ODT Guidelines

Medication-Assisted Treatment for Opioid Dependence: Guidelines for Pharmacists and Pharmacy Technicians

Alberta College of Pharmacy
Acknowledgements

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Executive summary
Background
Pharmacists and pharmacy technicians involved in dispensing medication-assisted therapies for opioid dependence must know, understand, and comply with the overall legislative framework that governs their practices. The following is a summary of the key policies and procedures for the dispensing of methadone maintenance treatment and buprenorphine-naloxone for opioid dependence. This executive summary is intended as a companion document to the ODT Guidelines (2014). This abbreviated version is intended to support the full document.
Available medication-assisted treatments for opioid dependence in Alberta

1. Methadone (brand name: Methadose™)
2. Buprenorphine-naloxone in a 4:1 ratio (brand name: Suboxone™)

Methadone and buprenorphine-naloxone can bring normal functioning back to an individual since they are opioids that cause little to no euphoric effects. Additionally, these medications have a long half-life to enable suppression of the withdrawal symptoms and cravings of opioid addiction that often contribute to relapse.

Note: All methadone prescriptions for patients being treated for opioid dependence must be dispensed using the commercially available methadone 10 mg/ml products. Pharmacists may no longer dispense compounded methadone since an indentical product is now commercially available and, as such, dispensing compounded methadone would therefore be considered manufacturing.

Table 1: Requirements for prescribing medication-assisted treatment for opioid dependence in Alberta

<table>
<thead>
<tr>
<th>Drug and indication</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone for opioid dependence</td>
<td>• All prescribers must have a methadone exemption for dependence granted by the Office of Controlled Substances (OCS), Health Canada.</td>
</tr>
<tr>
<td></td>
<td>• Prescribers must comply with training requirements required by the College of Physicians &amp; Surgeons of Alberta (CPSA).</td>
</tr>
<tr>
<td></td>
<td>o Initiating physicians must complete a methadone maintenance training (MMT) course and must have experience in an opioid dependence program or evidence of appropriate post-graduate training approved by CPSA.</td>
</tr>
<tr>
<td></td>
<td>o Maintaining physicians (those who treat patients who are already stabilized on methadone) must complete an MMT course and must have an ongoing association with an experienced initiating physician who agrees to act as a resource.</td>
</tr>
<tr>
<td></td>
<td>o Temporary prescribing physicians caring for patients in the hospital or in correctional facilities are not required to complete an MMT course and must obtain the methadone exemption from OCS within two business days of prescribing methadone for a hospitalized or incarcerated patient. Any changes in dose or prescribing of carries require consultation with an initiating or maintaining physician (preferably the patient’s own community-based methadone prescriber).</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Drug and indication</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone for pain</td>
<td>• All prescribers must have a methadone exemption for analgesia granted by OCS, Health Canada.</td>
</tr>
<tr>
<td></td>
<td><strong>Additional CPSA requirements:</strong></td>
</tr>
<tr>
<td></td>
<td>• Physicians who initiate methadone for pain must have experience in a pain or palliative care setting or must have evidence of appropriate post-graduate training.</td>
</tr>
<tr>
<td></td>
<td>• Physicians who maintain methadone for pain must have a letter of support from a pain or palliative care specialist for each patient.</td>
</tr>
<tr>
<td>Buprenorphine-naloxone (Suboxone™) for opioid dependence</td>
<td><strong>CPSA requirements:</strong></td>
</tr>
<tr>
<td></td>
<td>• Initiating physician: Physicians who initiate buprenorphine-naloxone must provide evidence of successful completion of an accredited buprenorphine course about prescribing for opioid dependence and have experience in the treatment of opioid dependence.</td>
</tr>
<tr>
<td></td>
<td>• Maintaining physician: Physicians who prescribe buprenorphine-naloxone in patients already stabilized on buprenorphine-naloxone during the maintenance phase must have completed an accredited buprenorphine course on prescribing for opioid dependency and must have an ongoing association with a physician with experience in the treatment of opioid dependence who agrees to act as a resource.</td>
</tr>
<tr>
<td></td>
<td>• Physicians who are temporary prescribers for patients in hospitals or correctional facilities do not require additional training but must have an association with a physician experienced in opioid dependence who agrees to act as a resource regarding any changes in dose or prescribing of carries.</td>
</tr>
<tr>
<td>Buprenorphine (BuTrans®)</td>
<td>• Prescribers do not require an exemption or additional training.</td>
</tr>
</tbody>
</table>
Additional prescribing circumstances

1. Pharmacists can dispense out-of-province prescriptions for methadone for dependence and/or buprenorphine-naloxone for dependence if they confirm the following:
   
   • The prescription is authentic, current, and appropriate;
   • For methadone prescriptions, that the prescriber has the appropriate exemption to prescribe methadone from the Office of Controlled Substances, Health Canada;
   • For buprenorphine-naloxone prescriptions, that the out-of-province prescriber has authority to prescribe narcotics within their provincial jurisdiction, and meets the prescribing requirements for buprenorphine-naloxone within his/her province. (Refer to TPP Information for the Prescriber and the Dispenser at http://www.cpsa.ab.ca/libraries/pro-tpp/Information_for_prescribers_and DISPENSERS.pdf?sfvrsn=0).

2. Veterinarians in Alberta are permitted to prescribe methadone and buprenorphine-naloxone within their scope of practice; exemption from OCS, Health Canada is required to prescribe methadone.

3. Hospital-based prescribers also require an exemption from OCS, Health Canada, and are only authorized to prescribe methadone for dependence for the duration of the patient’s admission to hospital. Hospital-based prescribers are not permitted to prescribe carries for methadone maintenance therapy (MMT). Carries are only permitted upon consultation with the patient’s initiating or maintaining physician.

Confirm exemptions by contacting one of the following:

• The College of Physicians & Surgeons of Alberta
  780-423-4764 or 1-800-561-3899 or email methadoneinfo@cpsa.ab.ca

• The Office of Controlled Substances, Health Canada
  1-613-946-5139 or 1-866-358-0453 or email exemption@hc-sc.gc.ca

Exemption confirmation for out-of-province prescriptions should be directed to the Office of Controlled Substances, Health Canada.

Note: Pharmacists are not permitted to prescribe or adapt prescriptions for methadone or buprenorphine-naloxone.
Requirements for the pharmacy premises

- Pharmacy operating hours of service should accommodate the needs of those requiring supervised/witnessed dosing without compromising patient safety or causing undue hardship to the patient.

- There must be a working refrigerator on the premises to store methadone preparations that require refrigeration. Pharmacy staff must monitor the refrigerator temperature and routinely record it to ensure that the cold chain is maintained for products contained within the refrigerator. Pharmacy staff must take appropriate action if temperatures fall outside acceptable limits.

- There should be an area within the pharmacy where the patient can protect and maintain their personal privacy during witnessed dosing.

- Security of the premises should acknowledge the potential risks of theft of substances of abuse such as narcotics. Controlled substances and narcotics should be stored in a locked and secure location.

- Note that in accordance with federal and provincial jurisdiction, pharmacists must document and report lost or stolen drugs.
Requirements for dispensing medication-assisted treatment for opioid dependence

Training requirements
In Alberta, there are no mandatory or formal training requirements for pharmacists or pharmacy technicians who dispense medication-assisted treatments for opioid dependence. All health professionals are expected to comply with the legal framework that governs their practice. Pharmacists and pharmacy technicians are expected to be competent to deliver the service provided within the scope of their individual practices.

Receiving a new patient on medication-assisted treatment for opioid dependence
Upon receiving a new patient, pharmacists are required to confirm that the prescription is written by a valid prescriber who meets the legislative requirements for the medication-assisted treatment prescribed to the patient (see previous section). The pharmacist must screen and assess the appropriateness of the treatment at the dose prescribed.

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

Dispensing requirements
- Compliance with the legislative framework that governs the practice of pharmacists.
- Pharmacists and pharmacy technicians are both authorized to dispense methadone or buprenorphine-naloxone. Only pharmacists are permitted to witness the dose ingestion as this requires an assessment of the appropriateness of treatment based on the patient’s clinical presentation.
- The prescription must be received on a triplicate prescription form and must comply with the rules and regulations of the Triplicate Prescription Program (TPP).
- The pharmacy must ensure that there is no gap in therapy on days that they are closed. While pharmacies are not required to be open seven days a week, the pharmacy is required to ensure that patients are able to acquire their doses on the days the pharmacy is closed. This may include (but is not limited to) collaboration with another pharmacy, opening for a short period of time, or weekend carries authorized by the prescriber.
- The prescription must contain the following information:
  - Patient’s name (where possible, include all given names);
  - Personal health number;
  - Patient’s date of birth;
  - Patient’s address;
  - Name of the medication;
  - Dosage of the medication;
  - The interval between dispensing days (for partial fill prescriptions);
  - Total quantity of the prescription written as a number and spelled out;
  - Instructions or directions for use, including instructions related to the requirement for witnessed dose ingestion and the frequency with which this must occur;
  - Instructions that identify the days in which a patient is permitted to receive carry doses (as applicable);
  - Prescriber’s name and phone number;
  - Prescriber’s unique TPP identification number as imprinted on the prescription;
  - Signature of the prescriber; and
  - Date of issue of the prescription by the prescriber (note that prescriptions are only valid for 72 hours and are not honoured after midnight of the third day) along with an end date for the written prescription.
- After dispensing, the final prescription must include all the above and:
  - The pharmacy assigned prescription number;
  - Quantity dispensed (e.g., amount dispensed/total amount ordered);
  - The signature and practice permit number of the pharmacist with the responsibility for assessing the prescription for appropriateness;
  - The date dispensed. Prescriptions to be held for dispensing at a later date must have documentation indicating that the dispensing was “deferred;”
  - The signature of the patient who received the dispensed medication.
Methadone doses must be accurately measured using a calibrated device that will minimize the error rate to no greater than +/- 0.1 ml. Due to the potential toxicity of methadone if given to children or opioid naive individuals, all devices used to measure methadone solutions should be used exclusively for methadone dispensing. Device should be labelled distinctly as “ONLY USE FOR METHADONE” and should have a poison auxiliary label affixed to the surface for clear identification by dispensing staff.

Methadone for opioid dependence can be dispensed using one of two commercially available formulations of methadone: a dye-free, sugar-free Methadose™ 10 mg/ml, or a cherry-flavoured Methadose™ 10 mg/ml.

- Dilution of the sugar-free, dye-free, unflavoured methadone formulation is required in Alberta to avoid injection abuse. If dispensing the clear formulation, dilute the dose in approximately 100 ml of a suitable diluent.
- Dilution of the cherry-flavoured methadone formulation is not required as it is a hypertonic sucrose solution for which injection abuse is minimal. Dilution of this formulation is optional, but it may also be further diluted if deemed necessary at the discretion of the pharmacist or prescriber.

**Additional dispensing information**

- The prescriber must include instructions for how the pharmacist should handle spoiled, lost, missed, and vomited doses. The instructions may be on the prescription or provided on a separate sheet to accompany the prescription.
- Pharmacists may ask prescribers for a dispensing schedule that lists each day’s observed dose(s) and each day’s permitted carries as deemed necessary by the complexity of the schedule or to enhance the clarity of the prescription.

