Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists

Part A: Methadone
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These tools have been developed by the Ontario Pharmacists Association for pharmacists in Ontario as a general guide to support those wishing to initiate a methadone program in their pharmacy setting. The resource materials provided in this toolkit are for general information purposes only and are NOT meant to be used “as is”.

This toolkit is complementary and is not inclusive of all recommendations and considerations. The information provided is not a substitute for sound clinical judgement from the health care professional. Pharmacists are to exercise their professional judgment in accordance with the Ontario College of Pharmacists (OCP) Standards of Pharmacy Practice. This tool is not a substitute for established clinical practice guidelines or regulatory requirements. It is not intended to supersede or replace guidelines, practice standards, policies or procedures issued by OCP, the Ministry or corporate employers. It is not intended, and should not be construed, as legal or professional advice or opinion.

While OPA strives to ensure the accuracy of the information provided in this document, information may be subject to change, and it is the responsibility of the user of this document to ensure they have the most up-to-date and complete information from available resources.

Acknowledgement

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The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long term care for funding this initiative.

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Addiction Management Principles

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Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviours. Addiction is characterized by inability to consistently abstain, impairment in behavioural control, craving, diminished recognition of significant problems with one’s behaviours and interpersonal relationships, and a dysfunctional emotional response.

Physical dependence is an adaptive physiological state that occurs with regular drug use and results in a withdrawal syndrome when drug use is stopped. It is usually associated with increased tolerance. Physical dependence tends to be a characteristic of substance use disorders, but alone does not imply addiction.

Tolerance is a condition in which higher doses of a drug are required to produce the same effect experienced during initial use. It is often associated with physical dependence.

Withdrawal is a characteristic of substance use disorders, but does not necessarily imply addiction. With regular use of a substance, biochemical and structural adaptations take place in the brain. Withdrawal is the group of symptoms and signs that a person experiences after a period of regular use, when the quantity of the substance in the brain is reduced.
What is Opioid Agonist Maintenance Treatment (OAMT)

It involves the prescribing of buprenorphine or methadone as part of a comprehensive program which includes counselling to help the person in treatment reduce or stop the harmful use of opioids. (Kleber, 2008)

Methadone is the most studied and longest used pharmacological treatment for opioid dependence; however, buprenorphine is another treatment option.

OAMT is a harm reduction approach — Any program or policy designed to reduce drug-related harm without requiring the cessation of drug use. (CAMH)

Harm reduction includes strategies that focus on reducing drug use and those that focus on reducing the harm of drug use.

OAMT has been shown to reduce —
- The use of opioids
- Criminal activity
- Patient mortality
- High risk behaviour and consequences such as HIV, STDs etc.
- Cost of law enforcement, health care and social services

OAMT improves
- Physical and mental health
- Social functioning
- Quality of life
- Pregnancy outcomes

There are limitations to the use of OAMT —
Methadone is a high risk medication with a narrow therapeutic range that can result in opioid overdose, especially at the beginning of treatment.

Buprenorphine has less overdose mortality risk but can still lead to death by overdose — especially if misused or combined with other CNS depressants or alcohol.

Both buprenorphine and methadone can produce adverse side effects and may interact with other medications.

Pharmacists can aid their patient’s recovery by supervising drug administration, monitoring their dosage, communicating with the treatment team, dispensing take-home doses in accordance with established guidelines and providing encouragement and support.

References:

Methadone maintenance 4 decades later, JAMA 300 (19), 2303-2305,Kieber HD (2008)

American Society of Addiction Medicine
http://www.asam.org/for-the-public/definition-of-addiction

Opioid Agonist Maintenance Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid use disorder (CAMH) 3rd edition

Primary Care Addiction Tool-kit 2010 (CAMH)
https://www.porticonetwork.ca/tools/toolkits/pcat
Initiating a Methadone Program in Your Pharmacy

Disclaimer: This tool has been developed by the Ontario Pharmacists Association as a resource to support pharmacists wishing to initiate a methadone program in their pharmacy setting. It is not a substitute for established clinical practice guidelines or regulatory requirements. The information provided is not a substitute for sound clinical judgement from the health care professional. While we strive to ensure the accuracy of the information provided in this document, information may be subject to change, and it is the responsibility of the user of this document to ensure they have the most up-to-date and complete information from available resources.

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Ontario College of Pharmacists Methadone Maintenance Treatment (MMT) and Dispensing Policy (June 2014)

Abbreviations: Ontario College of Pharmacists (OCP); College of Physicians and Surgeons of Ontario (CPSO); Centre for Addiction and Mental Health (CAMH); Designated Manager (DM)

Information to provide to OCP

Reporting to the College - Pharmacy Dispensing Methadone Form:
http://www.ocpinfo.com/library/forms/download/Methadone%20Dispensing%20Form.pdf

- Notify OCP within 7 days of initiating methadone dispensing practice (for MMT or pain)
- Hours and days of operation for your pharmacy (including holidays)
- Does pharmacy accept new patients
- Date(s) that DM and staff pharmacist(s) trained (or will be trained) to dispense methadone
- Type of methadone dispensing - MMT and/or pain
- Does the pharmacy transfer custody of methadone doses to an exempted physician or his/her delegate for administration at a clinic
  - NB: OCP must be notified of any future changes in the pharmacy’s status, such as:
    - Hours of operation
    - Accepting new patients
    - Type of methadone dispensing (MMT &/or pain)
    - If participating in transfer of custody
    - No longer dispensing methadone

Training Requirements

- Designated Manager must take CAMH ODT Core Course (or another OCP approved course) within 6 months of beginning methadone dispensing
- At least one staff pharmacist must take CAMH ODT Core Course (or other OCP approved course) within one year
  http://www.camh.ca/en/education/about/AZCourses/Pages/odtcore_odt.aspx

Training must be updated every five years. One of the following would be acceptable as a training update:
- OPA Live one day certificate program
- Completion of 5 online modules (including module on Policies Guiding Methadone Dispensing in Ontario)
  https://www.opatoday.com/professional/resources/education/learn

NB: Although not compulsory, the OPA Live one day certificate program and online modules would be beneficial for all pharmacists involved with methadone dispensing.

All pharmacists (regular and casual) who dispense methadone must be familiar with principles and guidelines outlined in both the current CAMH publication Opioid Agonist Maintenance Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid disorder and the CPSO-Methadone Maintenance Treatment Standards and Guidelines.

