ONTARIO PHARMACISTS ASSOCIATION

Advocating Excellence in Practice and Care

# Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists

## Part A: Methadone

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**Disclaimer**

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 a sole tool for clinical decisions.

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 also 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.

Note: During the COVID-19 pandemic, modifications to the standard guidelines have been made in order to reduce community transmission. Please refer to the CAMH document “COVID-19 Opioid Agonist Treatment Guidance” for further information on these modifications to treatment delivery.

**Acknowledgement**

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# Opioid Use Disorder (OUD)

**The Centre for Addiction and Mental Health (CAMH)** defines Opioid Use Disorder (OUD) as a treatable medical condition characterized by a problematic pattern of opioid use leading to significant impairment or distress. It involves physical and psychological dependence, where individuals continue using opioids despite negative social, physical, or personal consequences.

Key Aspects of OUD according to CAMH:

Definition: It is a chronic, relapsing condition involving compulsive, or hard-to-control, use of opioids.

Signs & Symptoms (DSM-5):

- Loss of Control: Using more or longer than planned, craving opioids, and difficulty cutting down.
- Functional Impairment: Failing to fulfill major roles at work, school, or home.
- Physical Dependence: Experiencing tolerance (needing more for the same effect) and withdrawal symptoms (e.g., pain, nausea, agitation) upon stopping.
- Continued Use: Using despite negative health, social, or dangerous consequences.

- Spectrum of Use: CAMH describes a spectrum from at-risk or hazardous use to severe addiction.
- Treatment: Involves evidence-based approaches, primarily **Opioid Agonist Therapy** (OAT), combined with behavioral and social supports.

The United Nations (UN) addresses opioid use disorder (OUD) primarily through the **United Nations Office on Drugs and Crime (UNODC)**and the World Health Organization (WHO), recognizing it as a critical, chronic, and relapsing health condition rather than just a criminal issue. The UN emphasizes that OUD is a major driver of global mortality, responsible for roughly 70% of the 128,000 deaths attributed to drug use disorders in 2019 (UNODC, *World Drug Report 2023* (United Nations publication, 2023).

Key Findings: Opioid and Stimulant Related Harms in Canada July 2024 to June 2025:

17 deaths per day (22% lower than previous 12 months)
14 hospitalizations per day (21% lower than previous 12 months)
59 Emergency Department visits per day (22% lower than previous 12 months)
94 Emergency Medical Services (EMS) responses per day (16% lower than previous 12 months)

53,308 apparent opioid toxicity deaths Jan. 2016 to June 2025
2787 apparent opioid toxicity deaths Jan. to June 2025 of which 97% were accidental
Jan. to June 2025 – 78% apparent opioid toxicity deaths occurred in British Colombia, Alberta and Ontario.
Most apparent opioid toxicity deaths occurred among males (72%) and among individuals aged **30 to 39 years (26%)** so far in 2025 (Jan to Jun)
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 57% involved fentanyl and 57% involved fentanyl analogues
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 83% involved opioids that were non-pharmaceutical
Of all apparent opioid toxicity deaths so far in 2025 (Jan to Jun), 68% also involved a stimulant

This update is based on data submitted to or extracted by the Public Health Agency of Canada on or before October 28, 2025: https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/

# Opioid Agonist Treatment (OAT)

Pharmacotherapy is the most effective treatment for opioid use disorder (OUD), and opioid agonist therapy (OAT) saves lives. The mortality risk is significantly reduced for people with OUD while in OAT treatment compared to out of OAT treatment.

Buprenorphine and methadone should both be considered as standard first-line treatment options for OAT. For people who initiate OAT with buprenorphine, clinicians should be aware of the higher risk of attrition after the first month of initiation and offer alternative opioid agonist medications in these circumstances . When considering methadone, clinicians should be aware of the higher risk of mortality during the first month compared with the remainder of the treatment period.