**Requirements for dispensing carries**

- The prescriber must authorize carry doses and prescribe them on a triplicate prescription form to include all the information consistent with the requirements of a methadone prescription for dependence.
- Consultation between the pharmacist and the prescriber or program is encouraged to ensure that the patient is suitable for carries. Generally, the prescriber will only consider carries when the patient is stabilized. The prescriber may consider weekend carries earlier where necessitated by a pharmacy’s operating hours.
- The maximum duration of methadone carries should be limited to 14 days in succession. Buprenorphine-naloxone carries do not need to be limited once a patient is stabilized. If the prescriber initiates buprenorphine-naloxone carries earlier than the recommendation on the product monograph, the pharmacist or prescriber should consider obtaining patient consent to acknowledge the “off-label” decision.
- Dispense methadone carries as single use doses. The cherry-flavoured Methadose™ formulation can be dispensed as a carry without further dilution, though, dilution is also possible if deemed necessary by the pharmacist or prescriber. The clear, sugar-free Methadose™ must be diluted in 100 ml of a coloured and flavoured crystalline drink such as grape-flavoured Kool-Aid™ or Tang™.
- Dispense buprenorphine-naloxone carries in the original foil wrap.
- Dispense carries in a light-resistant bottle/vial.
- Dispense all carries in a child-resistant container. Deviations from this standard are only permitted at the patient’s request, and the documented rationale within the patient’s records should include the patient’s acknowledgement and acceptance of this deviation. Adequate counselling must be provided on the potential dangers and toxicity to children and the public from inadvertent ingestion of doses intended for the patient.
- Store carries in a locked box or secured container for the patient to take home.
- Pharmacies must use their discretion for the packaging of buprenorphine-naloxone carry doses. Instruct patients to return empty carry bottles to the pharmacy for inspection and proper destruction. Do not reuse carry bottles for the same or for another patient.
- Affix all labelled instructions and auxiliary labels directly on each bottle.
- Have the patient acknowledge their responsibilities, obligations, and expectations for carries through a signed carry contract.
- Pharmacies must confirm that the prescriber has prescribed the carries in accordance to his/her standards and guidelines, and must collaborate with the physician to discuss concerns regarding prescriptions and decisions that may endanger the safety of the patient or the community.
- To confirm physician standards in Alberta, see the CPSA’s Alberta Standards and Guidelines for Methadone Maintenance Treatment for Dependence document: http://www.cpsa.ab.ca/Libraries/pro_methadone/alberta-mmt-standards-guidelines.pdf?sfvrsn=0
Labelling requirements for carries:
- Patient’s name;
- Pharmacy name, address and telephone number of the;
- Prescriber’s name;
- The prescription number;
- The date dispensed;
- The name of the active drug (i.e., methadone, buprenorphine-naloxone) and the total mg of drug in a single dose; and
- Cautionary warning label:
  - “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 a child or adult.” OR
  - “May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.”

Additional labelling specific to methadone carries:
- Label instructions should clearly specify the total amount to be consumed in one dose. The date that each individual bottle should be ingested as a single dose should also appear on the label of each single-use bottle.
  - Example: “Drug is diluted. Consume the entire contents of this bottle on [insert date].”
- A “keep refrigerated” label. (If diluted)
- Expiry date of the prepared bottle. (If diluted)

Note: pharmacies must maintain a dispensing record when preparing diluted carries to enable the tracking of products and diluents used to prepare the final product.

Sample carry label containing required information for a diluted methadone carry:

<table>
<thead>
<tr>
<th>Pharmacy name</th>
<th>Pharmacy address</th>
<th>Pharmacy phone number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient name</td>
<td>Prescription number</td>
<td></td>
</tr>
<tr>
<td>Methadone 100 mg diluted to 100 mL with Tang™ orange drink.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Drug is diluted. **Consume the ENTIRE contents of this bottle on** [insert the date of intended ingestion].

**KEEP REFRIGERATED IN A LOCKED AND SAFE AREA AWAY FROM THE REACH OF CHILDREN.**

**May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.**

**RETURN ALL USED AND UNUSED CARRY BOTTLES TO THE PHARMACY**

<table>
<thead>
<tr>
<th>Date dispensed</th>
<th>Expiry date of bottle</th>
<th>Prescriber’s name</th>
</tr>
</thead>
</table>

Sample carry label where Methadose™ is dispensed in an undiluted form (Note that Methadose™ cherry-flavoured concentrate 10 mg/ml does not require further dilution and may be stored at room temperature):

<table>
<thead>
<tr>
<th>Pharmacy name</th>
<th>Pharmacy address</th>
<th>Pharmacy phone number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient name</td>
<td>Prescription number</td>
<td></td>
</tr>
<tr>
<td>Methadone 100 mg cherry-flavoured syrup. (Note that the total 100 mg dose is contained within 10 ml of this syrup)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Consume the ENTIRE contents of this bottle on** [insert the date of intended ingestion].

**STORE AT ROOM TEMPERATURE IN A LOCKED AND SAFE AREA AWAY FROM THE REACH OF CHILDREN.**

**May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.**

**RETURN ALL USED AND UNUSED CARRY BOTTLES TO THE PHARMACY**

<table>
<thead>
<tr>
<th>Date dispensed</th>
<th>Expiry date of bottle</th>
<th>Prescriber’s name</th>
</tr>
</thead>
</table>
Requirements for witnessed dose administration

- Within the pharmacy, the pharmacist is responsible for witnessing dose ingestion of medication-assisted treatment for opioid dependence. This responsibility cannot be delegated to the pharmacy technician or another pharmacy staff member who is not a licensed pharmacist. Pharmacists involved in the administration of methadone or buprenorphine-naloxone through witnessed/supervised dosing are expected to maintain competency in identifying and assessing patients who may be at risk of harm from these drugs.

- Patients should take daily doses during the day so that adverse effects that might occur will be noticed during waking hours.

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

- If a pharmacist involved in medication-assisted treatments for opioid dependence delivers doses to another facility or location where witnessed dosing is to occur, he/she may witness the dose ingestion outside of the pharmacy premises if he/she is competent in assessing the appropriateness of dose ingestion. After witnessing the dose administration, the pharmacist must comply with the documentation requirements for witnessed administration.

- Documentation of witnessed doses involves recording the following:
  - Date and time of the witnessed ingestion,
  - Dose administered,
  - Signature of the pharmacist witnessing the ingestion,
  - Pertinent clinical information and observations in the patient’s profile as necessary, and
  - Withheld doses, including the justification for withholding the dose.

Methadone

- If dispensing the dye-free, sugar-free Methadose™, the methadone dose must be diluted in 100 ml of a suitable diluent for witnessed dose ingestion by the pharmacist.

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

- After the dose is swallowed, engage the patient in conversation or ask the patient to confirm that the drug has been ingested by opening their mouth and showing you. This request can be part of the patient agreement acknowledged and explained at the outset of the initial pharmacist-patient meeting.

Buprenorphine-naloxone

- Some physicians choose to administer initial doses of buprenorphine-naloxone as the patient may need to be retained for several hours of observation.

- If you are witnessing an initial buprenorphine-naloxone dose, the prescriber must clearly communicate to you the timing of the initial buprenorphine-naloxone dose, since the patient is expected to be in opioid withdrawal at the time of initial dose administration. Additionally, the prescriber should provide parameters on the triPLICATE prescription if additional dosing is to be permitted based on the patient’s response.

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

- The contents of the medicine cup containing the buprenorphine-naloxone sublingual tablets are provided to the patient for dissolution under the tongue.

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

- After the tablets are dissolved, ask the patient to lift up their tongue for observed confirmation that the tablets are no longer present.

- Patients may need to be retained for several hours during first dose administration or following each dosage change. Guidelines suggest that the patient
may need to be monitored for a minimum of one hour following dose administration to assess for withdrawal symptoms or opioid symptoms and may be invited back after three or four hours to be further assessed, pending the development of withdrawal symptoms and the severity of these symptoms, should they occur. The pharmacist should notify the prescriber and collaborate on the potential escalation of buprenorphine-naloxone doses if the patient experiences intense withdrawal. All authorization for additional doses must be through a triplicate prescription.

Withholding a dose
- Withhold the medication if the patient demonstrates symptoms or behaviours which bring to question the safety of the patient with dose administration.
- If you withhold a dose, contact the prescriber/program service provider.

Delegation of witnessed dosing
Only an authorized health professional with the appropriate scope and competence can be delegated to assess the patient and then supervise and witness the daily administration of methadone or buprenorphine-naloxone to a patient. Note that a pharmacy technician cannot witness ingestion, as patient assessment at time of ingestion must take place. The prescriber directly responsible for prescribing the methadone or buprenorphine-naloxone to the patient may delegate another health professional to witness the administration. Delivery of the dose or doses to the delegated professional by the pharmacy must ensure the following:

- The dose reaches the intended individual;
- The dose is secure and is delivered untampered (use a locked box as necessary);
- The dose is properly labelled to ensure proper administration;
- The delivery and receipt of the medication is documented; and
- The dose, date, and name of the individual who is delegated to witness the dose on the specific date(s) is documented.

Pharmacists may refuse requests authorizing delegated dosing if they have concern for the security of the delivery or the safety and risk to the patient or the public. This includes situations where the pharmacist has concerns regarding the delegated individual. Document refusal to dispense in the patient profile; attempt to discuss your decision and collaborate with the prescriber to reach another solution.

Requirements for collaboration with other healthcare professionals
- Report all missed, lost, stolen, vomited and spoiled doses to the prescriber.
- Develop a missed dose strategy/agreement with the prescriber in the event of missed doses where the prescriber is unavailable for consultation.
- Ensure that all dose changes are written on a triplicate prescription.
- Communicate to the prescriber any concerns about the patient’s therapy that may put either the patient or the public at risk.
- Communicate to the prescriber when a patient has been hospitalized, released from hospital, or incarcerated.

Report to law enforcement
- Lost or stolen doses of methadone, and
- Criminal activity that may put the patient or the public at risk.

Requirements for professional cognitive services
- Pharmacists and pharmacy technicians are expected to follow the standards of practice of their profession in providing professional cognitive services for medication-assisted treatment for opioid dependence. This includes acting professionally, maintaining a professional relationship with the patient and collaborating with health professionals within the patient’s circle of care, considering the appropriateness of therapy, identifying of drug therapy problems, appropriate intervention for drug therapy problems, and counselling patients to optimize safety and efficacy of the treatment.
- Pharmacists are expected to document their encounter and the services provided on the patient profile.

Documentation requirements
Pharmacists must follow patient record requirements detailed in Appendix A of the Standards of Practice for Pharmacists and Pharmacy Technicians (July 2011). The main documentation requirements include:

- Patient-specific record and profile;
- A signed two-way agreement between the patient and the pharmacy;
- Required documentation when filling a prescription;
- A copy of the triplicate prescription;
- Documentation of any drug therapy problems and how the pharmacist handled them;
- Documentation of the administration of the witnessed
medication to include the name of the medication, the time, date, dose, and witness signature;

- Documentation of the diluents and products used to prepare diluted methadone preparations, including lot numbers, expiry dates, quantities of the products used in the dispensing of diluted methadone preparations and an audit trail of the staff involved in the dilution and verification of the diluted methadone preparations;
- Documentation of carry doses leaving the pharmacy that identifies the date and time of transfer, and acknowledges the receipt of carries through the patient’s signature;
- Documentation of returned carries and any empty carry bottles that are not returned; and
- For doses that are delivered to another location outside of the pharmacy premises, documentation of the delivery details including signatures and names of the person(s) delivering and receiving the medication, date and time of delivery, dose, name and qualifications of person delegated to witness the dose at the external location.
Recommended readings for pharmacists and pharmacy technicians servicing medication-assisted treatments for opioid dependence


## Provincial and federal regulators

| Alberta College of Pharmacy | T: 780-990-0321  
|                            | TF: 1-877-227-3838  
| 1100-8215 112 St. NW | F: 780-990-0328  
| Edmonton, AB   T6G 2C8 | Web: abpharmacy.ca |
| College of Physicians & Surgeons of Alberta | T: 780-423-4764  
| 2700-10020 100 St. NW | TF: 1-800-561-3899  
| Edmonton, AB   T5J 0N3 | F: 780-420-0651  
|                           | To confirm prescriber exemptions: 1-800-561-3899  
|                           | Web: www.cpsa.ab.ca |
| Office of Controlled Substances, Health Canada | T: 613-946-5139  
|                             | TF: 1-866-358-0453  
| (Health professionals’ dedicated methadone line) |  
| E: exemption@hc-sc.gc.ca |  
| Web: www.hc-sc.gc.ca/contact/dhp-mps/hecs-dgesc/ocs-bsc-eng.php |
## Alberta methadone clinics