Required Documentation

- Written/faxed prescription from a prescriber with the appropriate Health Canada Section 56 Exemption to prescribe methadone (separate exemption for pain and MMT)
- Treatment Agreement: 2 way (pharmacist-patient) OR 3 way (prescriber-pharmacist-patient) is required for Methadone Maintenance Therapy (MMT). Issues to be addressed in agreement may include:
  - Expectations of all parties involved (hours of operation, consequences of inappropriate behaviour of patient)
  - Patient’s consent to access and share personal health information with other health professionals involved in their care
  - Notice to the patient that methadone dose will be withheld if the patient appears to be intoxicated or under the influence of other substances
• Patient’s acknowledgement that, if requested, they will be required to provide photo ID before receiving their dose
• Signature of Designated Manager (or delegated pharmacist) and the patient
• NB: Agreement should be reviewed and re-signed when the pharmacy makes substantial changes to their policies or procedures regarding methadone
  • Record of dispensing of daily observed and take home doses
  • Record of administration for MMT to include patient’s name, daily dose, date, time, and place of observed administration.
  • When a physician or delegate administers the methadone (i.e., transfer of custody), the dispensing pharmacist must be provided with copies of the daily administration record.
  • Record of daily reconciliation of methadone dispensed to and received from a treatment location under transfer of custody agreements
  • Record of destruction of unused doses in accordance with applicable laws and standards of practice.
  • If applicable, Institution¹-specific policy for dispensing methadone (e.g. hospital, licensed nursing homes, correctional facilities) which is auditable and traceable.

1 Institution is a facility that is licensed, approved or designated by a province in accordance with the laws of that province to provide care or treatment to persons or animals suffering from any form of disease or illness; or is owned or operated by the Government of Canada or the government of a province that provides health service. This would include correctional facilities–both federal and provincial.

Note: these are not to be considered transfer of custody scenarios

Dosage Form
• Daily doses must be prepared (witnessed and take home doses) using a manufactured product (10mg/mL solution) diluted to 100mL with a vehicle that does not lend itself to injection (e.g. Tang®)

• 100mL bottles for take home (i.e. carry) doses (self-sealing bottles now available)
• Childproof safety caps
• Lock box is recommended for take home doses. The necessity for a lockbox should be discussed in collaboration with the prescriber and patient. Consideration should be given to the risks unsecured methadone doses may pose while under the patient’s custody – both in transit and at home.

Required auxiliary labelling for take home doses
• “Methadone 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. MAY BE FATAL TO CHILD OR ADULT.” OR
• “Methadone may cause serious harm to someone other than the intended patient. MAY BE FATAL TO CHILD OR ADULT.”
• “Keep Refrigerated” auxiliary label for take home doses

Required References
The pharmacy must have access to the current:
• OCP Methadone Maintenance Treatment (MMT) and Dispensing Policy
  • http://www.oopinfo.com/regulations-standards/policies-guidelines/methadone2/
• Opioid Agonist Maintenance Treatment: A Pharmacist’s Guide to Methadone and Buprenorphine for Opioid Use Disorders (CAMH) – currently 3rd edition
  • http://store-camh.myshopify.com/products/p6500
• Methadone Maintenance Treatment Standards and Guidelines from the College of Physicians and Surgeons (CPSO)
  • http://www.cpso.on.ca/policies/guidelines/default.aspx?id=1984
• CPSO Policy: MMT for Opioid Dependence (Policy #2-10)
  • http://www.cpso.on.ca/Policies-Publications/Policy/Methadone-Maintenance-Treatment-for-Opioid-Dependence

Equipment
• An appropriate measuring device (e.g. calibrated pump) that is able to accurately deliver 0.1 mL increments.
  Note: Graduated cylinders are not suitable
• Disposable cups (approx.100ml) for observed doses
Additional Useful Resources

- Ontario Pharmacists Association’s Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists*

- Ontario Pharmacists Association’s Opioid Addiction and Substitution Therapy online modules* – complimentary
  - https://www.opatoday.com/224062

- CAMH Methadone Maintenance Treatment: Recommendations for Enhancing pharmacy services
  - https://www.nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_a_v4_5.pdf

- Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain (April 2010)
  - http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_a_v4_5.pdf

- CPSO Overdose Protocol (Available as Appendix I in electronic CPSO MMT 2011 guidelines)

- Naloxone dispensing and training resources

Web Resources

- College of Physicians and Surgeons of Ontario
  - http://www.cps.on.ca/CPSO-Members/Methadone-Program

- Ontario College of Pharmacists

- Centre for Addiction and Mental Health (www.camh.net)
  - https://www.porticonetwork.ca/web/opioid-toolkit

- Ontario Pharmacists Association Professional Development Website
  - https://www.opatoday.com/professional/resources/education

- Addiction Treatment Forum
  - www.attforum.com

- Connex Ontario Health Services Information
  - www.connexontario.ca/index.html

- Opioid Addiction and Dependency Recovery (ORbeOK) Canada
  - http://www.orbeok.ca/opioid_addiction_recovery_find_help_now/

- PCM Scientific Drug-Drug Interactions in Opioid Therapy
  - www.opioiddruginteractions.com

- Ontario Pharmacists Association Opioid Substitution Therapy Discussion Forum
  - http://methadoneforum.opatoday.com/

- CPSO Methadone News
  - http://www.cpso.on.ca/policies-publications/publications/methadone-news

Live Telephone Resources

- CAMH Addiction Clinical Consultation Service
  - 416-535-8501, press 2 (open Mon – Fri 8:30AM - 5PM)

- Ontario Pharmacists Association Opioid Substitution Therapy Drug Information Line
  - 1-888-519-6069 (open M-F 9AM-5PM)

- Health Canada (for verifying exemptions)
  - 613-946-5139
  - Toll free: 1-866-358-0453
  - Email: exemption@hc-sc.gc.ca

- CPSO Methadone Infoline (for prescribing)
  - 416-967-2600 ext. 603
Initiating MMT Services: A Brief Overview

Things to Consider Before Starting to Dispense Methadone

- Pharmacy days and hours of operation
- Pharmacy layout and work flow
- Need for a private area for counseling and witnessing methadone dose self-administration
- Staffing Impact: adequate personnel, training and competency, professional satisfaction
- Business Impact: Impact on new clients, current patients and clientele
- Impact on the surrounding community
- Collaborations with methadone prescribers
- Reimbursement
  - Will patients pay cash or bill to third party plan
- Service policies and limitations on
  - Hours when methadone is dispensed
  - Number of methadone clients
  - Number of methadone clients in store at one time
  - Service to methadone clients, regularly serviced by other facilities (i.e. guest dosing)
- Assessment
  - Assess staff competence to deliver methadone services
  - Procedures to minimize dosing errors and optimize work processes
  - Appropriate equipment (e.g. dispensing tools, measuring equipment, labels and labeling as regulated, child proof bottles, tamper evident caps or seals [best practice])
  - Documentation logs with information as regulated
  - Establish patient care process for patient assessment, dispensing, witnessed administration, and management of difficult situations