Results from a recent study suggest that any advantages from a reduced risk of mortality with treatment with buprenorphine/naloxone were outweighed by deficits in treatment retention. Evaluated in a jurisdiction where both medications were available in office-based settings, these findings do not support recommendations of buprenorphine/naloxone as first-line treatment over methadone.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2843176

OAT with slow-release oral morphine should be available and offered as a second-line treatment option as per the 2024 CRISM National Guidelines. The availability of slow-release oral morphine may vary across Canada, but it is recommended that this medication should be make widely available to ensure better equity.
https://www.metaphi.ca/wp-content/uploads/SROM.pdf
https://crism.ca/wp-content/uploads/2024/11/2024-Update-to-CRISM-Update-to-National-OUD-Guideline-20241111.pdf

The approach to providing OAT services is evolving in Ontario. The CPSO Methadone Maintenance Treatment Program Standards and Guidelines from 2011 was rescinded in March 2021. It was perceived that the exceptional status of methadone and the high degree of oversight, disincentivized physicians to offer OAT, thus limiting access for patients. As well, in 2018, Health Canada removed the Section 56 exemption requirement for methadone prescribers – to improve access to treatment,

**OAT as a Harm Reduction Approach**

OAT has been shown to reduce:

- Use of other opioids (Brand et al., 2003; Davioli et al., 2007; Gibson et al., 2008)
- Criminal activity (Lind et al, 2005) as OAT is legal and may keep patients away from the harmful consequences of acquiring and possessing illicit opioids and prescription opioids
- Patient mortality rates (Degenhardt et al., 2011; Gibson et al., 2008; Soyka et al., 2011) compared to people who continue to use illicit opioids

- Injection-related risk (including behaviours and transmission of HIV and sexually transmitted infections (Hart, 2007)
- Cost of law enforcement, health care and social services for patients who are unemployed, homeless or in other difficulties (Hart, 2007)

OAT improves (Brands et al., 2002):

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

In contrast to many short-acting opioids (e.g., heroin), long-acting opioids used for OAT:

- Are well absorbed and effective orally (methadone, morphine), sublingually (buprenorphine) or subcutaneously (buprenorphine XR injection)
- Take longer (e.g., 30 minutes vs. instantaneously) to produce an effect than opioids that are injected, smoked or snorted
- Are longer acting than other opioids (24 to 36 hours or longer vs. three to six hours) and are administered less frequently
- Do not cause drowsiness or euphoria in patients on an appropriate dose
- Do not cause significant impairment in thinking, behaviour or functioning when taken at an appropriate dose
- Do not dull normal emotions and physical sensations
- Diminish opioid craving
- Decrease drug-seeking behaviour
- Reduce the likelihood of euphoria from other opioids in stable patients
- Continue to be effective with long-term use without dose increases

**Limitations to the use of OAT**

- Methadone is a high-risk medication with a narrow therapeutic range that can result in opioid overdose, especially at the beginning of treatment. It may prolong QT interval, leading to an increased risk of fatal arrhythmias.
- Buprenorphine has a lower overdose mortality risk but can still have severe health consequences including death – especially, if misused or combined with other CNS depressants including alcohol.
- People (including health professionals) may inadvertently or inappropriately view patients as substituting one substance of dependence for another thus stigmatizing them further.
- Program practices may be experienced by patients as demeaning (e.g., observed urine collection, waiting in line at the pharmacy for their dose).
- OAT requires regular visits to the pharmacy and physician.
- Cost may be a barrier for some patients.
- Both buprenorphine and methadone can produce adverse side-effects and may interact with other medications.
- OAT practices may limit patient's 'flexibility' for work or travel.
- There may be limited availability of physicians and pharmacies that offer OAT in some areas

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.

*CAMH Opioid Agonist Maintenance Treatment: A pharmacist's guide to methadone and buprenorphine for opioid use disorder. Third edition 2015.*

Overdose Prevention Sites (which are also referred to as supervised injection services or safe consumption sites) are facilities that fall under the umbrella of harm reduction. These facilities are health services that provide a hygienic environment for people to consume substances under the supervision of medical professionals. In addition to supervised injection, individuals are provided with sterile supplies, education on safer consumption, overdose prevention and intervention, medical and counselling services, and referrals to drug treatment, housing, income support and other services. Overdose prevention sites have been known to reduce costs for the health care system, prevent blood borne illnesses such as HIV or Hepatitis C, helps individuals access support services and prevent overdose deaths. In addition, research shows that the existence of an overdose prevention site in a community does not lead to increased crime, and works to decrease public substance consumption. These facilities are helpful in reducing the harms related to substances, particularly opioids. Overdose prevention sites are an evidence-based component to a comprehensive treatment response.