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<th>Region</th>
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<tr>
<td>Calgary</td>
<td>Alberta Health Services (AHS) Opioid Dependency</td>
<td>403-297-5118</td>
<td>403-297-4985</td>
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<td></td>
<td>Program</td>
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<td></td>
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<tr>
<td></td>
<td>Second Chance Recovery</td>
<td>403-232-6990</td>
<td>403-232-6992</td>
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<tr>
<td>Edmonton</td>
<td>Alberta Health Services (AHS) Opioid Dependency</td>
<td>780-422-1302</td>
<td>780-427-0777</td>
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<td></td>
<td>Program</td>
<td></td>
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<tr>
<td></td>
<td>Metro City Medical Clinic</td>
<td>780-429-3991</td>
<td>780-429-3988</td>
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<td>Panorama Medical Clinic</td>
<td>780-471-4434</td>
<td>780-471-4438</td>
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<td>Lethbridge</td>
<td>North Side Medical Clinic</td>
<td>403-942-3003</td>
<td>403-942-4848</td>
</tr>
<tr>
<td>Medicine Hat</td>
<td>Chinook Alberta Methadone Program</td>
<td>403-504-1874</td>
<td>403-504-5038</td>
</tr>
<tr>
<td>Red Deer</td>
<td>Central Alberta Methadone Program</td>
<td>403-309-3652</td>
<td>403-309-6701</td>
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ODT Guidelines

Medication-Assisted Treatment for Opioid Dependence: Guidelines for Pharmacists and Pharmacy Technicians
Preface

Opioid dependence is a significant and growing health concern in our society. For those struggling with this chronic and often relapsing illness, the consequences can be significant. Intravenous abuse of legitimate or illicit drugs, disease transmission of blood-borne pathogens such as human immunodeficiency virus or hepatitis, criminal activity, loss of job, social isolation, financial hardship, loss of mental well-being, and morbidity and mortality from overdose are all risks that an opioid-dependent individual may face.

ODT Guidelines is a resource for pharmacists and pharmacy technicians in Alberta. It incorporates current best practices for medication-assisted management of opioid addiction with a focus on pharmacy best practices.

These guidelines describe mandatory components expected of pharmacies and personnel who dispense medication; however, they are also intended to inform and guide the efforts of pharmacists to deliver the entire “package” of care to patients being treated for addiction—that of dispensing, monitoring, patient counselling, record keeping, and collaborating with other health care professionals involved in the patient’s care.

This document replaces the 2012 Medication-Assisted Treatment for Opioid Dependence: Guidelines for Pharmacists and Pharmacy Technicians. Additionally, pharmacists and pharmacy technicians in Alberta must know, understand, and comply with the Standards of Practice for Pharmacists and Pharmacy Technicians developed and published by the Alberta College of Pharmacy. These standards are mandatory practice requirements which exist under the authority of Section 133 of the Health Professions Act, and are one component of the law that governs the practice of pharmacy in Alberta.

These guidelines highlight selected components of the practice standards as they pertain to the ODT Guidelines. For ease of communication and completeness, the standards highlighted will refer to those applicable to pharmacists. However, pharmacy technicians dispensing methadone and buprenorphine-naloxone to manage addictions are expected to meet all standards that apply to their profession and must provide the services that are appropriate within their scope of practice.

As the success of treating opioid dependency involves aspects beyond that of simply selecting and administering a medication, treatment for this multi-dimensional condition can be optimized through the concerted efforts and collaboration of a multidisciplinary team of trained professionals. This team may include physicians, pharmacists, nurses, case managers, social workers, and addiction counselors, all working together to provide the medical, psychological, behavioural, and social interventions to individuals ready to face their addiction.

Use these guidelines in conjunction with current and evolving evidence. As always, pharmacists and pharmacy technicians are expected to comply with national and provincial legislation regulating the dispensing of narcotics and prescription drugs in Alberta. Nothing in this document relieves you of that responsibility. Additionally, consider individual patient circumstances alongside sound professional judgment when using this document.

Alberta College of Pharmacy
Introduction

These guidelines:

1. Provide pharmacists and pharmacy technicians in Alberta with guidance for dispensing methadone and buprenorphine-naloxone.

2. Provide a framework for the dispensing of medication-assisted treatments for opioid dependence that identifies the basic clinical and service expectations to bring consistency to those who provide such services.

3. Summarize information about methadone and buprenorphine-naloxone that will enhance pharmacists’ and pharmacy technicians’ understanding about the treatments and optimize their delivery of patient care.

4. Align pertinent aspects from the College of Physicians & Surgeons of Alberta’s (CPSA) Standards & Guidelines for Methadone Maintenance Treatment for Dependence (January 2014) to optimize consistent messaging to patients and to enhance awareness of expectations that prescribers have of pharmacists who deliver care to patients with opioid dependence.

5. Clarify the role of the pharmacist as part of the multidisciplinary team involved in managing opioid dependence.

6. Provide guidance that optimizes retention to medication-assisted treatment for opioid dependence and that ultimately enhances the care of patients requiring addiction services.

7. Provide tools to help pharmacists and pharmacy technicians who deliver medication-assisted treatments for opioid dependence meet the regulatory requirements for such services.
Philosophy of medication-assisted treatment for opioid dependence

Opioid dependence
Opioids are a class of drugs entrenched in history, with some of their earliest natural agents (e.g., morphine and codeine) derived from the opium poppy, *Papaver somniferum*. Common opioids in use today include codeine, hydrocodone, oxycodone, morphine, hydromorphone, fentanyl, diacetylmorphine (heroin), methadone, and buprenorphine. These agents act by binding to opioid receptors, and are most commonly used as analgesics to reduce the perception of pain. Hydrocodone and codeine are also commonly used for their antitussive properties.

Individuals seeking to experience euphoric and psychoactive effects can become dependent on opioids through experimental or recreational use; however, many people become dependent on prescription opioids from legitimate use for pain management related to accidental injury or as a consequence of an underlying health condition. Though the *DSM-IV TR Criteria for Substance Dependence* does not consider physical dependence to opioids from long-term, appropriate use to treat pain to be a disorder or an addiction, regular and frequent use of opioids can result in opioid dependence disorder (see definitions in Appendix 1).

Opioid dependence disorder is considered a medical disease. It is a health issue that has implications for both the afflicted individual and the general public.

Treatment philosophy
The goal of a treatment program for opioid dependence disorder should be to provide broad access to effective medication-assisted treatments that are assessed, administered, monitored, and supported by experts trained in addiction to ensure optimal safety and efficacy from the therapy. These experts require the skills and knowledge to make appropriate decisions about the use of available treatments, but they must also understand the complex challenges of addiction and be able to provide guidance and support for the psychosocial aspects that can complicate the lives of individuals with opioid dependence.

Medication-assisted treatment for opioid dependence serves to bring normal functioning back to an individual. The benefits can be physiological, psychological, and social. Methadone and buprenorphine-naloxone cause little to no euphoric effect and their long half-life enables suppression of the withdrawal symptoms and cravings experienced in opioid addiction that often contributes to relapse.

Treatment success is not contingent on an individual being able to eventually stop medication-assisted treatment and to continue to remain abstinent from opioids, although this is an ideal outcome. Methadone itself can result in physiological dependence and for some, methadone or buprenorphine-naloxone therapy may be required chronically in order to prevent relapse.

A treatment strategy for opioid dependence should include the following key elements:

- Access to safe and effective medication-assisted treatments for opioid dependence;
- Access to quality care delivered by knowledgeable and trained professionals equipped to deal with the needs of the whole patient, which includes optimal treatment in conjunction with patient-centred psychosocial support and guidance;
- Harm reduction outcomes, such as those that:
  - Divert patients away from illicit drug and substance use and abuse;
  - Reduce the risk of morbidity and mortality from overdose or improper use of opioids;
  - Protect the individual and the public from the transmission of blood-borne pathogens;
  - Reduce criminal activity stemming from addiction;
  - Reduce fetal harm during pregnancy and optimize pregnancy outcomes; and
- Enable individuals to re-integrate into society as they overcome some of the social barriers resulting from their opioid dependence behaviours.

Methadone maintenance treatment (MMT) of opioid dependence through Alberta Health Services has been in place since 1971, while Suboxone™ received notice of compliance from Health Canada in 2007. Most recently, the availability of Methadose™, a commercially manufactured methadone for opioid dependence, has transformed MMT pharmacy services as the need to compound methadone for MMT is no longer required or permitted in all but the most exceptional of circumstances.
Drug choices for medication-assisted treatment for opioid dependence

The pharmacology of methadone and buprenorphine is the primary reason for their effectiveness as medication-assisted treatments for opioid dependence disorder. These drugs are used in withdrawal management and can be effective within an outpatient setting for those patients who have made a commitment to stop their use and/or abuse of opioids.

The slow absorption and longer half-life of methadone and buprenorphine result in more stable blood levels so that ingestion produces little to no euphoria and as blood levels remain relatively stable for a longer duration, this reduces the occurrence of intense withdrawal symptoms towards the end of the dosing period. Intense withdrawal symptoms can be unbearable, and are a key contributor to relapse in those seeking to overcome their opioid addiction through abstinence.

Patients with opioid dependency can experience improved well-being and psychosocial functioning while on these longer-acting therapies, which can result in pharmacodynamic stability that will eventually enable them to overcome drug seeking behaviours. Additionally, monitored therapy minimizes the risk of opioid overdose.

Methadone

Methadone, like other opioids, can be very toxic. Methadose™, a commercially manufactured methadone solution available as a 10 mg/ml red, cherry-flavoured syrup and a 10 mg/ml dye-free, sugar-free, flavourless solution, should be dispensed when providing methadone for MMT. It must be dosed and monitored by trained healthcare professionals, especially during the initiation/induction phase when patients are unstable. The mortality risk from methadone is highest during the first two weeks of treatment.

Additionally, pharmacists and prescribers must be vigilant in assessing the risk of exposure to others, particularly in patients authorized for self-administration of take-home doses of methadone (carries). Improper handling and storage of methadone within the patient’s home can result in unintended ingestion. This is especially of concern where children may be inadvertently exposed to the medication. Methadone can harm adults as well—doses as low as 40 mg can be lethal to an adult who is opioid naïve.

Methadone is a full opioid agonist and, as such, has no ceiling effect. Although it is generally more effective than buprenorphine in treating those dependent on higher opioid doses, the lack of a ceiling effect can pose an increased risk of harm from overdose, drug interactions, or other circumstances which can lead to increased methadone serum levels.

There can be a wide range of interindividual variability in the response to methadone. Peak plasma levels following oral administration range from one to five hours, and the elimination half-life can range from 15 to 60 hours.

Blood levels of methadone continue to rise during initial daily dosing until steady state is reached, typically within five to ten days; careful dose titration and monitoring for efficacy and toxicity are necessary, particularly during the initiation phase. During the maintenance phase of treatment, blood levels are relatively stable with few fluctuations minimizing the likelihood of withdrawal symptoms.

Suboxone™

Suboxone™ is an alternative option to methadone for addiction treatment within a community outpatient setting. Suboxone™ is available as a 2 mg and 8 mg sublingual tablet of buprenorphine in combination with naloxone in a 4:1 ratio.

Naloxone is an opioid antagonist that can displace opioids from their receptors, leading to withdrawal symptoms; however, it is not absorbed orally and does not exert a pharmacologic response when administered sublingually. Ultimately, Suboxone™ contains naloxone to deter the diversion through intravenous abuse.