Role of Pharmacist in MMT Program

- Assess patient care issues for the safe dispensing of observed and take home doses
  - Monitor for signs and symptoms of intoxication or overdose
  - Decline in patient’s appearance
  - Unusual patient behaviours
  - Social and housing issues that may require special dispensing needs
  - Process for missed, lost, stolen or vomited doses
  - Monitoring of drug interactions
  - Positive identification of the patient
  - Observe ingestion of witnessed doses

- Provide take home doses
- Awareness of when methadone doses must be withheld and physician immediately contacted (e.g. 3 or more missed doses in a row or as pre-established with prescriber; symptoms of intoxication such as slurred speech, stumbling gait, confusion, disorientation)
- Provide patient advice and information as necessary (e.g. inform of signs and symptoms requiring immediate attention at various phases of methadone treatment and dosing)
- Diversion Alertness
- Determine physician’s preferred method of communication (e.g. email, cell phone, etc.)
- Be familiar with the required guidelines for methadone dispensing
- Ensure all regulations are met in accordance with the pharmacist’s assigned role
- Dispensing, and billing roles pending staffing

Role of Pharmacy Technician in MMT Program

- Enter/process prescriptions
- Prepare individual patient doses
- Monitor return of empty bottles from take home doses
- Report discrepancies to supervising pharmacist (e.g. missing patient documentation, patient identification discrepancies, interaction codes, discoloration of solutions, unusual patient behaviour etc.)
- Billing/administrative issues as assigned by the pharmacy
- Maintain stock and required supplies

Methadone Label Requirements
(in addition to DPRA requirements for all prescriptions)

- Directions for use: Drink entire contents of bottle
- Dose in mg
- A notation that the drug product has been diluted (i.e., “in orange drink”)
- Date of ingestion for take home doses
- Required auxiliary label as per OCP Policy
- Take home doses require a child resistant cap and a “Keep Refrigerated” label

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long term care for funding this initiative.
Preparing Methadone Dose

- Accurately measure commercially available methadone solution (currently Methadose®)
- Diluents for methadone doses (witness and take home) may include; Tang®, Crystal Light®, Kool-Aid®, and other brands of artificially sweetened crystals. It is important to note that stability data is lacking for the mixture of Methadose® in these drinks. The vehicle component will develop microbial contamination, therefore it is recommended to refrigerate take home doses. In the absence of clinical stability and sterility data, USP 795 recommends a maximum beyond use date of 14 days for oral non-sterile preparations containing water, when stored at controlled cool temperature (ie. Temperature thermostatically maintained between 2 and 8 degrees Celsius).
- Take home doses prepared in these diluents must be protected from extremes in temperature when transferring custody to a physician’s clinic under delegation.

Initiating a New Patient

- Copy of picture identification
- Current contact information
- Treatment agreement: 2 way (pharmacist-patient) OR 3 way (prescriber-pharmacist-patient) agreement signed by all parties
- Explain hours of operation and usual process/procedure
- Verify prescriber exemption (pain or MMT, temporary) and expiry date with Health Canada
  - Contact Health Canada at exemption@hc-sc.gc.ca telephone 613-946-5139 / Toll Free: 1-866-358-0453
- If participating in the transfer of custody of methadone doses – must confirm that the physician has a ‘delegation exemption’ from CPSO granting the physician permission to delegate authority for the administration of methadone to another properly qualified regulated health-care professional *Contact CPSO 416-967-2600 ext.603
- Lock box and take home dose bottle return policy (as necessary)
- Counsel on safety and harm reduction

Physician -Pharmacist Collaboration

- Pharmacy and clinic hours of operation
- After hours contact information for physician and pharmacist
- Consistency in patient messaging and counseling
- Patient care issues
- Is a lock box required?
- Return take home dose bottles?
- Procedures for missed appointments and missed doses?
- How to notify prescriber of missed doses?

Patient Treatment Agreement

2 way (pharmacist-patient) or 3 way (prescriber-pharmacist-patient)

- Expectation of all parties and consequences may include:
  - Consent to access and share personal health information among health care professionals involved in their care
  - Pharmacy and clinic hours of operation
  - Consequences of inappropriate behaviour
  - Need for lock box and returned take home dose bottles (if applicable)
  - Inability to have methadone dose if patient appears to be intoxicated or under the influence of other substances
  - Notice to the patient that missed, lost, stolen or wasted doses will not be replaced without a prescription
  - Patient’s acknowledgement that, if requested, they will be required to provide photo ID before receiving their dose

Witnessing a Dose

- Positive identification of patient (photo ID)
- Pharmacist must assess the patient in order to safely administer the dose
- Confirm the dose with the patient
- Prepare the dose and administer in a disposable cup (with volume no less than 100mL)
- Ensure total volume is consumed
- Converse with patient to ensure dose was swallowed
- Cup is to be disposed behind the pharmacy counter
- Pharmacist and/or patient sign the record of administration
Documentation

- Documentation of methadone ingestion must include the patient’s name, daily dose, date, time and place where the administration was observed.
- All ‘No-shows’ (missed doses) communicated to prescriber.
- Patient receipt given, with dose documented especially important when a patient is guest-dosing at another pharmacy. (i.e. receipt may be used as evidence of last dose).

References

- CAMH: Opioid Agonist Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid use disorder 3rd edition
- CPSO: MMT Standards & Guidelines 2011
Methadone Dispensing at a Glance

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For Methadone Maintenance Therapy (MMT)
Confirm prescriber’s exemption with the Office of Controlled Substances (OCS)
Phone: 613-946-5139 or 1-866-358-0453
Email: exemption@hc-sc.gc.ca

Prescription should include:
• Dose written in numbers and words
• Specifies ‘in orange drink’ or another appropriate beverage
• Start and stop dates (use the word “inclusive” to minimize ambiguity)
• Specific details for days to be observed, and days that can be given as take home doses

Confirm Narcotic Monitoring System (NMS) requirements and evaluate NMS alerts.

Process and prepare the prescription using the DIN for commercially available methadone solution (e.g. Methadose™ 10mg/mL) indicated for opioid agonist treatment

Prescription label should make the following very clear:
1. The drug product (name, manufacturer) and amount in the bottle.
2. The total dose of methadone in milligrams contained in the bottle.
3. A notation that the drug product has been diluted (i.e., “in orange drink”).
4. The date for ingestion (for take home doses)

For take home doses include:
• Child resistant safety cap (required)
• “Keep in refrigerator” label
• Methadone auxiliary label which reads:
  “Methadone 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. MAY BE FATAL TO CHILD OR ADULTS.”
  or
  “Methadone may cause serious harm to someone other than the intended patient. MAY BE FATAL TO CHILD OR ADULTS.”