# Methadone Dispensing at a Glance

**For Methadone Agonist Therapy (MMT) only (not for pain)**

Prescription must include:

- Registration number of the certificate of registration for the prescriber (specific to each province's college)
- Name of the person for whom the methadone is prescribed
- Name and dose of methadone
- Directions for use of methadone
- Name and address of the prescriber
- Date the methadone is prescribed
- ID number of the patient and the type of ID used (e.g. Health Card, Driver's License)

As per CAMH Guidelines:

- Start and stop dates (use the word 'inclusive' to minimize ambiguity)
  Total quantity is not required as this can be clearly and exactly calculated based on start and stop dates
- Specific days of the week methadone doses are to be ingested/observed and days that dose(s) can be given as take-home/carry doses

Good practice for Prescribers:

- Dose spelled out in words, as well as in numbers
- Instructions to 'dispense in drink/juice'
- Name of the dispensing pharmacy (the patient has a choice, but the physician needs to know to ensure good physician-patient communication)
- Information about changes in dose (e.g., cancel previous prescription, dose change, carry change)
- Other instructions as needed

Confirm Narcotic Monitoring System (NMS) requirements and evaluate NMS alerts
https://ocpinfo.com/ocp-resources/six-important-tips-for-using-the-narcotics-monitoring-system/

Process and prepare the prescription using the DIN for one of the commercially available methadone solutions 10mg/ml indicated for opioid agonist treatment.

Prescription label should make the following clear:

- The drug product (name, manufacturer) and amount in the bottle
- The total dose of methadone in milligrams contained in the bottle
- A notation that the drug product has been diluted (i.e., 'in orange drink')
- The date for ingestion (for take-home/carry doses)

For take-home/carry doses, include:

- Child resistant safety cap
- Tamper-proof tape/cap (best practice)
- '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'

As per the Health Canada Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051), it is not permissible to compound a commercially available product. Compounded methadone is only permitted in the following rare cases:

- Therapeutic need* – patient is unable to tolerate all commercially manufactured products
  NB: ODB requires the physician to submit a request to the Exceptional Access Program along with a completed Adverse Drug Reaction form
- Lack of product availability

- A concentration less than the commercially manufactured 10mg/ml solution is required
- It is not a patient choice based on preference.

Where a compounded product is prescribed and dispensed, the pharmacist shall label with the expiry date and concentration in accordance with NAPRA Model Standards for Pharmacy Compounding of Non-sterile preparations. https://www.napra.ca/publication/model-standards-for-pharmacy-compounding-of-non-sterile-preparations/

**Take-home/carry doses**

- Do not dispense methadone take home doses unless authorized by prescriber. Arrangements may be needed due to pharmacy closures on holidays or weekends. This will require additional discussion with the prescriber and patient about 'guest-dosing' at an alternative pharmacy if carries are not permitted.
- Methadone may not be delivered to a patient using traditional pharmacy methods – it requires patient evaluation, witnessing a dose and direct transfer of the carry/take-home dose to the patient by the pharmacist. Using only a chain of signatures is not sufficient.
- May only be given to the patient.
- Lock box and return of take-home bottle(s) 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.

**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 verify with picture ID
- Confirm the dose with the patient by asking them their dose before it is consumed
- If a patient is receiving methadone from two different pharmacies, have an effective communication system to confirm last dose or missed doses.

**Pharmacology of Methadone**

- Readily absorbed, onset of effect is 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:

- Nausea and vomiting
- sweating (dose related) is exacerbated by heat and social situations (it 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

- Dental problems caused by or related to dry mouth (there may be other medications, such as anti-depressants, used by a methadone client that may also cause increased dryness of the mouth). With low saliva, generalized bacterial plaque accumulates as a result of poor oral health

Less Common-Methadone specific:

- psychoactive changes (mood changes or cognitive impairment)
- cardiovascular effects (QTc prolongation and cases of TdP-torsades de pointes)
- urinary hesitancy or retention
- opioid withdrawal symptoms if stopped abruptly

Rare-Methadone specific:

- cutaneous effects (flushing, itchiness, skin rash)
- peripheral edema (swelling of feet or ankles)

# Methadone Drug Interactions

Methadone can interact with other medications.  Pharmacists should always ask about all other drugs the patient is taking including prescription medications and herbal remedies.

Mixing methadone with other drugs that depress the central nervous system ca be extremely dangerous. Other opioids, alcohol and benzodiazepines should be avoided.  This is especially risky when you first start taking methadone. Using other drugs while taking methadone can also cause your dose of methadone to affect you differently.

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.

**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 a 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.
- Be advised of hazards of using illicit substances 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.
- Counselled 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. They also have CNS depressant effects.
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.