Buprenorphine is a partial opioid agonist at the μ (mu) receptor. It is associated with a reduced risk of death in overdose compared to full opioid agonists such as methadone because it has a ceiling effect to adverse effects such as respiratory depression. This is why many clinicians consider buprenorphine-naloxone to be a safer drug than methadone. However, buprenorphine’s ceiling effect may also result in limitations since its effectiveness plateaus once a certain serum level is reached.

Higher doses or serum concentrations will not result in additional benefit. The main advantages of Suboxone™ over methadone as a medication-assisted treatment for opioid dependence are that:

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

The main disadvantages for Suboxone™ are:

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

Factors in drug choice
The choice of therapy between these two options will depend on a number of factors including (but not limited to):

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

Appendix 2 contains a more comprehensive overview and comparison of methadone and buprenorphine-naloxone.
1.0 Role of the pharmacist in medication-assisted treatment for opioid dependence

Practice standards and responsibilities

Standards
Pharmacists dispensing or supervising the dispensing of drugs for opioid dependence treatment (i.e., methadone and/or buprenorphine combinations) must act professionally and must:

- Practice in accordance with the law that governs their practice. (S1)
- Ensure they are competent in the area of addictions and drug abuse. (S1.7)
- Be aware of the chemistry, pharmacology, and therapeutics of the drugs they are dispensing to determine appropriateness of the drug for the patient. (S3, S4, S5, S6)
- Ensure that the prescription is appropriate, current, authentic, and complete for each patient. (S6)
- Determine if there is a drug therapy problem and take appropriate action as necessary. (S3.1, S3.4, S4, S5)
- Follow proper dispensing procedures that optimize accuracy including proper packaging, labelling, and checking. (S7, S21)
- Confirm the patient’s identity and ensure that the patient has sufficient information about the therapy to receive the intended benefit of the therapy. (S2, S8)
- Ensure the proper procedures and environment are in place when administering the drug, and be prepared to handle emergencies. (S1, S16)
- Ensure that the correct patient receives the correct drug in the prescribed dose that is authorized by a qualified prescriber. (S1, S6, S7, S8, S17)
- Ensure patient safety when administering or witnessing the drug administration. (S2, S3, S4, S5, S16, S17)
- Create and maintain appropriate patient records for dispensing and administration. (S18)
- Be aware of changes in the law that governs their practice and adjust their practice to ensure compliance with the changes. (S1.2, S1.3)
- Act collaboratively with colleagues in the best interest of patient care. (S1.4)
- Ensure that those whom they supervise act within the limits of their profession or training. (S20)

Responsibilities
- Pharmacists dispensing methadone must ensure that the prescriber has a valid exemption to prescribe methadone for dependence.
- Pharmacists dispensing methadone or buprenorphine-naloxone for out-of-province prescribers must be able to confirm the authenticity of the prescription and the prescriber. Additionally, they must confirm that the prescriber has a valid exemption to prescribe methadone for dependence from Health Canada. For buprenorphine-naloxone prescribing, they must make a reasonable effort to ensure the prescriber meets the requirements within the provincial jurisdiction in which the prescriber is licensed.
- Pharmacists and pharmacy technicians involved in dispensing methadone or buprenorphine-naloxone must remain responsible for the delivery of all components of activities that meet with the standards and expectations of their regulated profession.
The Narcotic Control Regulations of Canada do not place any prohibitions on pharmacists wishing to dispense methadone or buprenorphine-naloxone. Similarly, the Alberta College of Pharmacy (ACP) and provincial jurisdictions within Alberta do not impose additional provincially legislated requirements for those wishing to dispense these agents.

Individual pharmacies and pharmacy owners are encouraged to inform ACP if they are involved in methadone maintenance treatment (MMT) or providing services for medication-assisted treatment for opioid dependence, so that ACP can maintain a central repository of locations to inform and direct addiction service providers and the general public for access to such services.

The roles and core services provided by pharmacists in medication-assisted treatment of opioid dependence include (but may not be limited to) the following:

- Screening patients to identify inherent risks;
- Confirming that the prescriber has a valid exemption to prescribe methadone for dependence;
- Educating patients about medication-assisted treatments for dependence;
- Providing and reviewing the treatment agreement (i.e., patient-pharmacy agreement or patient-prescriber/provider-pharmacy agreement);
- Dispensing the prescribed medication;
- Witnessing daily ingestion of the medication;
- Monitoring for compliance, adverse effects, and risk of harm;
- Providing patient care to optimize the effectiveness and safety of the therapy;
- Communicating the expectations of the patient in optimizing efficacy and safety of the therapy;
- Monitoring the patient’s progress on medication-assisted treatments for opioid dependence;
- Monitoring for instability such as patterns and frequency of missed, lost, or vomited doses and timely notification of the patient’s physician when such issues occur;
- Documenting and record keeping;
- Communicating with other members within the patient’s circle of care to share information that optimizes efficacy and safety of therapy, including copies of other prescriptions such as benzodiazepines and opioids (as patients may be under the care of several physicians, this can enable prescribers to make more informed clinical decisions);
- Providing or facilitating access to supportive care; and
- Properly storing medication, not only on the pharmacy premises, but also during transportation to other facilities to protect diversion and/or inadvertent exposure to the public.
Practice standards and responsibilities

Standards

- A pharmacist who administers a drug must ensure that the environment in which they administer the drug is clean, safe, and appropriately private and comfortable for the patient. (S16)
- A licensed pharmacy must have an area that ensures patient confidentiality. (SOLP 4.12, 4.13, 4.14)
- The product must be stored and labelled appropriately following preparation. (S17.2)
- Drugs must be stored in the licensed pharmacy at appropriate temperatures, under appropriate conditions, and in accordance with any manufacturer’s requirements to ensure stability. (SOLP 5.2)
- Pharmacies must be equipped with a refrigerator in good working order. Temperature of the refrigerator must be monitored and recorded regularly to ensure the cold chain has not been disrupted. Pharmacy staff must take appropriate action if temperatures fall outside acceptable limits. (SOLP 4.7, 5.2 and 5.3)

Responsibilities

- Pharmacists must not engage in a service if they do not have the adequate qualified resources and the appropriate environment and operations to ensure the appropriate provision of the service to the patient.
- Pharmacists must document and report lost or stolen drugs in accordance with federal and provincial jurisdiction.

Pharmacies offering services for medication-assisted treatments for opioid dependence must accommodate daily witnessed administration and ensure that staff are competent in providing these services. Pharmacies are expected to provide the following:

- Pharmacy operating hours that accommodate the needs of those requiring supervised/witnessed dosing without compromising patient safety or causing undue hardship to the patient. Pharmacies that do not operate seven days a week must ensure that arrangements are made to enable the patient to acquire their doses on the days the pharmacy is closed. This may include collaboration with an affiliated pharmacy, opening at selected times on the day(s) the pharmacy is closed to service pre-scheduled patients who require witnessed daily doses, arrangements with a hospital pharmacy, and/or authorization for a carry on selected days that the pharmacy is closed, as deemed safe for the patient.

- A working refrigerator on the premises to store prepared methadone products that require refrigeration (e.g., diluted Methadose™). Pharmacy staff must monitor and routinely record the refrigerator temperature to maintain the cold chain for products contained within the refrigerator. Pharmacy staff must take appropriate action if temperatures fall outside acceptable limits.

- A space within the patient services area that has suitable sound barriers to prevent unauthorized individuals from overhearing conversations, and suitable visual barriers to maintain patient privacy. The premises should ensure confidentiality and privacy during patient consultations, witnessed dose administration, and provision of carries. Pharmacies may consider scheduling individual appointments for witnessed doses to minimize wait times or patient overlap.

- Security of the premises that addresses the potential risks associated with medication-assisted opioid dependence treatment services and the risks to the community that can result from theft of methadone or buprenorphine. As with other narcotics, preparations containing methadone and buprenorphine should be stored in a locked and secure location at all times (i.e., during hours of operation and when the premises are closed for business). Staff must be attentive to the need for close supervision of narcotics and must report and notify the appropriate authorities when loss or theft of methadone and other narcotics occur.

1 Standards for the Operation of Licensed Pharmacies.
3.0 The collaborative relationship

### Practice standards and responsibilities

#### Standards
- Pharmacists and pharmacy technicians providing medication assisted-treatments for opioid dependence must establish and maintain professional relationships with their patients and must work collaboratively with colleagues including other regulated health professionals. (S1, S2)
- A pharmacist who administers a drug must take all steps necessary to ensure that the drug is administered safely. (S2, S3, S4, S5, S16, S17)
- A pharmacist or pharmacy technician must create and maintain patient records for services provided. (S18)

#### Responsibilities
- Pharmacists must maintain appropriate records when dispensing medication-assisted treatment for opioid dependence that will verify that patients have provided informed consent before the initiation of treatment. A mutual agreement form to confirm the roles, expectations, and obligations of each party can provide a record of this discussion to protect both parties.
- Pharmacists and patients must report all missed, lost, stolen, spoiled, and vomited doses of methadone to the prescriber.
- Pharmacists and patients must report all missed, lost, stolen, and spoiled doses of buprenorphine-naloxone to the prescriber.

Opioid dependence disorder is a chronic and relapsing disease. Pharmacies providing methadone and addiction treatment services are providing chronic care, typically on a daily basis. Pharmacists may work closely and directly with the prescriber or with a team of service providers from an opioid dependency program. The success of treatment hinges on close communication between service providers, pharmacists, and patients.

Pharmacists who take on the care of such patients should always arrange for an initial meeting with the patient to discuss the services that they will provide, along with the obligations and expectations of both the pharmacy staff and the patient within this relationship.

A written two-way pharmacy-patient agreement serves to outline key information and agreements between the service provider and the patient, and can go a long way to troubleshoot any misunderstandings that may occur in the future. Both the patient and the pharmacist should read and sign the agreement.

The delegated pharmacist must have the training, understanding, and competence in addiction therapy to be able to appropriately instruct and inform the patient during the meeting. Some pharmacies may wish to use a three-way agreement\(^2\) which includes the prescriber or program service provider within the collaborative relationship. See Appendix 3 for samples of both types of agreements.

An agreement can consist of statements in which the patient acknowledges that he/she understands the specific information provided by the pharmacy staff and prescriber or program service provider. Additionally, it may clarify expectations of both the service provider and the patient as it relates to professional services, sharing of information, and conduct. The following identify some of the common components of a pharmacy-client agreement:

- Acknowledgement of store hours and agreed pick-up times;
- The process for confirming patient identity prior to receiving a dose;
- Agreement of conditions where doses and services will be withheld;
- Agreement of process for missed, lost, spoiled, or vomited doses;
- Agreement of expected conduct within the pharmacy;
- Acknowledgement of collaboration and sharing of health information with the prescriber for the safety and benefit of the client; and
- Agreement for rules and expectations for carried doses.

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\(^2\) Note: Three-way agreements are possible within a highly collaborative team where the individual care providers share a mutual trust and understanding of each of their individual roles and contributions towards the patient’s care. The three-way agreement can also serve as evidence to the patient of the close working relationships between the prescriber and pharmacy and of their mutual agreement for compliance and conduct. However, in many cases, the prescriber and program clinic initiate patient agreements specific to their own needs during the initial patient consultations, and in such situations, the two-way agreement may be a more practical choice.
The staged care model of service delivery (Figure 1) involves the collaboration of a number of providers delivering various levels and types of care as the patient transitions through the treatment path towards a better sense of well-being. A primary care physician may care for patients who are stabilized during the maintenance phase. During periods of instability, the physician may transition the patient back to the opioid dependence program for more intensive monitoring and support.

Pharmacists often see patients at both stages of care and are in an ideal position to assess their response to treatment, monitor for adverse effects, and to communicate any concerns to the prescriber or program. Additionally, pharmacists can play an important role in communicating reminders from the prescriber/program about the requirement for urine tests, blood work, and follow-up medical appointments.