In the exceptional cases, where a compounded product is prescribed and dispensed, pharmacist shall label with expiry date and concentration in accordance with OCP Guidelines for Compounding Preparations
http://www.ocpinfo.com/regulations-standards/policies-guidelines/compounding/

For Pain
Confirm prescriber’s exemption with the Office of Controlled Substances (OCS)
Phone: 613-946-5139 or 1-866-358-0453
Email: exemption@hc-sc.gc.ca

Dispensing for pain patients differs from dispensing for MMT in several ways, including:
• Methadone may be dispensed in a liquid or tablet form
• Liquid does not require dilution in Tang® or other vehicle
• Pain patients may receive more than one day’s dose at a time and may require “split” daily dosing

Label must include:
• The usual labelling requirements of a standard prescription
• In the exceptional cases, where a compounded product is prescribed and dispensed, pharmacist shall label with expiry date and concentration in accordance with OCP Guidelines for Compounding Preparations
• http://www.ocpinfo.com/regulations-standards/policies-guidelines/compounding/

Include:
• Child resistant cap
• Device to accurately measure dose (e.g. Oral syringe with instructions on use)
• Methadone auxiliary label which reads:
  “Methadone 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. MAY BE FATAL TO CHILD OR ADULTS.”
  or
  “Methadone may cause serious harm to someone other than the intended patient. MAY BE FATAL TO CHILD OR ADULTS.”

In the exceptional cases, where a compounded product is prescribed and dispensed, pharmacist shall label with expiry date and concentration in accordance with OCP Guidelines for Compounding Preparations
http://www.ocpinfo.com/regulations-standards/policies-guidelines/compounding/
Initiating a new patient

- Request a copy of picture identification
- Ensure current contact information is recorded (home, work, cell)
- Collect a signed Treatment Agreement - two way agreement (pharmacist-patient) as a minimum, but a three way agreement (physician-pharmacist-patient) is preferred if possible
- Explain the pharmacy’s hours of operation, usual process and procedures
- Check type of exemption (pain or MMT, temporary) and expiry date with Health Canada
- Contact Health Canada at exemption@hc-sc.gc.ca telephone 613-946-5139/Toll Free: 1-866-358-0453
- If participating in the transfer of custody of methadone doses – must confirm that the physician has a ‘delegation exemption’ from CPSO granting the physician permission to delegate authority for the administration of methadone to another properly qualified regulated health-care professional *Contact CPSO 416-967-2600 ext.603
- Lock box and take home dose bottle return policy (as necessary)
- Counsel on safety and harm reduction

Preparing methadone doses

- Diluents for methadone take home doses may include; Tang®, Crystal Light®, Kool-Aid®, and other brands of artificially sweetened crystals. It is important to note that stability data is lacking for the mixture of Methadose® in these drinks. Therefore, take home doses prepared in these drinks must be protected from extremes in temperature due to sterility of mixed solution
  - It is recommended to refrigerate carries to keep the vehicle fresh. The shelf life of the diluted Methadose® depends on the shelf-life of the juice/drink used for dilution. In the absence of clinical stability and sterility data, USP 795 recommends a maximum beyond use date of 14 days for oral non-sterile preparations containing water, when stored at controlled cool temperature (ie. Temperature thermostatically maintained between 2-8°C).
  - Document all spillage or wastage of methadone. Health Canada no longer requires prior authorization requests for the local destruction of narcotics and controlled drugs.

Witnessing a methadone dose

- Positively identify the patient (using picture ID if necessary)
- Pharmacist to assess the safety of administering a dose - Do not give patient their dose if patient i appears to be intoxicated or under the influence of other substances
- If upon assessment, pharmacist determines that it is safe/appropriate for patient to receive their dose - confirm dose, measure, and prepare the dose in a cup for the patient to drink

Take home doses

- Do not dispense methadone take home doses unless authorized by prescriber
- May only be given to the patient
- Locked boxes and return of take home bottles can be considered best practices - this process should be established with the prescriber and explained to the patient
- Use of tamper evident tape, caps or seals is best practice to enhance safety and monitoring
- Once patient qualifies, the take home dose schedule is determined by the prescriber. The usual number of take home doses can range from one to a maximum of six (with a few minor exceptions determined by the prescriber under CPSO Guidelines)

Minimizing risk

- Use tamper evident-tape or self-sealing bottles
- Best practice is to have all measurements checked by at least two pharmacy staff (one of whom must be registered with the College)
- Positively identify all patients; call them by name and use picture ID
- Confirm the dose with the patient before it is consumed
- Ensure a copy of the CPSO Overdose Protocol (MMT Program Standards and Clinical Guidelines, Appendix I: http://www.cpsq.on.ca/policies-publications/cpgs-other-guidelines/methadone-program/mmt-program-standards-and-clinical-guidelines) are readily available to all dispensary staff
- If a patient is receiving methadone from two different pharmacies, have an effective communication system to confirm last dose or missed doses.
Methadone

Pharmacology of methadone
- Readily absorbed-onset of effects within 30 minutes
- Usual peak plasma levels: two to four hours after ingestion
- Elimination half-life is 22-48 hrs
- Steady state levels in 5-7 days
- Metabolism: primarily by cytochrome P450-3A4 in liver; minor roles for CYP1A2, 2B6, 2C8, 2C9, 2C19 and 2D6.
  - Primary metabolite is EDDP which is inactive and is used as a marker in urine drug screens

Methadone adverse effects
Note: This is a list of the more common side effects or symptoms and is not intended to be all-inclusive

Common with all opioids
- sweating (dose related) is exacerbated by heat and social situations (can be misinterpreted as withdrawal)
- constipation
- sexual dysfunction and neuroendocrine effects
- weight changes (usually weight gain)
- drowsiness/sedation (slurred speech, cognitive impairment, 'nodding off' or ataxia) sleep disturbances-insomnia (may also be related to other causes such as depression, anxiety, PTSD or rumination of past trauma) or sleep apnea

Less Common-methadone specific
- psychoactive changes (mood or cognitive impairment)
- cardiovascular effects (QTc prolongation and cases of TdP-torsades de pointes)
- Urinary hesitancy or retention

Rare-methadone specific
- cutaneous effects (flushing, itchiness, skin rash)
- peripheral edema (swelling of feet or ankles)
- dental problems (including dry mouth)

References
- CAMH: Opioid Agonist Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid use disorder, 3rd edition
- OCP: MMT & Dispensing Policy 2014
- CPSO: MMT Standards & Guidelines 2011
Methadone Maintenance Dosing Guide

Disclaimer: This tool has been developed by the Ontario Pharmacists Association as a resource to support pharmacists wishing to initiate a methadone program in their pharmacy setting. It is not a substitute for established clinical practice guidelines or regulatory requirements. The information provided is not a substitute for sound clinical judgement from the health care professional. While we strive to ensure the accuracy of the information provided in this document, information may be subject to change, and it is the responsibility of the user of this document to ensure they have the most up-to-date and complete information from available resources.