**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

| **Medications that can decrease plasma levels/effects of Methadone** | **Medications that can increase plasma levels/effects of Methadone** | **Medications that may be affected by Methadone** |
|---|---|---|
| Amprenavir<br>Barbiturates<br>Efavirenz<br>Fusidic acid<br>Indinavir<br>Lopinavir<br>Nelfinavir<br>Nevirapine<br>Phenytoin<br>Primidone<br>Rifampin<br>Risperidone<br>Ritonavir<br>Somatostatin<br>St. John's Wort<br>Urinary acidifiers | Amitriptyline<br>Benzodiazepines<br>Cimetidine<br>Ciprofloxacin<br>Clarithromycin<br>Delavirdine<br>Disulfiram<br>Erythromycin<br>Fluconazole<br>Fluoxetine<br>Fluvoxamine<br>Indinavir<br>Ketoconazole<br>Paroxetine<br>Sertraline<br>etc. | Abacavir<br>Amprenavir<br>Desipramine<br>Didanosine<br>MAOI's<br>Nifedipine<br>Stavudine<br>AZT |

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

**Resources**:

CAMH Opioid Agonist Treatment: A pharmacist's guide to methadone and buprenorphine for opioid disorder 3rd edition
NB: Appendix 2 is not exhaustive.
To order- https://www.camh.ca/en/camh-news-and-stories/get-the-latest-on-opioid-agonist-guidelines

Drugs.com
https://www.drugs.com/drug-interactions/methadone.html

Addiction Treatment Forum
https://atforum.com/wp-content/uploads/Methadone_Interactions_with_other_drugs.pdf

# Initiating a Methadone Program in Your Pharmacy

Ontario College of Pharmacists Opioid Policy, 2018
(*Formerly Methadone Maintenance Treatment (MMT) and Dispensing Policy June 2014)*
http://www.ocpinfo.com/regulations-standards/policies-guidelines/opioid-policy/

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:**

Notify OCP within seven days of initiating methadone dispensing practice (for MMT) by submitting completed Methadone Dispensing Notification Form – send by email to pharmacyapplications@ocpinfo.com, or fax to 416-847-8399, or mail to the attention of Pharmacy Applications & Renewals at 483 Huron St. Toronto, ON M5R 2R4
http://www.ocpinfo.com/library/forms/download/Methadone%20Dispensing%20Form.pdf

A) Pharmacy information (Trading Name, Name of Owner/Corporation, Accreditation no., Postal Code)
   Start and stop date of methadone dispensing
B) Description of methadone services (MMT?)
   Does pharmacy accept new patients?
   Does the pharmacy transfer custody of methadone doses to an exempted physician or his/her delegate for administration at a clinic?
C) Name and OCP number of Designated Manager;
   And date CAMH course completed or course registration date
   And signature
   Name and OCP number of staff pharmacist;
   And date CAMH course completed or course registration date
   And signature
D) Designated Manager Acknowledgment signed and dated

NB: OCP must be notified of any changes to the information specified above (e.g., change in hours)

**Training Requirements**

Designated Manager must take the CAMH Opioid Use Disorder Treatment (OUDT) Course (or comparable course*) within 6 months of beginning methadone dispensing.
https://www.camh.ca/en/education/continuing-education-programs-and-courses/continuing-education-directory/opioid-use-disorder-treatment-oudt-course
*it is the responsibility of the pharmacist to ensure the course taken is equivalent to the CAMH OUDT course

In addition to the DM, within one year, at least one staff pharmacist must complete this training.

Training must be updated at a minimum every five years.
One of the following would be acceptable as a training update:

OPA's Methadone, Buprenorphine and the Community
Webinar and in-person options. See opatoday.com for upcoming sessions.
*or*
OPA's Addictions and Opioid Agonist Therapy Education
Completion of 5 online modules, including Policies Guiding Methadone Dispensing in Ontario
https://opatoday.com/product/opioid-substitution/

Ideally, all pharmacists providing methadone services should have knowledge of the best evidence and relevant clinical practice guidelines. Although not mandatory, OPA methadone training courses would be beneficial for all pharmacists involved with methadone dispensing.

All pharmacists (regular and casual) who dispense methadone must be familiar with the principles and guidelines outlined in the current CAMH Opioid Agonist Maintenance Treatment: A pharmacist's guide to methadone and buprenorphine for opioid disorder 3rd edition

**Required Documentation**

Pharmacists should record relevant and pertinent details with regards to opioid therapy in an accessible and standardized manner in accordance with OCP Documentation Guidelines.

https://www.ocpinfo.com/regulations-standards/practice-policies-guidelines/documentation-guidelines/

Documentation of any decisions that requires professional or clinical judgment involving a change in therapy (holding dose, what to do when dose vomited etc.), Documentation should include: the decision, the rationale for the decision, expected patient outcome and plan for monitoring and follow up.