Figure 1: Staged care delivery
4.0 Prescription standards and requirements

### Practice standards and responsibilities

#### Standards
Pharmacists dispensing or supervising methadone for dependence and/or buprenorphine combinations must:

- Ensure that the prescription complies with legislated requirements, including specific requirements that apply to the therapy ordered. (S1)
- Confirm the patient’s identity. (S8)
- Ensure that the prescription is appropriate, current, authentic, and complete for each patient. (S6)
- Determine if there is a drug therapy problem and take appropriate action as necessary. (S4, S5)
- Follow proper procedures when dispensing. (S1)
- Create and maintain patient records. (S18)
- Provide ongoing care and support to optimize patient safety while the patient remains in their care for the treatment prescribed. (S2, S3, S4, S5, S16, S17)

#### 4.1 Prescription requirements
Pharmacists and pharmacy technicians must dispense methadone or buprenorphine-naloxone pursuant to receiving a prescription order that meets the following requirements:

1. The prescription is written on a triplicate prescription form (TPP). The pharmacy must receive two copies of the actual TPP form or a faxed form from the prescriber’s office.
   - a. With an original prescription, retain the pharmacy copy in the pharmacy and submit the second copy to the College of Physicians & Surgeons of Alberta (CPSA).
   - b. With a faxed prescription, the prescriber’s office must either destroy the original prescription or mark “VOID” clearly on the prescription after faxing it to the pharmacy. (For further details, see Triplicate Prescription Program: Information for the Prescribes and the Dispenser at [http://www.cpsa.ab.ca/libraries/pro_tpp/Information_for_prescribers_and_dispensers.pdf?sfvrsn=0](http://www.cpsa.ab.ca/libraries/pro_tpp/Information_for_prescribers_and_dispensers.pdf?sfvrsn=0))

2. The prescription contains the following information:
   - a. Patient’s name (where possible, include all given names);
   - b. Personal health number;
   - c. Patient’s date of birth;
   - d. Patient’s address;
   - e. Name of the medication;
   - f. Dosage of the medication;
   - g. Indication for the methadone (i.e., dependence treatment, analgesia, or both);
   - h. The interval between dispensing days, indicated for partial fill prescriptions;
   - i. Total quantity of the prescription, in both numeric and written form;
   - j. Directions for use, including instructions related to the requirement for witnessed ingestion and the frequency with which this must occur;
   - k. Instructions that identify the days in which a patient is permitted to receive carry doses (as applicable);
   - l. Prescriber’s name and phone number;
   - m. Prescriber’s unique TPP identification number as imprinted on prescription;
   - n. Signature of the prescriber;
   - o. Date of issue of the prescription by the prescriber (Note: Prescriptions are only valid for 72 hours and cannot be honoured after midnight of the third day since the prescription was written. If the start date is clearly indicated on the triplicate prescription and the prescription is received by the pharmacy within 72 hours of when it is written, it may be honoured even if the start date commences more than 72 hours from the writing of the prescription); and
   - p. End date for the written prescription.

3. A valid prescriber authorized and signed the prescription.
4. For methadone, the prescriber must have the appropriate exemption for methadone (i.e., dependence, analgesia, or both).

5. For buprenorphine-naloxone, a prescriber must complete an online buprenorphine prescribing course required by the College of Physicians & Surgeons of Alberta.

6. The prescription must be legible and thoroughly understandable.

7. The prescription must meet the applicable requirements for completeness mentioned in Standard 6 of the Standards of Practice for Pharmacists and Pharmacy Technicians.

8. The prescriber must provide the pharmacist with a new triplicate prescription for any change from a previously stable dosage amount or for the provision of a replacement dose.

Confirming exemptions
Pharmacists dispensing methadone must ensure that the prescriber has a valid exemption to prescribe methadone for dependence. Pharmacists can confirm prescriber exemptions by contacting one of the following:

- The College of Physicians & Surgeons of Alberta
  780-423-4764 or 1-800-561-3899 or email methodoneinfo@cpsa.ab.ca
- The Office of Controlled Substances, Health Canada
  1-613-946-5139 or 1-866-358-0453 or email exemption@hc-sc.gc.ca

The College of Physicians & Surgeons of Alberta (CPSA) requires physician methadone prescribers licensed in Alberta to meet specific training requirements associated with the prescriber’s methadone prescribing practice (i.e., Initiating, Maintaining, or Temporary prescriber).

Additional notes
- Methadose™ is available in two formulations. Only initiating physicians of methadone can prescribe methadone to be dispensed in a non-crystalline suspension.
  - Pharmacists must dispense the sugar-free Methadose™ formulation in a diluted juice or crystalline drink deemed compatible with the methadone. This is to reduce the likelihood of diversion and to mask its bitter taste. If the prescriber directs the pharmacist to deviate from this standard, the pharmacist must confirm that the direction has come with consultation and agreement of an initiating physician and must clearly document the rationale on the prescription.
  - The cherry-flavoured formulation of Methadose™ does not require dilution in a crystalline drink because it is hypertonic (contains 40% sucrose), and therefore unlikely to be diverted. However, the prescriber or pharmacist may decide to dilute the cherry-flavoured formulation as well.

• Pharmacists must ensure that the prescriber provides clear instructions on how to handle spoiled, lost, and missed doses. This may be part of the written prescription or may be in the form of general instructions received with the methadone prescription. Additionally, the pharmacist should follow the CPSA guidelines for the management of spoiled, lost, and missed methadone doses. The guidelines are available at: http://www.cpsa.ab.ca/Libraries/pro_methadone/alberta-mmt-standards-guidelines.pdf?sfvrsn=0.

• Pharmacists must ensure that the prescriber provides clear communications about special instructions expected or permitted for the methadone, and that this is clearly documented as part of the prescription order (e.g., twice daily witnessed administration, twice daily administration with the first daily dose witnessed and the second daily dose permitted as a carry) and/or added to the patient’s file which contains special instructions that dispensing staff are required to review each time the drug is dispensed.

Filling out-of-province prescriptions
Pharmacists may dispense out-of-province methadone and buprenorphine-naloxone prescriptions provided that they ensure that the prescription is current, appropriate, authentic, and complete. Pharmacists must confirm that the out-of-province prescriber has a valid exemption for methadone, and must also ensure that the rules of the respective provinces are met (refer to Triplicate Prescription Program: Information for the Prescriber and the Dispenser at http://www.cpsa.ab.ca/libraries/pro_tpp/Information_for_prescribers_andDispensers.pdf?sfvrsn=0). If the province participates in a triplicate prescription program or a similar equivalent, you must mail the copy of the prescription to the respective program.
Note: Methadone and buprenorphine-naloxone prescriptions dispensed from a hospital pharmacy for inpatient use do not have to meet the above three requirements.

- Pharmacists should discourage the use of unapproved abbreviations that may cause confusion or misunderstanding and should clarify abbreviated instructions with the prescriber as required (e.g., DWI—daily witnessed ingestion).

- Pharmacists may ask prescribers for a dispensing schedule which lists each day’s observed dose(s) and each day’s permitted carries as deemed necessary by the complexity of the schedule or to enhance the clarity of the prescription.

- Pharmacists should check that the last date for the methadone prescription falls on a day that the pharmacy is open for business to avoid missed doses or patient distress from seeking a new prescription and an alternate provider.

Once the pharmacy dispenses a prescription, it should contain the following additional information:

1. The pharmacy-assigned prescription number;
2. Quantity dispensed (e.g., amount dispensed/total amount ordered);
3. The signature and practice permit number of the pharmacist who assessed the prescription for appropriateness;
4. The date dispensed; prescriptions to be held for dispensing at a later date must have documentation indicating that the dispensing was “deferred;” and
5. The signature of the patient who received the dispensed medication, to acknowledge their receipt of the medication.
5.0 Dispensing

### Practice standards and responsibilities

**Standards**
- Pharmacists and pharmacy technicians dispensing a Schedule 1 drug must ensure that they fill the prescription correctly, that they use appropriate dispensing procedures, that they properly package and label the drug, and that a final check is performed. (S7)
- Pharmacists and pharmacy technicians must label diluted products with a beyond-use date and ensure that the products are not to be used after this date. (S10)
- A pharmacist or pharmacy technician who repackages drugs must take appropriate steps to protect patient safety. (S21)
- Records must demonstrate an audit trail of staff involved in each process in the dispensing and administration of the final product. (S7, S10, S21)

**Responsibilities**
- Measuring devices used in the dispensing of methadone solutions must meet error allowance requirements for weights and measures. Methadone doses must be accurately measured using a calibrated device that will minimize the error rate to no greater than 0.1 ml
- Because of the potential of toxicity and lethality of errors involving methadone, it is vital that pharmacies organize their dispensing areas and evaluate work processes to optimize safety to staff and patients. This includes ensuring that all devices used to measure methadone solutions are used exclusively for methadone dispensing and that they are labelled and identified distinctly, and stored separately from other equipment.
- Pharmacies must include beyond-use dates on the labels of all diluted methadone products. Pharmacies choosing to use beyond-use dates in excess of 14 days should provide support for stability and sterility from guidelines, published literature, or laboratory batch testing.
- For health reasons and risk mitigation, pharmacists and pharmacy technicians must not reuse carry bottles.

### 5.1 Dispensing Methadose™

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

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

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

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

To calculate the amount of Methadose™ to dispense in millilitres that will contain the prescribed dose, divide the prescribed dose in milligrams by the concentration of the product.

**Calculation:**

\[
\text{Prescribed dose (mg)} = \ \frac{\text{Measured volume (ml)}}{10 \text{ mg/ml}}
\]

**Example:** 80 mg of methadone is prescribed.

\[
80\text{mg} = \ \frac{x \text{ ml}}{10 \text{ mg/ml}}
\]

\[
x = 8 \text{ ml of Methadose™}
\]
Storage
An unopened bottle of Methadose™ has a shelf life of approximately four years from the date of manufacture. The expiry date will appear on the bottle. Once opened, it can be stored at room temperature (15-30°C) for six months.

Diluted preparations must be refrigerated.

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

• The dye-free, sugar-free, unflavoured oral concentrate must be diluted using approximately 100 ml of a suitable crystalline diluent such as grape Kool-Aid™ or orange Tang™ to mask the bitter taste of methadone and to discourage diversion. Although dilution is not required for the cherry-flavoured formulation, there may be situations where dilution should be considered—for example, when dispensing small volumes where surface adhesion of the concentrate to the dispensing device or bottle may result in inaccurate or variable dose delivery, where risk of potential abuse and/or diversion is suspected, or when dispensing carries.
  o The CPSA requires that only “Initiating” methadone prescribers are to order a prescription for methadone dispensed in a non-crystalline formulation.

• Ensure that equipment or devices used for dispensing and dilution meet standards for accuracy of measuring devices. Measuring devices used in the dispensing of methadone must be accurately measured using a calibrated device that will minimize the error rate to no greater than 0.1 ml (typically oral syringes or manual/electronic pumps meet this accuracy requirement). Graduated cylinders are not recommended.

• Distinctly label equipment and devices used to measure Methadose™ and use these devices exclusively to dispense methadone where possible. Keep this equipment in a designated area to avoid mix-ups.

• The stability and sterility of Methadose™ diluted with a crystalline drink such as Kool-Aid™, Tang™, or Crystal Light™ is unknown as published studies are not available. Dispensing guidelines within many provincial jurisdictions have identified the duration of stability of methadone in various diluents from a collection of past literature (see Table 1); however, available literature does not address the issue of sterility, which includes the likelihood of bacterial growth in the prepared solution stored under refrigerated or unrefrigerated conditions. The information in Table 1 is provided as best existing guidance to allow you to use professional judgment when assigning best-before dates to diluted Methadose™.

