “stickier”.

- Pharmacists are reminded that monitoring of adverse events may be necessary during the transition period of compounded methadone solution to Methadose solution.
- Due to the differences in formulations it is important for methadone prescribers and pharmacists to communicate these changes to patients.
- The new strength of methadone used to prepare the methadone dose may also pose a public safety risk during this time of transition, therefore careful management and communication between methadone prescribers and pharmacy staff involved in the preparation of doses is encouraged.

Our pharmacy system software is not designed with a decimal place for the quantity dispensed. How can I input the correct quantity of 7.5ml for a 75mg dose?

- Please contact your pharmacy software vendor to activate the decimal point on your software if necessary. Software vendors have confirmed that decimal points can be accommodated on software systems.
Appendix B:
Sample Pharmacist – Patient Agreement

As your pharmacist(s), we believe in the principles of the methadone maintenance program, and the valuable role it can play in improving people’s lives. To help you succeed in the program we make the following promises:

- We will treat you professionally and respectfully.
- We are part of your health care team and will communicate with your methadone prescriber when necessary. The kinds of issues we will discuss with your prescriber(s) include:
  - Missing one or more drinks
  - Refusal to drink full dose of methadone
  - If you are intoxicated when you arrive at the pharmacy
  - Doses for replacement of lost, stolen or vomited methadone
  - If you see another prescriber and are prescribed mood-altering medications
- We will provide methadone to you exactly as your practitioner prescribed it. We are not able to give you extra doses, early doses, or methadone to take home unless your practitioner prescribes it.
- We are required to watch you drink your dose of methadone and have a conversation with you afterward.
- We will not dispense your methadone to anyone other than yourself and may require you to present identification.

As our patient, we have a number of expectations of you, too.

- You will attend the pharmacy during regular pharmacy hours.
- You are asked to respect our neighbourhood. Please ensure that all pharmacy packaging material and litter are disposed of in the garbage containers provided.
- All of our patients are expected to be respectful of others, including staff, other patients and our neighbours.
- You must store all take-home doses of methadone (carries) safely and securely in your home in a lock box.
- You may be refused your methadone at the pharmacist’s discretion if any of the following occurs:
  - You appear intoxicated
  - You are prescribed opioids or other mood altering medications from another prescriber without prior approval
  - If you are required to pay for your dose(s), and cannot make payment
  - If you are not being respectful to staff, other patients, or our neighbours
- If you do not take your methadone for three consecutive days you will have to see your doctor for a new prescription.

__________________________________________  ____________________________
Pharmacist’s Signature                  Patient’s Signature

__________________________________________  ____________________________
Pharmacist’s Name                  Patient’s Name

__________________________________________  ____________________________
Date                  Date

End of Appendix B
Appendix C:
Facsimile Transmission of Prescriptions Template

Prescriber Name ______________________
Registration # _______________________
Clinic Name __________________________
Prescriber Address _____________________
Prescriber Telephone # ________________

Patient Given & Surname ______________________
Patient PHIN ____________________________
Patient DOB _____________________________
Patient Address __________________________

Rx#1
Supply a total of ____ doses to be dispensed in quantities
of ____ every ____ days, OR, refill ______ times.

Rx#2
Supply a total of ____ doses to be dispensed in quantities
of ____ every ____ days, OR, refill ______ times.

Confidential Facsimile to:
Pharmacy Name: ______________________
Pharmacy Fax #: _______________________
Date _________________________________
Time ______________________________

If a prescription for methadone or buprenorphine/naloxone is being faxed, the daily dosage must be clearly indicated below (in addition to being noted on the M3P form itself):

Practitioner Certification

- This prescription represents the original of the prescription drug order.
- The pharmacy addressee noted above is the only intended recipient and there are no others.
- The original prescription has been invalidated and securely filed, and will not be transmitted elsewhere at another time.
- Quantity is stated in words and numerals.

This telecopy is confidential and is intended to be received by the addressee only. If the reader is not the intended recipient thereof, you are advised that any dissemination, distribution or copying of this facsimile is strictly prohibited.

Use of this form for purposes or by persons not authorized under the Controlled Drugs and Substances Act and its regulations is a criminal act. End of Appendix C
Appendix D:

**Sample Emergency M3P Documentation**

This form is for use in the event of an emergency that requires a faxed M3P prescription. Please complete and fax to the pharmacy with the M3P prescription. Direct consultation between the pharmacist and the prescriber must occur. The pharmacist must obtain written documentation from the prescriber prior to dispensing any medication.

<table>
<thead>
<tr>
<th>Prescriber:</th>
<th>Patient Name:</th>
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<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>Pharmacy and Pharmacist:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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</tbody>
</table>

**Brief Description of the emergency situation:**

As the prescriber, I request the above named pharmacy to accept a faxed transmission of the M3P prescription form for the above named patient. I understand that the M3P prescription must be faxed to and received by the pharmacy prior to the pharmacy dispensing the medication. I guarantee delivery of the original M3P prescription to the pharmacy.