Methadone Pharmacokinetics

- Methadone is a long-acting, orally effective full mu-opioid receptor agonist – it exhibits no ceiling effect. Ceiling effect is the point at which the increasing effects of partial agonists reach maximum levels and do not increase further, even if doses continue to rise.
- NB: Methadone does not exhibit ceiling effect properties; therefore, dosing must be managed in a manner so as to always minimize risk of overdose.
- Administration once per day mixed with orange drink (e.g. Tang®) or another suitable drink which does not lend itself to injection - QS to 100mL
- Onset of Action: 30 minutes
- Time to peak plasma concentration after ingestion: 2 to 4 hours
- Steady state: 5 to 7 days
- Elimination half-life 22-48 hrs.

Some important dosing facts about Methadone Maintenance Therapy

- Most deaths with methadone treatment occur during the initiation phase as the dose is adjusted.
- Accidental overdoses in adults of as little as starting dose of 40 mg have led to deaths after 3 days of treatment.
- For non-tolerant adults, a single day’s maintenance dose as low as 50-100 mg can be lethal.
- For children, an accidental overdose of 10 to 20 mg can be fatal.
- The effectiveness of methadone maintenance therapy is tied to adequacy of methadone dosing. Adequate dosing can result in treatment retention and reduction in illicit opioid use.
- Patients should be on same dose for at least three consecutive days with no missed doses before dose increase.
  
  NB: ALL missed doses must be communicated to the prescriber.

The Phases in methadone dosing include the following:

Initiation or Induction Doses ‘Start Low’

Goal is to reduce withdrawal or abstinence symptoms safely
- Initial dose of methadone should not exceed 30 mg for the first three consecutive days.

- Initial dose should be less than 20 mg/day if patient is at higher risk for methadone toxicity and less than 10mg/day if the patient has recently been abstinent from opioids

Early Stabilization Phase (0-2 weeks) ‘Go Slow’

Goal is to balance the need to adequately and quickly achieve an optimal dosage against the risk of overdose.
- Dose increases should be in increments of no greater than 10-15 mg
- Increase 5-10mg every 3-5 days if at increased risk of methadone toxicity
- If the patient has been recently abstinent, increase no more than 5mg every 5 or more days
- Patients should be on same dose for at least 3 consecutive days with no missed doses before dose increase.
- Dose increases should not occur more frequently than every 3 to 5 days
- Patient should not be taking any other sedatives (including alcohol, sedating non-prescription drugs) to reduce risk of methadone toxicity
- Patient should consume their dose in the morning so they can be observed for central nervous system (CNS) depression
- Family and friends should be advised to watch for symptoms of overdose
- Any sedation or drowsiness (slurred speech, ataxia, ‘nodding off’) may be early signs of overmedication and the patient should go to the hospital emergency department
- If one dose is missed, there should not be a dose increase until the patient has been on the same dose for a minimum of 3 days
- If two consecutive doses are missed, cancel the prescription as the patient should be reassessed by the physician - restart their initial dose (10-30mg daily) for at least 3 days, then re-assess after the third consecutive dose
- Doses must be held and the prescriber contacted if a patient appears to be intoxicated (e.g. slurred speech, ataxia, drowsiness, smell of alcohol, other unusual behaviour)

Methadone Maintenance Dosing Guide

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long term care for funding this initiative.

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Late Stabilization Phase (2-6 weeks or up to 80mg/day)

Goal is to achieve an optimal dose as quickly and safely as possible.

- Most patients in this phase are taking 50-80mg methadone and are experiencing only partial relief of withdrawal symptoms
- Dose increases should be no more than 5-15mg every 3 to 5 days (usually 5-10mg dose increases) until 80mg is reached - a higher increase of 10-15mg is reserved for those who remain in withdrawal for much or most of the day.
- If there are three consecutive missed doses, cancel the prescription, as the patient must be reassessed by the prescriber. The dose should be decreased by 50% of the current dose or to 30mg per day. Followed by increases of no more than 10mg per day for a maximum of 3 days.
- Then reassess by day 3-4
- After 4 (or more) consecutive missed doses, cancel the prescription as the patient must be reassessed by the prescriber. The dose should be 30mg daily or less - then increase the dose no more than 10-15mg every 3-4 days until reach 80mg daily. Then increase the dose by 10mg daily every 5-7 days for dose increases above 80mg daily
- Monitor for signs of overmedication
- Doses must be held and the prescriber contacted if a patient appears to be intoxicated (e.g. slurred speech, ataxia, drowsiness, smell of alcohol, other unusual behaviour)

Maintenance Phase (6 or more weeks)

Goal is to achieve an optimal dose where methadone can relieve opioid withdrawal symptoms for at least 24hrs., block opioid-induced euphoria and reduce opioid craving, while avoiding euphoria, sedation and other significant adverse effects.

- For most patients, the dose is between 60 and 120mg
- During this phase (when the dose is 80mg or more), the physician shall increase the dose by no more than 5-10mg every 5-7days.
- After at least 2 months in methadone maintenance treatment, patients can be considered for take home doses, if clinically stable and no problematic substance use for at least 1 week. Further take home doses are granted at a rate of one every 4 weeks if patient continues to remain stable, as determined by history and urine drug screening.
- Usually there is a maximum of six take home doses per week
- In some exceptional cases, the number of take home dose may be accelerated (as permitted - refer to CPSO MMT Program Standards and Clinical Guidelines)

Methadone Toxicity

- Motor retardation-circulatory collapse (slow pulse and low blood pressure)
- Respiratory depression-infrequent or shallow breathing, change in skin colour
- Respiratory rate < 10 to 12 breaths/minute. Respiratory depression can be delayed by up to 10 hours following a methadone overdose.
- Pinpoint pupils
- Euphoria-severe sedation including stupor and coma
- Dysphoria-cardiac arrest

Tapering Methadone

- Decision to taper is best made with the support of the methadone prescriber, counsellor, pharmacist, friends, and family.
- Slow taper more successful than rapid taper—a slow and gradual reduction in dose, dropping 5mg every 3 to 14 days. At this rate there should be very few, if any, physical symptoms during the taper.
- Once the dose is lowered to 20mg, the tapering may be slowed down to an even more gradual reduction, to reduce or eliminate any symptoms.
- Other factors associated with successful taper:
  - abstinence from drug use
  - social stability
  - medical and psychiatric stability
  - Patients should be strongly discouraged from abruptly discontinuing methadone because of the high risk of relapse to opioid use and potential for severe withdrawal symptoms.
Patient Information Sheet on Methadone Overdose
(from CPSO Methadone Maintenance Treatment Guidelines Appendix I)

Methadone overdose (receiving a larger dose of methadone than intended) is a serious medical emergency.