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

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

• When diluting Methadose™, pharmacists and pharmacy technicians must record the date of dilution, the lot number, and the expiry date of both the Methadose™ and the diluent based on the expiry of the product or opened bottle, whichever is shorter. This information should be documented on the dilution record (see sample in Appendix 4.2), the patient’s electronic profile, or directly on the triplicate prescription, whichever is most feasible, and it must be available to audit or track the diluted preparation.

• Pharmacies should conduct stability and sterility tests of their prepared formulations to support decisions to extend expiry dates beyond the guidance provided in this document. Pharmacies should use reputable resources and validated tests and maintain a record of their findings to support decisions that have been made.

Note: Published guidance on the stability of methadone solutions is reported in many provincial guidelines based on a study from the early 1990s. However, there is a need for more updated testing to acknowledge both the stability and sterility of prepared products under various compounding conditions. Formulations prepared in juices should have an expiry that does not exceed the shelf-life of the juice under the conditions of storage recommended upon opening the bottle. In general, dispensing methadone in fruit juices or diluents not identified below or within a product monograph is discouraged due to the lack of sufficient evidence for stability and sterility upon extended storage of the mixture, especially beyond immediate ingestion upon dilution.

---

3 Metadol™ product monograph (March 2009).
Table 1: Methadone stability in various diluents for carries

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


5.2 Dispensing carries

A “carry” refers to a dose of methadone or buprenorphine-naloxone that the patient is authorized to take home for self-administration.

The prescriber initiates authorization of carries and should provide instructions on a triplicate prescription form. Carry privileges should only be granted to patients who are physically and psychologically stable on treatment during the maintenance phase. The prescriber should gradually increase the number of permitted carries over time and with careful monitoring of the patient's compliance with therapy. Carries are generally continued and increased if the patient is able to demonstrate ongoing stability with their therapy. The maximum duration of carries can be limited by the expiry date of the treatment.

Granting carries, especially methadone carries, can pose a risk to the household and community where the patient lives since there is the risk that doses may be lost, misplaced, stolen, or improperly stored such that accidental exposure may pose a risk to others in the household and the community at large. Maintain a signed carry agreement with the patient to acknowledge the expectations and obligations of both the patient and the pharmacy in the granting of carries (see Appendix 3 for a sample carry agreement).

The pharmacist's role regarding carries may include (but is not limited to):

1. Ensuring the prescription authorizing carries is appropriately written to identify ingestion days and carry intervals;
2. Assessing the stability of the patient;
3. Assessing the social situation, environment, and arrangements in which the patient lives to determine safety and risk of permitting carries for those who cohabit with the patient;
4. Educating to ensure the patient understands how the product should be taken and stored, in order to optimize efficacy and safety;
5. Packaging and labelling to optimize safety and compliance with proper administration;
6. Monitoring compliance with carries. Initially,
Pharmacists may randomly ask that the patient present to the pharmacy during the allowed carry period for a witnessed ingestion. Pharmacists should also ask the patient to return used bottles at the time for inspection. This will help to ensure that the patient has taken the doses correctly and that diversion has not occurred;

7. Communicating with prescribers if issues and concerns arise. Patients who demonstrate improper use of carries, or who frequently request replacement for lost, stolen, or spoiled carry doses, should have their carry privileges withdrawn until they can demonstrate stability and competence with unwitnessed dosing; and

8. Maintaining a record when preparing diluted carries to enable the tracking of products and diluents used to prepare the final product.

Typically, the prescriber does not consider methadone carries until a patient has been on methadone for at least two to three months and is stable on the treatment. The maximum duration for carries of methadone should be limited to 14 consecutive days given the beyond-use dates of prepared diluted solutions.

Pharmacists should be aware of the following requirements for dispensing carries:

- The prescriber must initiate authorization for carries. Consultation between the pharmacist and the prescriber/or program is encouraged to ensure that the patient is suitable for carries. Temporary prescribers are only permitted to issue carries for hospitalized or incarcerated patients upon consultation from a community-based methadone prescriber.
- The maximum duration of methadone carries should be limited to 14 days in succession.
- Methadone carries must be:
  - Dispensed as single use doses;
  - Packaged in a locked box or secured container for the patient to take home;
  - Prepared in a child-resistant container. Deviations from this standard should only be permitted at the patient’s request. Document the rationale within the patient’s records and include the patient’s acknowledgement and acceptance of this deviation. Provide adequate counselling on the potential dangers and toxicity to children and the public from inadvertent ingestion of doses intended for the patient; and
  - Prepared to their final formulation; further dilution or mixing should not be necessary.
- If requested by the pharmacist, patients must return empty carry bottles to the pharmacy for inspection and proper destruction. Do not re-use carry bottles for the same or for another patient.

Labelling requirements for carries

- Patient name;
- Pharmacy name, address and telephone number;
- Prescriber name;
- Prescription number;
- Date dispensed;
- The name of the active drug (i.e., methadone, buprenorphine-naloxone) and the total mg of drug to be consumed in a single dose ingestion; and
- A cautionary warning label:
  - “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 a child or adult.” OR
  - “May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.”

**Additional labelling specific to methadone carries**

- Label instructions should clearly specify the total amount to be consumed in one dose. The date that each individual bottle should be ingested as a single dose should also appear on the label of each single-use bottle. The date of dispensing needs to be clearly distinct from the date of intended ingestion.
  - Example: “Drug is diluted. Consume the entire contents of this bottle on (insert date).”
- A “Keep refrigerated” label (if diluted)
- Expiry date of the prepared bottle (if diluted)

<table>
<thead>
<tr>
<th>Pharmacy name</th>
<th>Pharmacy address</th>
<th>Pharmacy phone number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient name</td>
<td>Prescription number</td>
<td></td>
</tr>
<tr>
<td>Methadone 100 mg diluted to 100 mL with Tang™ orange drink.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug is diluted. <strong>Consume the ENTIRE contents of this bottle on</strong> [insert the date of intended ingestion].</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>KEEP REFRIGERATED IN A LOCKED AND SAFE AREA AWAY FROM THE REACH OF CHILDREN.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RETURN ALL USED AND UNUSED CARRY BOTTLES TO THE PHARMACY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date dispensed</td>
<td>Expiry date of bottle</td>
<td>Prescriber’s name</td>
</tr>
</tbody>
</table>

Figure 2: Sample carry label containing required information for a diluted methadone carry
5.3 Dispensing buprenorphine-naloxone

Dispensing requirements for buprenorphine-naloxone are the same as those for methadone, with a few exceptions. Follow the standards of practice for appropriate dispensing and labelling described under Standard 7 in the Standards of Practice for Pharmacists and Pharmacy Technicians.

Exceptions and special considerations for buprenorphine-naloxone carries

- Buprenorphine-naloxone carries do not need to be limited to 14 days. Once a patient is stabilized and suitable for buprenorphine-naloxone carries, the prescriber can dictate the quantity his/her discretion. The Canadian Suboxone™ product monograph recommends that the patient be stabilized on therapy and on treatment for at least two months before considering carries. Resources differ in this recommendation. If the prescriber initiates carries earlier than the recommendation on the product monograph, the pharmacist or prescriber should consider obtaining patient consent to acknowledge the decision.

- Dispense buprenorphine-naloxone carries in the original foil wrap as buprenorphine-naloxone is hygroscopic.

- Dispense carries in a light-resistant bottle or vial.

- Dispense carries in a child-resistant container. Only permit deviations from this standard at the patient’s request. Document the rationale within the patient’s records and include the patient’s acknowledgement and acceptance of this deviation. Provide adequate counselling regarding the potential dangers and toxicity to children and the public from inadvertent ingestion of doses intended for the patient.

In addition to the items outlined in the label requirements for methadone, buprenorphine-naloxone labels for carries must include:

- The instructions for administration, which can include the date(s) that individual tablets should be administered or, if not taken daily, the days of the week for administration by the patient. Once carry doses reach monthly quantities, the pharmacist is permitted to follow the usual labelling and packaging procedures for narcotic and controlled substances;
  - If the number of carries permitted is small, the pharmacist or pharmacy technician may choose to dispense each tablet in individually labelled prescription vials and to have all the vials returned as proof of ingestion;

- One of the following cautionary warnings:
  - “Buprenorphine-naloxone may cause serious harm to someone other than the intended patient. Not to be used by anyone other than the patient for whom it was intended.”
  - “May be toxic or lethal if ingested by a child or adult other than the intended patient. Accidental ingestion is considered a medical emergency and requires immediate medical attention.”

Instruct patients to return empty carry vials to the pharmacy for inspection and proper destruction (as applicable). Do not re-use carry vials for the same or for another patient.

5.4 Dispensing for delivery for delegated administration

Only the pharmacist can supervise and witness the daily administration of methadone by a patient. In exceptional circumstances, a prescriber/program service provider may direct the pharmacist to have a dose delivered to another delegated health professional for witnessed administration. Pharmacists may refuse these requests if they have concern for the security of the delivery and/or the safety and risk to the patient or the public. However, you must clearly communicate these concerns and discuss them with the prescriber/program service provider to resolve issues in the
best interest of their patient.

Document the request and final decision in the patient records. If the patient requires delivery, make every effort to ensure the dose reaches the intended individual(s). Use a reliable and secure method of transportation and follow-up to ensure that the dose has been delivered untampered.

It is the delegated individual’s responsibility to record the ingestion; the dispensing pharmacist can make note of the delivery for witnessed dosing by another observer. A “locked box” is advisable to transport the dose(s) to the intended recipient(s) along with packaging and labelling consistent with that used for carries. This applies to deliveries involving buprenorphine-naloxone.
6.0 Administration

Practice standards and responsibilities

Standards

• Pharmacists and pharmacy technicians must act professionally and must establish and maintain professional relationships with their patients. (S1)
• A pharmacist who administers a drug must ensure that the environment within which the drug will be administered is clean, safe, and appropriately private and comfortable for the patient. (S16.3)
• Pharmacists who witness the dosing of medication-assisted treatments for opioid dependence must be competent to assess and monitor the patient and the therapy being administered. (S1, S3, S4, S5, S6, S8, S16, S17)
• A pharmacist who administers a drug must ensure that they have policies and procedures for handling emergencies. (S17)
• A pharmacist or pharmacy technician must create and maintain patient records for pharmacist services provided. (S18)

6.1 Methadone maintenance treatment

Daily witnessed methadone dosing
Daily witnessed dosing of methadone for dependence is recommended for all patients during the initiation phase and until the prescriber and/or treatment team is satisfied with the patient’s progress and deems the patient to be stabilized on maintenance therapy and at a low risk of relapse.

Pharmacists are primary providers of daily witnessed dosing services. Pharmacists need to ensure accuracy of the dispensed product and must verify the identity of the patient and assess the patient for drug-related problems that may compromise the safety of the administered therapy.

Pharmacists administering the dose should do the following before providing the dose:

• Positively identify the patient by asking for their photo identification (ID) as agreed through the patient agreement. Keep a copy of the photo ID on the patient’s profile as a reference for all pharmacy staff who may serve the patient.
• Assess the patient for intoxication from other substances.
  o Ask the patient to remove their sunglasses and observe their eyes for pin-point pupils, alertness or sedation.
  o Talk to the patient and ask questions to determine if they are slurring or incoherent.
  o Ask the patient to walk to the counter and observe their gait.
  o Have the patient come close enough to allow you to smell for signs of alcohol or other substances of abuse such as marijuana.
  o Assess the patient’s general demeanor and behaviour in comparison to what you are aware of as their usual behaviour.
• Review the patient’s profile to see if there are any alerts or notes from other pharmacy staff.
• Review the patient administration records for returned carries (as applicable), and ask the patient if there have been any missed doses.
• Ask if the patient has:
  o Started or taken any new drugs, either prescription or non-prescription, including natural health products;
  o Experienced any unusual symptoms since the last dose. If yes, ask the patient to describe these symptoms; and
  o Had any relapses or used a pain medication since the last dose. If yes, ask what was taken and how much.
If you deem the patient to be suitable to receive the prescribed dose, provide the dose to the patient for observed administration. Then:

- Witness the oral ingestion of the methadone liquid that has been dispensed. This may or may not require dilution (see Section 5.0).
- Engage the patient in conversation after they have swallowed or ask them to confirm that they have ingested the drug by opening their mouth and showing you. This request can be part of the patient agreement acknowledged and explained at the outset of the initial pharmacist–client meeting.
- Record the witnessed administration in the patient’s file including the date and time of ingestion, dose administered, and the initials or signature of the witnessing pharmacist which must be sufficiently legible to accurately identify the person who witnessed the ingestion. Include documentation of the patient’s condition and progress at this time.