<table>
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<tr>
<th>Prescriber’s Name:</th>
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<table>
<thead>
<tr>
<th>License#</th>
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</table>

<table>
<thead>
<tr>
<th>Prescriber’s Signature:</th>
</tr>
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</table>

<table>
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<tr>
<th>Date Signed:</th>
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**End of Appendix D**
Appendix E: Sample Ingestion and Carrier Log

Patient’s Name: Patient’s Picture:
Patient’s Address or DOB:
Witness/Carry Schedule:

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Dose</th>
<th>Drink(✓)</th>
<th>Number of Carries</th>
<th>Pharmacist’s Initials</th>
<th>Patient’s Signature</th>
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End of Appendix E
Appendix F:
Suboxone (Buprenorphine / Naloxone) – Important Practice Notes

SUBOXONE® (BUPRENORPHINE/NALOXONE) – IMPORTANT PRACTICE NOTES FOR PHARMACISTS

1. Who can prescribe Suboxone® (buprenorphine/naloxone)?

Health Canada grants federal exemptions to physicians for methadone prescribing, with provincial supervision performed by the College of Physicians & Surgeons. Conversely, the criteria and requirements necessary to obtain an exemption to prescribe Suboxone is determined by the provincial medical colleges. In Manitoba, it is necessary for the physician to hold a methadone exemption, take a 6 hour on-line Suboxone course, and apply to the College of Physicians & Surgeons of Manitoba. The College of Physicians & Surgeons of Manitoba keeps an updated list of physicians who can prescribe methadone and Suboxone. It is the responsibility of the prescribing physician to verify that the prescribing physician has the appropriate exemption. This information can be confirmed by calling the College of Pharmacists Office at (204)233-1411.

2. How is buprenorphine/naloxone different from methadone?

Buprenorphine/naloxone comes in the form of a sublingual tablet. Witnessing of doses is necessary, just like methadone, as per the contract between patient, clinic and pharmacy. It may take 2 to 3 minutes for the tablet to dissolve.

The pharmacological properties of buprenorphine can cause precipitated withdrawal syndrome if administered to an individual who has taken a sufficient dose of a full agonist opioid and is physically dependent on opioids. Therefore the correct timing and dosage of buprenorphine/naloxone according to the patient’s last dose of opioid is important.

The purpose of including naloxone with buprenorphine is to prevent inappropriate IV usage. Rapid binding of naloxone to the mu-opioid receptor precipitates a rapid opioid-withdrawal syndrome when injected. Pharmacists should caution patients on this effect.

Buprenorphine is longer acting than methadone and therefore some patients may be able to take it three times a week rather than daily. Buprenorphine has a “ceiling” effect, so doses over 24 mg are unlikely to be beneficial. Most patients report fewer side effects on buprenorphine/naloxone (less sedation, less constipation, more normal sexual function) and the risk of deaths from over-sedation is less than with Methadone.

Fatalities due to respiratory depression have occurred when buprenorphine was used in combination with CNS depressants such as benzodiazepines, alcohol, or other opioids. The pharmacist must always assess the patient with respect to other drug and medication use prior to providing buprenorphine/naloxone.

3. Contact with the Prescribing Practitioner

Pharmacies must contact the patient’s primary healthcare provider/prescriber if major behavioral difficulties are observed (sedation, missing repeated doses) and dosages missed. If a patient misses more than 5 doses, the prescription must be cancelled and the patient must contact the clinic staff in order to resume buprenorphine/naloxone.

4. Education

Pharmacists must be knowledgeable in all pertinent aspects of buprenorphine/naloxone use when involved in Suboxone® dispensing in order to prevent errors and dose calls. Education is available for pharmacists working with patients on Suboxone®. A free six hour professional development program covering the treatment of opioid dependent patients is available online at www.suboxonee.ca. All pharmacists who have patients at their pharmacy on Suboxone® should complete this program. The College also offers a Principles for the Provision of Opioid Dependence Treatment by Manitoba Pharmacists Certificate Program. Many other opioid dependence treatment training programs are available in Canada. Pharmacists are encouraged to contact Kim McInnis, Assistant Registrar at the College office (204)233-1411 ext 250, to discuss further resources.

End of Appendix F
Appendix G:
Methadone Compounding Issues

This section has been retained for reference during the Methadose™ implementation period.

*Methadone Solutions*

Methadone solutions should be prepared using standard compounding techniques. All containers and graduates used in the preparation and storage of methadone solutions should be used for methadone only and labeled accordingly. Some pharmacies use the “POISON” auxiliary label with the international symbol of the skull and cross bones on all graduates and stock bottles that contain methadone as an extra precautionary measure. Scales need not be limited to methadone compounding use.

Add a few drops of blue food colouring to the final stock solution to distinguish it from other liquids in the pharmacy. This will help prevent methadone from inadvertently being mistaken for water. The blue colour should not affect the colour of the final solution when mixed with juice.

A compounding log should be retained to record when solutions were prepared, how much was prepared, who prepared the product, and who performed the final check. The lot number and expiry date should be noted on the container to ensure that staff dispenses all methadone within a reasonable amount of time. A sample compounding log can be found in Appendix H.

Methadone for maintenance should always be dispensed to patients using a stock solution concentration of 10 mg/ml. Add sufficient quantity of Tang® (or other suitable beverage - water is not suitable) to each individual dose to a final volume of 60 to 100 ml. The volume of methadone should be no more than half of the total dispensed volume to discourage intravenous administration of the product.

*Labelling Stock Bottles and Graduates*

Methadone solutions must be clearly labeled. Ensure that the drug name, strength, use-date, and appropriate warning label are affixed to all containers for methadone within the dispensary.

*End of Appendix G*
## Appendix H:
Sample Compounding Log

<table>
<thead>
<tr>
<th>Date</th>
<th>Lot # Powder</th>
<th>Expiry date powder</th>
<th>Quantity powder</th>
<th>Quantity solution</th>
<th>Use-by-date solution</th>
<th>Prepared by initials</th>
<th>Pharmacist’s check initials</th>
</tr>
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End of Appendix H

References
ii Personal communication, December 2007. Dr. Adrian Hynes, Health Sciences Centre psychiatrist.
iii Personal communication, Dr. Lindy Lee. Date: October 22, 2014.
viii College of Physicians and Surgeons of Manitoba, draft Manitoba Methadone and Buprenorphine Maintenance Recommended Practice