Methadone is a long-acting medication and can stay in your body for many hours. Even if you have been on methadone for a long time, taking more methadone than your body is used to can be dangerous. Even what may seem like a small dose increase can be dangerous. If you are new to methadone or have not been taking your regular dose, even for a few days, you are at increased risk of overdose.

Taking too much methadone can result in difficulty breathing (slow or shallow breathing), drowsiness, small pupils, and, in some cases, coma and death.

For this reason, your nurse, pharmacist or MMT physician has deemed that IT IS ESSENTIAL THAT YOU GO TO THE EMERGENCY DEPARTMENT to be observed for a minimum of 10 hours, and maybe longer, depending on your symptoms.

There is good treatment available in the emergency department that can reverse the effects that you may get from taking too much methadone.

References:

CPSO: MMT Program Standards and Clinical Guidelines 2011

CAMH – Opioid Agonist Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid use disorder 3rd edition

CAMH: MMT Client Handbook


The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long term care for funding this initiative.
Methadone Drug Interactions

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Pharmacists are encouraged to regularly access the most up-to-date information on drug interactions from reliable drug information sources as part of their clinical assessment and new information is becoming known daily.

Appendix 2 in the 3rd edition - Opioid Agonist Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid disorder (CAMH) is not exhaustive.


Pharmacists and Methadone Drug Interactions

- Keep an accurate, updated medication profile, including OTC, herbal and illicit drugs
- Develop a working knowledge of methadone drug interactions
- Watch for additive toxicity, particularly with CNS depressants and drugs known to increase QT interval
- Need quick access to current list of interactions
- Determine clinical significance of drug interaction.
- Use alternative, non-interacting drugs when possible
- If potentially interacting drug must be used, adjust methadone dose based on patient response
- Make dose adjustments slowly and in small increments to avoid toxicity or symptoms of withdrawal. Severity of signs/symptoms of withdrawal or over sedation may help determine extent of dose change required
- If potential increase in methadone levels, advise patient in advance of signs or symptoms to watch for and what to do
- When possible, avoid concurrent administration of drugs with overlapping side effect profiles
- Consider pre-existing disease states as an alternative cause for symptoms, other than a drug interaction.
- Consider complexity of prescribed regimens on patient adherence
- Patients should be carefully monitored when starting or discontinuing a medication that may interact with methadone.
- Many interactions can be managed by monitoring for symptoms (e.g. Opioid withdrawal symptoms or excess sedation) and making dose adjustments as needed.

Patients and Methadone Drug Interactions

- Provide all health care providers with an updated list of all medications used (including OTC, herbal and illicit)
- Carry a list of all medications (Best Possible Medication Record)
- Consult with their doctor or pharmacist before taking any new prescription, OTC, herbal or dietary supplements.
- Advised of hazards of using illicit or drugs intended for someone else
- Patients who are on an interacting medication should be educated about the importance of adhering to their medication regimen.
- Counselling to quickly report any sudden or unexpected signs/symptoms of methadone withdrawal or overmedication
- If potential increase in methadone levels, advise patient in advance of signs or symptoms to watch for and what to do.
- Verbally instructed on what the drug is for, how to take it, and how to reduce risk of side effects or interactions
- Adherence to prescribed medications emphasized
- Special consideration for patients with liver or kidney disorders, pulmonary or heart ailments, pregnancy
- Instructed in advance on what to do in an emergency if their supply of methadone and/or other medications runs out

Pharmacodynamic Interactions of Methadone

Additive Effects: When methadone is combined with a medication or illicit drug that has similar pharmacological profile, the effects may be additive – e.g. Potentiation of CNS or respiratory depressant effects, constipation, nausea or urinary retention. CNS depressant effects of alcohol and benzodiazepines are additive when combined with methadone – putting patients at increased risk of respiratory depression and sedation. This can result in death.

OTC medications containing dimenhydrinate and diphenhydramine can be abused and are problematic when used by patients on methadone.

Anticholinergic medications can potentiate the effects on the bowel, causing increased risk of severe constipation, possibly leading to paralytic ileus. It can also increase the risk of urinary retention.

Methadone Drug Interactions

The Ontario Pharmacists Association wishes to acknowledge the Ministry of Health and Long term care for funding this initiative.
Patients taking drugs that are associated with a prolonged QT interval are at risk of developing an arrhythmia (Torsade de Pointes – TdP) which may be fatal. (reference www.crediblemeds.org) Avoid medications known to prolong QT interval in patients taking methadone.

Methadone, especially at higher doses (greater than 150mg) is an independent risk factor for QTc prolongation.

**Pharmacokinetic Interactions**

Many of the interactions with methadone occur through involvement of the microsomal P450 system – especially those that are also metabolized by CYP3A4. Methadone may also be metabolized to a lesser extent by the CYP1A2, 2B6, 2C8, 2C9, 2C19 and 2D6 enzymes.

Effects of induction of methadone metabolism tend to occur slowly. Maximal effects generally occur at one to two weeks and can result in methadone withdrawal symptoms.

Inhibition of methadone metabolism occurs rapidly and toxic effects (sedation, respiratory distress) can present in 1-2 days – patients need to be monitored for a longer time.

Chronic use of alcohol can enhance hepatic metabolism of methadone through enzyme induction. However, acute alcohol use reduces methadone metabolism by competing for metabolic enzyme activity. Patients presenting as intoxicated or smelling of alcohol must be refused their dose and referred to the prescriber.

Theoretically, grapefruit juice could cause elevated plasma levels of methadone – clinical significance is unknown.

A list of medications that can increase or decrease plasma levels/effects of methadone is detailed in CAMH-Opioid Agonist Treatment 3rd edition - Appendix 2, Table A2-2 and A2-3, pg. 106-116. NB: This list is current as of this publication.

### Medications that can decrease plasma levels/effects of methadone (Table A-2):
- Amprenavir
- Barbiturates
- Efavirenz
- Fusidic acid
- Indinavir
- Lopinavir
- Nelfinavir
- Nevirapine
- Phenytoin
- Primidone
- Rifampin
- Risperidone
- Ritonavir
- Somatostatin
- St. John’s Wort
- Urinary acidifiers

### Medications that can increase plasma levels/effects of methadone (Table A2-4):
- Abacavir
- Amprenavir
- Desipramine
- Didanosine
- MAO’s
- Nifedipine
- Stavudine
- AZT

Check with your Drug Information Centre or an online reference for current, up to date information.