If a pharmacist involved in medication-assisted treatments for opioid dependence delivers doses to another facility or location where witnessed dosing is to occur, they may witness the dose ingestion outside of the pharmacy premises if they are competent in assessing the appropriateness of dose ingestion. After witnessing the dose administration, the pharmacist must comply with the documentation requirements for witnessed administration.

**Withholding the medication dose**
Pharmacists can withhold the medication if the patient demonstrates symptoms or behaviours which cause the pharmacist to question the safety of the patient with dose administration. Contact the prescriber or program service provider if you withhold a dose.

Pharmacists should identify potential reasons for withholding medication in the contract with the patient. These could include clinical reasons that may increase the risk of harm to the patient, such as intoxication with other medications or substances, excessive sedation, psychiatric symptoms, and/or positive urine or blood tests for other substances of abuse. Additionally, the patient may have his/her pharmacy services terminated for inappropriate behaviour within the pharmacy which can include abuse of staff or other customers, criminal behaviour, and inability to pay for the medication. Termination of a patient relationship by a pharmacist must follow Standards 2.9 and 2.10 in the *Standards of Practice for Pharmacists and Pharmacy Technicians*.

**Managing missed methadone doses**
It can be harmful to administer methadone to a patient who has missed several daily doses. The prescriber/program service provider and pharmacist should collaborate to determine at what point to refuse therapy for the patient in order to protect them from toxicity that may result from non-compliance.

In all situations, a patient who has missed three consecutive daily doses of methadone should have their therapy withheld until the prescriber is consulted to discuss dose adjustment and the patient’s safety risks from non-compliance. The pharmacist should clearly document the patient’s reason(s) for missing the doses. Dose changes will require a new triplicate prescription. Pharmacists and pharmacy technicians should inactivate all old prescriptions to avoid errors.

**General guidance**
- Document any missed, lost, or vomited doses on the patient’s records and report them to the prescriber/program service provider. Include the reason(s) for the missed doses. If the patient has authorized it, you can also report to the family physician or addiction counselors who may be in the circle of care for the addiction management.

- Develop a missed dose strategy/agreement with the prescriber in the event that the patient misses doses and the prescriber is unavailable for consultation.

The following is a guide for the management of missed methadone doses. Pharmacists must use their own professional judgment in using this and other information to manage individual circumstances.
Table 2: Managing missed methadone doses

<table>
<thead>
<tr>
<th>Number of missed methadone doses</th>
<th>Clinical action</th>
<th>Dosing adjustment guideline (Note: Must be authorized by prescriber through TPP)</th>
</tr>
</thead>
</table>
| ONE missed dose                  | • Report to and consult with prescriber  
• Document in the patient records to include reason(s)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | One missed dose permits continuation at the original dose; no dosage change is required |
| More than TWO non-consecutive missed doses within a seven day period | • Report to and consult with prescriber  
• Document in the patient’s record and include reason(s)  
• Prescription duration cannot be extended due to missed doses                                                                                                                                                                                                                                                                                                                                                           | No further doses until the patient is reassessed by the prescriber |
| TWO consecutive missed doses     | • Report to and consult with prescriber  
• Document in the patient’s record and include reason(s)  
• Determine, evaluate, and discuss issues for non-compliance with patient and prescriber  
• Evaluate the patient’s symptoms of withdrawal or intoxication  
• Follow up with the patient’s response to therapy  
• Determine and confirm with the prescriber if the patient is to assume usual dose by the next dose  
• Cancel existing prescription and obtain new prescription from prescriber                                                                                                                                                                                                                                                                                  | CPSA Guideline: Restart at 75% of original dose |
| THREE or more consecutive missed doses | • Withhold further doses until prescriber is contacted  
• Report to and consult with prescriber  
• Document in the patient’s record and include reason(s)  
• Determine, evaluate, and discuss issues for non-compliance with the patient and prescriber  
• Evaluate the patient’s symptoms of withdrawal or intoxication  
• Follow up with the patient’s response to therapy if dosing is resumed  
• Cancel existing prescription and obtain new prescription from prescriber                                                                                                                                                                                                                                                                 | CPSA Guideline: Restart at 50% of original dose or re-initiate on methadone |

Dosing adjustment guideline (Note: Must be authorized by prescriber through TPP)

One missed dose permits continuation at the original dose; no dosage change is required.

No further doses until the patient is reassessed by the prescriber.

CPSA Guideline: Restart at 75% of original dose.

CPSA Guideline: Restart at 50% of original dose or re-initiate on methadone.

Adapted from (January 2014) Alberta Standards and Guidelines for Methadone Maintenance Treatment for Dependence, College of Physicians & Surgeons of Alberta (CPSA).
Split maintenance dosing of methadone
Methadone is usually administered as a once daily dose; however, in some situations, the prescriber may consider a split dosing regimen based on patient response. The prescribing and dispensing of split doses should be supported by the demonstration of withdrawal symptoms within 24 hours of the daily dose along with signs and symptoms of excessive methadone dosage within four hours of an administered daily dose. Situations where this has been considered include dosing in pregnancy, particularly during the initiation phase of therapy and during the third trimester, as well as dosing in fast metabolizers of methadone. In such a situation, the prescriber and the pharmacist should assess the convenience, risks, and necessity of two observed doses within one day. The prescriber may consider carries for the second dose, but the decision should be made based on optimizing safety of both the patient and the community.

A carry dose may be a smaller dose than the daily observed dose if the prescriber deems that this will reduce the risk to the patient or the community.

Lost/stolen methadone doses
Evaluate situations of lost/stolen doses individually to judge the authenticity of the patient’s communication and the potential risks of authorizing a replacement dose. Encourage patients to report lost or stolen dosages to the authorities. Report lost/stolen doses to the prescriber; if the prescriber deems a replacement dose necessary, he/she must write a new triplicate prescription. It is the responsibility of pharmacists and other health care professionals to report lost or stolen methadone doses to the proper authorities if it is deemed to be a risk to the community/public.

Vomited methadone doses
Evaluate redosing of methadone following vomiting on a case-by-case basis. Replacement doses should only be considered if the emesis is witnessed by the pharmacist or pharmacy staff and if it occurred within 15 minutes of consumption. If in doubt, it is always safer to have the patient experience withdrawal than to overdose on methadone. Vomited doses require that the pharmacist contact the prescriber to write a new prescription as necessary.

The College of Physicians & Surgeons of Alberta provides general guidelines for physicians for managing vomited doses. The guidelines recognize that witnessed vomiting that occurs more than 15 minutes after ingestion should not be redosed at the full dose. You may wish to have the patient return and observe them for symptoms of withdrawal before considering a partial dose—consider a partial dose at 50% of the full daily dose. If a patient vomits a dose 15 minutes or more following ingestion, it should not be replaced.

Do not replace unwitnessed vomited doses unless there are clear withdrawal signs and symptoms. If there is a pattern or frequency of vomited doses, the prescriber or program needs to reassess the patient for suitability for methadone therapy.

Managing accidental overdose
Accidental overdose is a medical emergency and the patient and/or his/her caregivers should be told to go to the local hospital for assessment and treatment. The risks from the overdose will depend on a number of factors such as the amount of medication ingested compared to the patient’s usual dose, the duration of time the patient has been on treatment and their past tolerance to opioids, any past history of a similar event and what occurred at that time, and concomitant therapies and health conditions.

The patient should be escorted to the hospital or an ambulance should be called if the patient is experiencing shortness of breath or any symptoms of opioid toxicity.

Accidental ingestions involving children or opioid naïve individuals are medical emergencies requiring ambulance escort. The pharmacist should tell the patient to stop all other medications until seen by a physician, and should alert the patient’s prescriber and/or program to the issue.

Induced vomiting of methadone is unreliable and may not be effective even five minutes from the time of overdose.

6.2 Buprenorphine-naloxone treatment
Daily witnessed dosing of buprenorphine-naloxone is recommended for all patients during the initiation phase and until the prescriber is satisfied with the patient’s progress and deems the patient to be stabilized on buprenorphine-naloxone therapy and at a low risk of relapse. Some prescribers may choose to administer initial doses of buprenorphine-naloxone in their own clinics as the patient must be in opioid withdrawal at the time of dose administration and may need to be retained for one or more hours of observation. Some patients will be asked to return to the clinic three to four hours after administration for monitoring, or if they are in an uncomfortable state of withdrawal.

The prescriber must clearly communicate to the pharmacist the timing of the initial buprenorphine-naloxone dose if the pharmacy is to monitor the first witnessed dose. The prescriber must authorized all doses through a triplicate prescription.

For initial witnessed doses of buprenorphine-naloxone:

- Tell the patient to come early in the day and inform the patient of the potential duration of stay pending the prescriber’s instructions.
- Administer the initial dose when the patient is in withdrawal. This is generally considered to be after 12 hours of having taken a short-acting opioid and 24 hours after the last dose of a long-acting opioid. If the patient
was on methadone, the first dose may need to wait for 36 hours after the last dose. (Note: methadone has a variable half-life in individuals. Clinicians generally use a range of three to five days from the last methadone dose before initiating the first buprenorphine-naloxone dose.)

- Monitor the patient for at least an hour after dose administration.
- Remember that some patients may need to be retained for several hours or be asked to return in three to four hours to be observed for response or pending the development of withdrawal symptoms and the severity of these symptoms.
- Consider notifying the prescriber to collaborate on the potential for dose escalation based on patient response; however, all doses administered must be authorized by the prescriber on the triplicate prescription.

Pharmacists administering the dose should do the following before providing the dose:

- Positively identify the patient by asking for their photo identification as agreed through the patient agreement.
- Assess the patient for intoxication from other substances.
  - Ask the patient to remove their sunglasses and observe their eyes for pin-point pupils, alertness, or sedation.
  - Talk to the patient and ask questions to determine if they are slurring or incoherent.
  - Make them walk to the counter to observe their gait and to allow you to smell for signs of alcohol or other substances of abuse such as marijuana.
  - Assess their general demeanor and behaviour in comparison to what you are aware of as their usual behaviour.
- Examine the patient administration records, returned carries (as applicable), or ask the patient if there have been any missed doses.
- Ask the patient if they have started any new drugs, either prescription or non-prescription, including natural health products.
- Ask the patient if they have had any relapses.

Pharmacists should withhold medication if they clinically assess the patient as being unsuitable to receive the medication, and should contact the prescriber/program service provider.

If the pharmacist deems the patient suitable to receive the prescribed dose, the pharmacist should provide the dose to the patient for observed administration. Suboxone™ is available as a tablet for sublingual administration that is packaged within a foil pouch.

- Unwrap the tablet, taking care not to touch the tablet with bare fingers. Wear disposable gloves when handling tablets to avoid skin contact as sublingual tablets are sensitive to moisture and humidity once exposed.
- Place the tablet inside a disposable, single-use medicine cup (preferably a clear, transparent cup).
- If administering more than one tablet to achieve the desired dose, advise the patient to take multiple tablets sublingually at the same time if possible. You may split tablets into halves to facilitate sublingual dissolution.