**Treatment Agreement**

A written two-way (pharmacist-patient) OR three-way (prescriber-pharmacist-patient) agreement serves as best practice to outline expectations and prevent miscommunication.
(sample agreement in CAMH Opioid Agonist Treatment 3rd edition – Appendix 4)

Items 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
- 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
- Signature of Designated Manager (or delegated pharmacist) and the patient

NB: This 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/witnessed and take-home/carry doses. This 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 in a clinic/treatment location (i.e., if transferring custody of doses), the dispensing pharmacist must be provided with copies of the daily administration record. Records of daily reconciliation of methadone dispensed to and received from a clinic/treatment location under transfer of custody agreements must be checked and verified. Record of destruction of unused doses in accordance with applicable laws and standards of practice must also be maintained.

If the pharmacist intends to transfer custody to a physician/delegate to administer in the clinic, the means of transport must be secure, auditable, and traceable. The pharmacist must be able to identify who has care and control of the doses at any point in time (i.e. chain of signature) prior to transferring custody as they are accountable for security and integrity until the doses are either dispensed to the patient or dispensed to the physician/delegate.

Please note: This does not provide for delivery of methadone doses to patients through a pharmacy's delivery service. The pharmacy delivery service will not account for evaluation of the patient, witnessing observed doses or secure transfer of carry/take-home doses.
www.ocpinfo.com/practice-education/practice-tools/fact-sheets/methadone

If applicable, written institution[1]-specific policies for dispensing methadone (e.g., hospital, licensed nursing homes, correctional facilities)

1 An 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**

All doses (observed/witnessed and take-home/carry doses) must be prepared using a manufactured product (10mg/mL solution) diluted to at least 100mL with a vehicle that does not lend itself to injection (e.g., Tang®)

**Equipment Needed**

- An appropriate measuring device (e.g., calibrated pump) that can accurately deliver 0.1 mL increments. Note - graduated cylinders are not suitable.
- Disposable cups (approx.100ml) for observed doses,
- 100mL bottles for carry doses
- Childproof safety caps are required; tamper proof caps are recommended.
- A lock box is recommended for take home/carry 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 a risk 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 (may be typed as part of the prescription label)

**Required References**

The pharmacy must have access to the current text:

CAMH Guide Opioid Agonist Maintenance Treatment, 3rd edition

- To order - https://store-camh.myshopify.com/products/p6500

# Initiating MMT Services: A Brief Overview

**Things to Consider Before Starting to Dispense Methadone**

Pharmacy hours of operation – hours for methadone administration? Open seven days per week?

Pharmacy layout and workflow – private area for preparing methadone doses without distraction
A private area/semi-private alcove 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

Develop policies on:

- Hours when methadone is dispensed
- Consider the number of clients that can comfortably be served in the pharmacy at one time
- Number of methadone clients in pharmacy at one time
- Service to methadone clients who are regularly serviced by other facilities (i.e., guest dosing)
- Assess staff competence to deliver methadone services in a non-stigmatizing environment
- Procedures to minimize dosing errors and optimize work processes
- Appropriate equipment (e.g., dispensing tools, measuring equipment, labels and labeling as regulated, child proof liquid 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/witnessed and carry/take-home doses.
- Monitor for signs and symptoms of withdrawal, intoxication and/or overdose.
- Observe for changes in patient's appearance or behaviour
- Aware of social and housing issues that may require special dispensing needs
- Ensure a process is in place for handling missed, lost, stolen or wasted doses
- Identify and address methadone drug interactions
- Positive identification of the patient
- Observe ingestion of witnessed/observed doses
- Provide carry/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., signs and symptoms requiring immediate attention at various phases of methadone treatment and dosing, harm reduction education)
- Diversion alertness
- Determine physician's preferred method of communication (e.g., email, cell phone, etc.) especially after office hours
- 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 pending staffing
- Check prescriptions for technical accuracy
- Prepare individual patient doses
- Monitor return of empty bottles from carry 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 carry/take-home doses

Required auxiliary labels as per OCP Policy

- 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 (may be typed as part of the prescription label)

**Preparing Methadone Dose**

- Accurately measure commercially available methadone solution using an appropriate measuring device (e.g. calibrated pump) accurate to 0.1ml increments
- Diluents for methadone doses (witnessed/observed and take home/carry) 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® or commercially prepared methadone 10mg/ml liquids 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 (i.e., Temperature thermostatically maintained between 2 and 8 degrees Celsius)
- Take-home/carry doses prepared in these diluents must be protected from extremes in temperature when transferring custody to a physician's clinic using delegation