**References:**

Opioid Agonist Treatment: A pharmacist’s guide to methadone and buprenorphine for opioid use disorder (CAMH) 3rd edition

Mobile APP - Drug-Drug Interactions in Opioid Therapy by Professor Elinore McCance-Katz
### Methadone FAQs

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<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
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<tbody>
<tr>
<td>Do physicians require an exemption to prescribe methadone for pain?</td>
<td>Under federal legislation, Canadian physicians require an exemption (Section 56) issued by the Office of Controlled Substances to prescribe methadone for Opioid Dependence. A separate exemption is required for physicians who wish to prescribe methadone for pain management.</td>
</tr>
<tr>
<td>Can methadone prescriptions be accepted from prescribers out of province?</td>
<td>Yes, any prescription can be accepted from out of province, as long as the prescriber is authorized to practice in the province or territory in which the prescription was written. As with any prescription, the authenticity should be confirmed, as well as the appropriateness of the drug and dose. In addition, the prescriber’s methadone exemption must be confirmed with Health Canada.</td>
</tr>
<tr>
<td>As a methadone dispensing pharmacist how often am I required to update my training?</td>
<td>Practice is constantly changing and new innovations in treatment occur. Pharmacists are required to have retraining at least every 5 years. One option for a methadone refresher course is OPA’s one day live <em>Methadone, Buprenorphine, and the Community Certificate Program</em>. The other option is OPA’s complimentary on-line methadone and buprenorphine/naloxone education modules which would require the completion of 5 modules including the mandatory module titled <em>Policies Guiding Methadone Dispensing in Ontario</em>. You can register for both programs at <a href="https://www.opatoday.com/professional/resources/education/learn">https://www.opatoday.com/professional/resources/education/learn</a>.</td>
</tr>
<tr>
<td>Are my “relief/casual” pharmacists required to complete the CAMH training?</td>
<td>It is the Designated Manager’s responsibility to ensure all pharmacists, including relief and casual pharmacists, working in their pharmacy have the skills, knowledge and judgment to dispense methadone.</td>
</tr>
<tr>
<td>A patient is not able to attend the pharmacy due to a physical and/or mental condition for their witness dose. Can my driver deliver the dose and witness the dose self-administration?</td>
<td>Methadone deliveries should only take place in exceptional circumstances, whereby the pharmacist has collaborated with the prescriber and they have determined that delivery is the only option to ensure continuity of care. Furthermore, in such rare circumstances it is important to note that the methadone would have to be delivered and dosing directly observed by the pharmacist. Only the pharmacist has the proper training to ensure it is safe (e.g., not appearing to be intoxicated) for the patient to ingest methadone, as well as to ensure the entire dose is swallowed to minimize diversion.</td>
</tr>
<tr>
<td>Is a pharmacy assistant or regulated technician able to witness and document an observed dose of methadone?</td>
<td>A patient ingesting methadone in the pharmacy must be directly observed by the pharmacist. The pharmacist has the training to ensure it is safe (e.g., no signs of intoxication) for the patient to ingest methadone, as well as to ensure the entire dose is swallowed to minimize diversion. A pharmacy technician can assist with dose preparation and elements of the documentation process.</td>
</tr>
<tr>
<td>A prescription for methadone allows for one observed dose today and 9 carries. Is there a limit to only 6 carries at a time, or can the patient be given all 9 carries today?</td>
<td>The CPSO MMT Program Standards and Guidelines allow for stable patients to have “special carries” for more than one week under special circumstances. As this is for exceptional circumstances only, the rationale should be discussed with the prescriber and documented accordingly.</td>
</tr>
</tbody>
</table>
A methadone patient arrives after a dental procedure with a prescription for Tylenol® with Codeine No. 3 (i.e. "Tylenol #3") and amoxicillin. What should the pharmacist do with respect to clinical recommendations to the prescriber? Are there issues with sharing personal health information with the dentist and with the methadone prescriber?

The pharmacist should first consider if the dentist is aware that the patient is taking methadone. This could be discussed with the patient and/or the dentist directly. The pharmacists should be comfortable in communicating his/her concerns with the dentist, since:

- The dentist falls within the patient's "circle of care"; and
- Consent for such collaboration would have already been established as part of the patient's treatment agreement.

**TRANSITION TO METHADOSE™**

<table>
<thead>
<tr>
<th>Why are pharmacies no longer permitted to compound methadone? (Ref 2)</th>
<th>Pharmacies are no longer permitted to compound methadone due to the availability of a commercially manufactured product (Methadose®) which is indicated for opioid agonist maintenance therapy. Pharmacists are reminded that it is not permissible to compound a commercially available product as per the Health Canada Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there any circumstances where the exceptional dispensing of a compounded product may be permitted? (Ref 2)</td>
<td>Compounding is permitted in the event of a therapeutic need or lack of product availability and must be completed per the OCP Guidelines for Compounding Preparations. It would also include cases where a patient requires a concentration of methadone less than that provided by the manufactured product (10mg/mL solution), or the patient is unable to tolerate the commercially available product.</td>
</tr>
<tr>
<td>Methadose™ is available as either a cherry flavoured solution or an unflavoured, sugar-free, dye-free solution – which form is recommended? (Ref 3)</td>
<td>All doses of methadone must be diluted to 100 mL using a vehicle such as orange flavoured Tang® (or other flavored drink); therefore, the unflavoured, sugar-free, dye-free Methadose™ solution is the recommended product for pharmacies to use as stock solution to prepare methadone maintenance treatment (MMT) doses.</td>
</tr>
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</table>

**DILUENT**

| How can I handle a situation where the prescription directs a patient’s methadone dose be dispensed and diluted to a decreased volume (e.g. 50mL)? (Ref 4, pg. 92) | Such a request is not best practice, does not reflect CAMH guidelines, and the pharmacist must consider the risk of diversion. It would be appropriate to contact the prescribing physician, verify the reasons for this clinical decision, and document accordingly. |
| Does dilution have to be to 100mLs? My patient is complaining of difficulty swallowing such a large volume. (Ref 2 & Ref 4, pg 92) | OCP Policy and CAMH Guidelines both state that doses are to be diluted to 100mL. If the patient has difficulty swallowing the entire dose, the pharmacy could give the patient additional time to consume the dose slowly. It is important that the risk of diversion is considered and the patient is supervised throughout the time required to consume the entire 100mLs. |
| Can Cherry flavoured Methadose™ be diluted in water and given? Is Tang® a required vehicle or is water just as good? | Water is not a suitable vehicle. In addition to reducing the risk of diversion, another purpose of the vehicle is to prevent injection of the methadone solution. Tang® (or other similar diluent) is an effective option, and should be used as a vehicle with ALL methadone doses as per the CAMH Guidelines and OCP Policy. |
| Is Methadose™ compatible with Crystal Light? I have a diabetic patient who is requesting a sugar free option. | Methadose™ can be dispensed with Crystal Light for patients who require a sugar free alternative. |

**MEASURING DEVICE**
What are the requirements for the safe and accurate measuring of methadone doses? (Ref 2) | Methadone doses must be accurately measured using a device able to deliver 0.1mL increments. The reliability of graduated cylinders can vary significantly and such devices are not suitable for accurate dose measurement.  