**Initiating a New Patient**

- Copy of picture identification
- Current contact information (keep regularly updated)
- Two or three-way treatment agreement signed by all parties
- Explain hours of operation and usual process/procedure
- Lock box and take-home/carry 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 for patient care issues
- Is a lock box required by the prescriber
- Tamper proof caps/seals required by the prescriber/clinic?
- 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 and/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
  Sample patient-pharmacist agreement can be found in references pages of
  CAMH Guide Opioid Agonist Maintenance Treatment, 3rd edition - Appendix 4

**Witnessing a Dose**

- Positive identification of patient (photo ID)
- Only the pharmacist can assess the patient in order to safely administer the dose
- Confirm the dose with the patient
- Prepare the dose and administer it in a container that will hold at least 100 mL of liquid (disposable cup or bottle)
- Ensure total volume is consumed and converse with patient to ensure dose was swallowed
- Cup is to be disposed of in the pharmacy
- 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) to be communicated to prescriber
Patient receipt given, with dose documented- especially important when a patient is guest-dosing at another pharmacy.

Provision of Naloxone kits:
Naloxone is a Schedule II medication that can be provided by a pharmacist through funding from the Ontario Ministry of Health and Long-Term Care for 'emergency use' to temporarily prevent overdoses from opioids including methadone. Pharmacists must do a patient assessment and get the appropriate training to provide patient/agent education.
https://www.ocpinfo.com/practice-education/practice-tools/support-materials/naloxone-guidance/?hilite=naloxone

# Methadone Maintenance Dosing Guide

Methadone is prescribed in a way that balances the risk of adverse effects to the patient and people in their environment while optimizing the benefits, including retention in treatment and decreased health and quality-of-life harms related to substance abuse.

The pharmacokinetics of methadone varies greatly from person to person; so, after the administration of the same dose, considerably different concentrations are obtained in different subjects, and the pharmacological effect may be too small in some patients, too strong and prolonged in others. Methadone is mostly metabolized in the liver. https://pubmed.ncbi.nlm.nih.gov/15501692/#:~:text=The%20pharmacokinetics%20of%20methadone%20varies,strong%20and%20prolonged%20in%20others.

**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. Therefore, dosing must be managed in a manner 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
  Note: Split daily dosing may be beneficial to patients with the following conditions: chronic pain, pregnancy, rapid metabolism (due to genetics or drug interactions)
- 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 Agonist Therapy**

- Most deaths with methadone treatment occur during the initiation phase or within the first two weeks as the dose is adjusted.
- Accidental overdoses in adults of as little as a 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 agonist 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; although the frequency of dose adjustment ranges are based on various clinical parameters (stage of titration, base dose, risks of toxicity etc.). There should be no missed dose before a dose increase.
- The META-PHI methadone guidelines for prescribers specifies patients should have had 4 of the 5 previous doses (not necessarily 3 consecutive doses) for dose to be increased.
  https://www.metaphi.ca/wp-content/uploads/MethadoneGuidance.pdf
- All missed doses must be communicated to the prescriber.

**Phases in Methadone Dosing**

**Induction (or Initiation) Doses 'Start Low'**.

In determining initial methadone doses, opioid tolerance and risks for toxicity should be considered. Patients' experiences with methadone, knowledge of their own tolerance, and preferences should be discussed.

An initial dose of 10mg or less should be prescribed; then doses increased by no more than 5mg every 5 days (as necessary) for patients who:

- Are recently abstinent or use intermittently
- Have unknown tolerance to opioids due to unclear history or lack of collateral information
- Use low-potency opioids (e.g., codeine)

An initial dose of 5-20mg should be prescribed; then doses increased by 5-10mg every 3-5 days (as necessary) for patients who:

- Have established tolerance via patient history or collateral information (e.g., UDT results)
- Have risk factors that include:
    - High or multiple CNS depressant use (e.g., alcohol, antipsychotic, benzodiazepine, gabapentoid)
    - Medical illness involving respiratory compromise (e.g., chronic obstructive pulmonary disease)

An exception would be if a patient uses fentanyl. See META PHI fentanyl guidelines r- starting dose recommended is 30 mg, including for those with risk factors listed.

- Have changes in drug metabolism

An initial dose of 5-30mg should be prescribed; then increase doses by 5-15mg every three to five days (as necessary) for patients who both:

- Have high tolerance of high-potency opioids from daily use and have UDT confirmation of recent opioid use
- Do not have risk factors for excessive CNS depression (as listed above)

***Determining starting doses***

Based on an assessment of the above factors, we recommend the following starting doses for methadone (monotherapy) initiation in the outpatient setting:

- **Low tolerance and/or high risk of toxicity:** Initial dose of 5–10 mg (buprenorphine should be considered in these cases)
- **Moderate tolerance and risk of toxicity:** Initial dose of 10–20 mg
- **Moderate tolerance and no major risk factors for toxicity:** Initial dose of 20–30 mg
- **High tolerance and risk of toxicity:** Initial dose of 20–30 mg
- **High tolerance and no major risk factors for toxicity:** Initial dose may be up to 40 mg
- **Very high tolerance AND no major risk factors for toxicity AND known recent experience of high-dose methadone at a steady state[6]:** Initial doses of up to 50 mg may be considered (the rationale for the higher starting dose and the patient's consent should be documented)

  Clinicians should be cognizant of their own expertise; those with less experience with methadone prescribing may choose to initiate doses more conservatively.

  Before planning a starting dose above 30 mg, it is advisable to obtain some form of collateral information regarding fentanyl use, which can include a urine drug test, evidence of fentanyl use on previous urine drug tests, and/or records of emergency department visits or hospitalizations associated with fentanyl use. The limitations of urine testing should be noted; for example, a urine test that is positive for fentanyl indicates exposure at some point in the last one to two weeks but is not an indicator of tolerance. People who have been recently abstinent from fentanyl may have a positive test but will have lost some of their tolerance and should be started at lower doses

https://metaphi.ca/wp-content/uploads/MethadoneGuidance.pdf

Reassess patients frequently during the first two weeks of treatment because they are at the highest risk of fatal overdose during this period. Discuss the risks and strategies to reduce it (e.g., use only small amounts of additional opioids; do not use alone; have a naloxone kit available).

Reassess the patient with every subsequent dose increase.

Recent Changes in Opioid Therapy:

Recent Ontario guidance suggests starting methadone at higher doses (30mg) for people with very high opioid tolerance including for people on benzodiazepines. Doses can be increased by 10-15mg every 3-5 days until about 80mg, and thereafter typically by 10mg increments.
In practice, you may begin to see starting doses up to 40mg for select patients with previous experience of methadone, known very high opioid tolerance and very low risk of toxicity.
https://www.bccsu.ca/opioid-use-disorder/

People who use fentanyl often need doses above 120mg to address both withdrawal symptoms and cravings. Those on these higher doses should be monitored for sedation and side effects.
https://pharmacyconnection.ca/navigating-changes-to-opioid-agonist-therapy-and-how-to-support-patients/

**Titration and stabilization Phase**

The dose should be increased 5-10mg every five to seven days to manage withdrawal symptoms and cravings.

**Maintenance Phase**
An appropriate maintenance dose is determined through clinical judgment i.e., one which provides 24hours without opioid withdrawal and reduction of opioid cravings while not causing sedation or toxicity.

Consideration should be given to tapering down the dose for patients experiencing opioid-induced side effects (e.g., sweating, hypogonadism, severe constipation, adrenal insufficiency. Also, collaborate with the patient to balance the benefits, disadvantages and risks of methadone treatment.

Rapid metabolism is confirmed with serum methadone levels and/or observing emergence of withdrawal after an observed dose.

There is no consensus on the best way to assess the need for split dosing. Consideration should be given to clinical stability before offering split dosing. It often requires providing evening doses as take-home doses as most patients are unavailable to attend a pharmacy for witnessed dosing.

Assessment of post-dose sedation at peak serum levels should be done for patients on high doses of methadone.

**Missed Doses**

**Repeated missed doses during the titration stage are a barrier to reaching a therapeutic dose of methadone. For patients who repeatedly face challenges achieving three consecutive doses, we recommend considering a dose increase for individuals with demonstrated tolerance to methadone and high-potency opioids who meet the following criteria:**

- **At a dose of 60 mg or less**
- **At least four doses in the preceding five days**
- **Ongoing withdrawal at the current dose**
- **Ongoing fentanyl use**
- **Lack of sedation**

**A dose increase immediately after a missed dose is not recommended. If a dose was missed one day before the day of the assessment, we recommend continuing that dose for one more day and prescribing a dose increase for the following day without requiring an additional clinical visit. Specify on the prescription that the pharmacist should assess the patient and hold the dose if they appear sedated.**

**META:PHI's 2021 document Methadone Treatment for People Who Use Fentanyl:**
**Recommendations for different clinical scenarios in which someone who has taken methadone within the past two weeks is seen on Day 5**

**https://metaphi.ca/wp-content/uploads/MethadoneGuidance.pdf (page 24-25)**

NB: Guidelines for patients who use fentanyl--decrease dose by 50% after four missed doses; to 30 mg after five missed doses.