OCP Policy specifically states that “Methadone doses must be accurately measured using a device that is able to deliver 0.1mL increments”. Are there devices available in Ontario known to meet this standard? Is one more accurate than another? | Oral syringes and graduated cylinders do not meet the minimum standard for methadone dispensing. Manual laboratory grade pumps (eg. Dispensette®) and automated methadone dispensing equipment (Methameasure®) are appropriate options. With proper calibration and training of staff, both the manual and automated options can measure the volume to be dispensed to increments of 0.1mL.  

The automated system has added safeguards and documentation components. For safety, the system ensures doses aren’t pumped twice for the same patient, and will maintain an inventory of the remaining volume in the stock bottle. For each dose, there is documentation of the time, volume dispensed, user, lot #, patient ID, and signature capture.  

Is there a device that is preferred by OCP? | OCP does not have a position on one pump type over another. Pharmacies must ensure that any device or equipment they choose can measure accurately to increments of 0.1mL and that the calibration and cleaning of this equipment is done regularly and documented.  

How often should devices be calibrated? | The automated pump systems have protocols in place to calibrate daily or several times a day and to document this step. Manual pumps should also be calibrated daily, or at a minimum, once weekly and a calibration log maintained in the pharmacy.  

**STABILITY**  

How long is a dose stable once the dilution vehicle has been added? | The methadone component of the dose can remain stable even after mixing with diluent; however, the vehicle (e.g., juice) component will develop microbial contamination much more quickly. It is recommended to refrigerate take home doses to keep the vehicle fresh. The shelf life of the diluted Methadose® depends on the shelf-life of the juice/drink used for dilution. In the absence of clinical stability and sterility data, USP 795 recommends a maximum beyond use date of 14 days for oral non-sterile preparations containing water, when stored at controlled cool temperature (ie. Temperature thermostatically maintained between 2-8°C).  

Do methadone take home doses need to be stored in the fridge? | Yes. Once diluted with a vehicle, methadone take home doses should be stored in the fridge to reduce microbial contamination. When storing doses in the fridge, patients should store them in a locked box to prevent accidental ingestion by a child.  

Is there a difference in stability if the doses have been prepared using an automated machine vs using a manual pump? | The type of pump used should not impact on the stability of doses. It is important for pharmacies to maintain clean equipment and workspaces at all times to reduce any contamination of doses.  

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**References:**  
1. Drug and Pharmacies Regulation Act (1990), s. 1 and s. 158  
2. Ontario College of Pharmacists: Methadone Maintenance Treatment (MMT) and Dispensing Policy. (2014).  
7. Controlled Drugs and Substances Act - S.C. 1996, c. 19 (Sec. 56).  
8. CPSO MMT Program Standards and Clinical Guidelines, CPSO, 2011  
Appendix A - Methadone Measuring Equipment Chart

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As per the OCP Methadone Maintenance Treatment (MMT) and Dispensing Policy\(^1\) oral syringes, graduated cylinders and manual pumps that do not dispense in at least 0.1mL increments no longer comply with regulatory requirements for measuring and dispensing methadone. The two main methadone dispensing tools available to Ontario Pharmacists are calibrated manual pumps and automated pumps. The only automated pump currently available in Canada is Methameasure\(^\circledR\).

The following chart highlights the difference between calibrated manual pumps and automated pumps.

<table>
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<tr>
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<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Mechanical liquid bottle top dispenser that uses a floating piston design. Available in analog, digital and fixed volume configurations. Several ranges of volumes are available.(^2) The minimum increment volume required is 0.1mL.(^1)</td>
<td>Comprises of a computer controlled precision pump(s) in a cabinet that can dispense methadone in increment volumes of 0.1mL.(^3) (Click here for video demonstration: <a href="http://www.methameasure.ca">www.methameasure.ca</a>)</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>Accuracy per the manufacturer’s monograph is 0.5%, except for the 0.05 – 0.5 mL volume model where accuracy is 1.0%.(^2)</td>
<td>Accurate to 0.1%.(^4)</td>
</tr>
<tr>
<td><strong>Bottle Compatibility</strong></td>
<td>Fits 45mm reagent bottles and can be adjusted to fit other sizes with the use of adapters.</td>
<td>Compatible with all methadone solutions and both forms of Methadose 10mg/mL.</td>
</tr>
<tr>
<td><strong>Equipment Maintenance</strong></td>
<td>Disassembles easily to simplify cleaning and maintenance. As methadone crystallizes when exposed to air, regular cleaning is required to ensure accuracy. According to Pharmasystems monograph: “When each stock bottle is complete, we recommend that you circulate the Dispensette(^\circledR) with hot water”(^5) Must be recalibrated every 3 to 12 months depending on use. Annual factory re-calibration is recommended to ensure ongoing accuracy (for an additional fee).(^5)</td>
<td>The Methadone pump must be calibrated daily using a three step check. Depending on system use, tubing will require replacement due to wear and tear (no additional fee under normal conditions).</td>
</tr>
<tr>
<td><strong>Pharmacy System Integration</strong></td>
<td>Standalone system.</td>
<td>Fully integrated with all major pharmacy systems: Kroll, PharmaClik RX, Fillware, Telus, WinRX and RX-Pro. Allows for integrated patient identification with the use of biometrics and photo identification. Can also be used as a standalone system if preferred.</td>
</tr>
</tbody>
</table>
| Pharmacy Workflow Integration | The Pharmacist is responsible for all processes involved in methadone dispensing; with direct involvement in assessment of patient and administration of dose. Calibrated pumps are manual and do not maintain any records, and therefore it is not possible for a pharmacist to verify the dispensed volume after a vehicle has been added to complete the preparation of the dose to a total volume of 100mL. | The complete process (identification, checking, dispensing, dilution with vehicle, reporting and administering of medication) is seamless, full volume can be dispensed in 10 seconds or less, and each step and user is documented by the system. A patient receiving one witness dose & 6 carries can be served in under one minute.3

Provides the following reports to assist with record keeping:

- administration (including prescription number, lot number and expiry date of methadone dispensed);
- missed dose;
- custody transfer
- advanced preparation.

System also provides:
- Display notes functionality allows the user to see important notes relating to the patient prior to dispensing / administering of the medication.
- Bottle returns functionality automated to make tracking simple.
- Helps to track if the patient has paid for their medication |

| Source | Product catalogue and operating manual for BrandTech Dispensette®. [www.brandtech.com](http://www.brandtech.com) 

1. OCP Methadone Maintenance Treatment (MMT) and Dispensing Policy, June 2014
3. [http://www.methameasure.ca/faq.html](http://www.methameasure.ca/faq.html)