A stable methadone dose should be re-established after several missed doses. This may not be the same as the previous dose.

One replacement dose of methadone (no more than 50 percent of the regular dose) should be offered if the patient has emesis witnessed by a health care professional occurring withing 15 minutes of an observed dose. If emesis occurs during pregnancy, the dose should be spread over 30 minutes and consider observing for 15-20 minutes after dosing. A new prescription is required for this replacement dose.
https://ocpinfo.com/ocp-resources/navigating-changes-to-opioid-agonist-therapy-and-how-to-support-patients/

**Signs of Opioid Intoxication**

- Sedation ('nodding off')
- Slowed or slurred speech
- Motor retardation
- Euphoria
- Dysphoria
- Pinpoint pupils

Opioid intoxication occurs when opioids are taken in excess of the individual's level of tolerance and may progress into overdose. Medical attention is required if patients exhibit signs of sedation, motor retardation or slurred speech.

**Signs of Overdose**

- Difficulty:
  - walking
  - talking
  - staying awake
- Blue or grey lips or nails
- Very small pupils
- Cold and clammy skin
- Dizziness and confusion
- Extreme drowsiness
- Choking, gurgling or snoring sounds
- Slow, weak or no breathing
- Inability to wake up, even when shaken or shouted at

If you think someone is overdosing, call 9-1-1 right away, or your local emergency help line

https://www.canada.ca/en/health-canada/services/opioids/overdose.html

Give the person naloxone if it's available. Naloxone is a medication that can temporarily reverse an overdose if it is administered right away. You can give naloxone while you wait for professional help to arrive.

https://www.ocpinfo.com/practice-education/practice-tools/support-materials/naloxone-guidance/

# Resources

OCP Opioid Policy
https://www.ocpinfo.com/regulations-standards/practice-policies-guidelines/opioid-policy/

OPA's Methadone and Buprenorphine/Naloxone Toolkit for Pharmacists
https://www.opatoday.com/methadone-and-buprenorphine-naloxone-toolkit/

OPA's Addictions and Opioid Agonist Therapy Education (FREE)
https://opatoday.com/product/opioid-substitution/

The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain
https://www.cmaj.ca/content/cmaj/suppl/2017/05/03/189.18.E659.DC1/170363-guide-1-at-updated.pdf

OCP Update on Opioid Use Disorder Treatment
https://pharmacyconnection.ca/update-on-opioid-use-disorder-treatment/

Addiction Treatment Forum
http://atforum.com/

Connex Ontario: Addiction, Mental Health, and Problem Gambling Treatment Services
https://www.connexontario.ca/en-ca/

OPA's Opioid Substitution Therapies Discussion Forum
http://methadoneforum.opatoday.com/

CAMH Making the Choice, Making It Work, Treatment for Opioid Addiction 2nd edition
(Formerly Methadone Maintenance Treatment: Client Handbook)
https://www.camh.ca/-/media/health-info-files/publications/making-choice-en.pdf

CAMH Opioid Agonist Maintenance Treatment 3rd edition 2015. Available for purchase at-
https://store-camh.myshopify.com/products/p6500

CRISM 2018 National Opioid Use Disorder Guideline
https://crism.ca/projects/opioid-guideline/
& 2024 update https://www.cmaj.ca/content/196/38/E1280

NAPRA Model Standards for Pharmacy Compounding of Non-sterile Preparations
https://napra.ca/general-practice-resources/model-standards-pharmacy-compounding-non-sterile-preparations

CAMH Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder May 2021
https://www.camh.ca/-/media/files/oat-info-for-clients.pdf

Meta:Phi Network
https://www.metaphi.ca/resources/?keywords=methadone&orderby=title&order=ASC&view=grid

**Live Telephone Resources**

CAMH Addiction Clinical Consultation Service
- 416-535-8501, press 2 (M-F 8:30AM - 5PM)

Opioid Agonist Therapies Support for Professionals
- Email: methadone@opatoday.com (M-F 10AM – 3PM)