Once the patient receives the medication, the pharmacist must:

- Witness the sublingual administration of the buprenorphine-naloxone tablet. You cannot delegate this task to the pharmacy technician.
  - It can take one to ten minutes for the sublingual tablet to completely dissolve, and the patient must stay within sight of the pharmacist witnessing the dose.
- Ask the patient to open their mouth and lift up their tongue so you can confirm that the tablets have dissolved. Awareness of this procedure can be part of the patient agreement that you and the patient acknowledged and explained at the initial pharmacist–client meeting.
- Record the witnessed administration in the patient’s file, including at minimum the date and time of administration and the initials of the witnessing pharmacist. You can include documentation about the patient’s condition and progress at this time.

If a pharmacist involved in medication-assisted treatments for opioid dependence delivers doses to another facility or location where witnessed dosing is to occur, they may witness the dose ingestion outside of the pharmacy premises if they are competent in assessing the appropriateness of dose ingestion. After witnessing the dose administration, the pharmacist must comply with the documentation requirements for witnessed administration.

Managing missed buprenorphine-naloxone doses
As the inherent risks of missing doses of buprenorphine-naloxone are considered to be less harmful than non-compliance with methadone, buprenorphine-naloxone is often a preferred treatment in patients who may be deemed to be at risk of non-adherence to therapy and who are dependent on more moderate doses of opioids.

Pharmacists must report to the prescriber patients on buprenorphine-naloxone who have missed several daily doses as a result of opioid use. If a patient misses buprenorphine-naloxone doses as a result of recent opioid use, delay dosing until at least 12 hours have passed since the time of opioid intake and confirm that the signs of opioid withdrawal
are clearly evident before resuming doses. The duration to withhold the dose of buprenorphine-naloxone in such a scenario varies according to the half-life of the opioid used by the patient and the prescriber’s clinical judgment.

From a clinical perspective, patients who miss five days or less of buprenorphine-naloxone are able to resume their previous buprenorphine-naloxone dose. However, the extent of doses missed and the reasons for having missed the doses may identify patients who require follow-up to reassess their circumstances.

**General guidance**
- Document any missed or lost doses on the patient’s records and report them to the prescriber. Include the reason(s) for the missed doses. If the patient has authorized it, report this information to the family physician or addiction counselors who may be in the circle of care.
- Develop a missed dose strategy/agreement with the prescriber in the event that the patient misses doses and the prescriber is unavailable for consultation.
- Consult the following table for a guideline on how to manage missed doses in various scenarios. Though this is one of several published guidelines for the management of buprenorphine-naloxone, pharmacists must use their own professional judgment in using this and other information to manage individual circumstances.

**Lost/stolen buprenorphine doses**
Evaluate situations of lost/stolen doses individually to judge the authenticity of the patient’s communication and the potential risks of authorizing a replacement dose. Encourage patients to report lost or stolen dosages to the authorities. Report lost doses to the prescriber and, if the prescriber deems a replacement dose necessary, he/she must write a new triplicate prescription.

**Vomited buprenorphine doses**
Buprenorphine is absorbed sublingually within one to ten minutes, bypassing the gastrointestinal tract. Vomited doses generally do not require replacement.

**Managing accidental overdose**
Induced vomiting after buprenorphine-naloxone sublingual tablets is ineffective. If you suspect overdose, treat it as a medical emergency.

**Table 3: Managing missed buprenorphine-naloxone doses**

<table>
<thead>
<tr>
<th>Number of missed consecutive days</th>
<th>Dose</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than seven days</td>
<td>Greater than 8 mg</td>
<td>Restart at 4 mg</td>
</tr>
<tr>
<td>Six to seven days</td>
<td>Greater than 8 mg</td>
<td>Restart at 8 mg</td>
</tr>
<tr>
<td>Six or more days</td>
<td>6 to 8 mg</td>
<td>4 mg (50% reduction)</td>
</tr>
<tr>
<td>Six or more days</td>
<td>2 to 4 mg</td>
<td>None</td>
</tr>
</tbody>
</table>


From a clinical perspective, references vary in the guidance for managing missed buprenorphine-naloxone doses. Ultimately, there should be an agreement between the prescriber and pharmacist about the expectations for management as both the clinical aspects and individual patient compliance and behavioural aspects need to be considered.

If buprenorphine-naloxone must be re-initiated or doses changed due to missed doses, the prescriber must write a new prescription and the pharmacy must cancel any other buprenorphine-naloxone prescriptions.

The intended duration of therapy as authorized must not be exceeded because of missed consecutive doses.
7.0 Cognitive services

Practice standards and responsibilities

Standards

- Pharmacists and pharmacy technicians providing medication-assisted treatments for opioid dependence must establish and maintain professional relationships with their patients. (S2.1, S2.2)
- Pharmacists must provide appropriate information to optimize the efficacy and safety of the treatment. (S1, S2, S3, S4, S5, S6, S7, S8)
- Pharmacists must consider drug therapy problems and use professional judgment, taking into account patient-specific considerations for appropriateness. (S1, S4, S5, S6)
- Each time a pharmacist or pharmacy technician dispenses a Schedule 1 drug or blood product pursuant to a prescription, or sells a Schedule 2 drug:
  - The pharmacist or the pharmacy technician must confirm the patient’s identity, and
  - The pharmacist must provide the patient with sufficient information to enable the patient to receive the intended benefit of the drug therapy. (S8)
- A pharmacist or pharmacy technician must create and maintain patient records for pharmacist services provided by that pharmacist. (S18)

Responsibilities

- A pharmacist who provides cognitive pharmacy services for medication-assisted treatment of opioid dependence should do so in a private consultation area.
- A pharmacist who engages in cognitive services for medication-assisted treatment of opioid dependence should receive formal training on the provision of opioid dependence treatment to ensure that their knowledge is current and accurate.

7.1 Dose management

Pharmacists’ roles

Pharmacists may have limited input in the initial dosages ordered by the prescriber, but the pharmacist is responsible for confirming that the dose is appropriate based on the extent of opioid dependence and other factors such as concomitant medications that may pose a risk for drug interactions or other adverse effects.

Pharmacists are also typically the front-line professional entrusted with witnessing doses and can therefore assess the clinical effect of and response to the daily administered dose. They play a key role in monitoring response and compliance to therapy and communicating to prescribers when they encounter potential problems that may compromise efficacy or safety of the therapy.

Pharmacists are expected to communicate to the prescriber any signs and symptoms of intoxication, withdrawal, or other adverse effects, and they are required to inform and consult prescribers about missed, lost, or vomited methadone doses. The same consultation with the prescriber is expected for buprenorphine-naloxone, with the exception of vomited doses of the sublingually administered tablet, which generally do not need to be replaced.

Pharmacists providing medication-assisted treatment for opioid dependence should be aware of common doses used during the various phases of treatment, and they should recognize the signs and symptoms of toxicity, adverse reactions to therapy, and withdrawal symptoms. They should also be able to identify and troubleshoot the potential risks and effects from drug interactions.

Methadone dosing

The starting and maintenance dosages of methadone have not been established through well-designed clinical trials. There are many individual considerations for dose initiation and ongoing therapy. However, methadone has been used for more than 40 years for opioid dependence, and dosing guidelines are available in most jurisdictions.

What follows are CPSA’s recommendations for methadone dosing from the 2014 Standards and Guidelines for MMT for...
Dependence.

Methadone dosing: Initiation phase
Patients are at the highest risk of methadone overdose and toxicity (including death) during the first two weeks of MMT. The initial dose prescribed for a patient should take into consideration the patient’s level of opioid tolerance, concomitant therapies that may impact drug levels and/or pose a risk of toxicity from methadone, and concomitant medical conditions including cardiovascular disease and mental health issues.

Initiating doses are prescribed by “initiating” physicians. All doses in the initiation phase must be daily witnessed doses, and patients should not be taking other prescribed opioids.

- Prescribers should not consider carry doses during the initiation phase.
- Monitoring of the patient during the initiation phase should include assessing for both intoxication from excessive dosing and withdrawal side effects resulting from inadequate dosing.
- Prescribers should decrease doses if there are signs and symptoms of intoxication typically occurring within three to four hours of dosing. Decrease doses if the patient experiences intolerable side effects.

Patients at low risk for methadone toxicity
- The starting dose can be 30 mg or less.
- Dose should be increased at no greater than 10 mg every three days during the early and late stabilization phases.

Patients at moderate risk for methadone toxicity
- The starting dose can be 20 mg or less.
- Dose should be increased at no greater than 10 mg every four days during early and late stabilization phases.

Patients at high risk for methadone toxicity or who have been abstinent from opioids for seven or more days
- The starting dose is 10 mg or less.
- Dose should be increased by no more than 5 mg every five or more days during the early and late stabilization phases.

Methadone dosing: Stabilization phase
- Doses should be increased only after the patient has been assessed in person by the physician and after the physician has confirmed that the patient is experiencing true withdrawal symptoms in spite of adherence to therapy.
- The dose may not be increased more than 10 mg every five to seven days during the stabilization phase.
- Doses should be increased only after the patient has been assessed in person by the physician and after the physician has confirmed that the patient is experiencing true withdrawal symptoms in spite of adherence to therapy.
- The dose may not be increased more than 10 mg every five to seven days during the stabilization phase.

Patients at high risk for methadone toxicity or who have been abstinent from opioids for seven or more days
- The starting dose is 10 mg or less.
- Dose should be increased by no more than 5 mg every five or more days during the early and late stabilization phases.

Methadone dosing: Maintenance phase
In the maintenance phase, both the dose and the patient are stable on methadone therapy. The optimal maintenance dose of methadone should prevent withdrawal symptoms, prevent opioid-induced euphoria, and reduce cravings for 24 hours without causing sedation or other significant side effects. Dose requirements typically range between 60 mg to 120 mg daily; however, methadone does not have a minimum or maximum effective dose. Prescribers should base the appropriate dose on ongoing monitoring of response from step-wise dose initiation.

- Patients may be transferred to the care of a maintaining physician during this phase. The maintaining physician must consult with the initiating physician before any change in dose and/or if the patient shows more than one indicator of instability.
- The maintaining physician should administer a urine toxicology test (UTT) a minimum of every three months for a stable patient in the maintenance phase of treatment.
- The patient should have clinical contact with the maintaining physician at least every three months, or as otherwise recommended by the initiating physician.

Buprenorphine-naloxone dosing: Initiation phase
- Buprenorphine-naloxone used for addiction treatment is administered as a sublingual tablet. As it is a partial agonist, there is a risk that it may cause a precipitated opioid withdrawal at the initiation of therapy. Therefore the drug should only be initiated when the patient demonstrates withdrawal. This may take up to 12 hours after the last dose of opioid and more than 24 hours after the last dose of methadone. (Note: Methadone has a variable half-life in individuals. Clinicians generally use a range of three to five days from the last methadone dose before initiating the first buprenorphine-naloxone dose).
- High dose rapid initiation is considered safe and effective and there is less risk of respiratory depression than with full agonists. High dose rapid initiation will result in the most rapid stabilization. The Suboxone™ product monograph advises initiating dosing at 4 mg with an additional 4 mg added later during the same day as required based on patient response. The dose can be titrated upwards to as much as 8 mg by day two and up to 16 mg by day three. The maximal daily dose is 24 mg and this may be reached within the first week of initiation therapy.
The dose used will depend on concomitant drugs used by the patient such as benzodiazepines or alcohol, as these can enhance toxicity.

The prescriber should decrease doses if there are signs and symptoms of intoxication typically occurring within one to four hours of dosing. The prescriber should also decrease doses if the patient experiences intolerable side effects.

The prescriber should make dose adjustments in increments of 2 mg to 8 mg (buprenorphine-naloxone is only available as 2 mg and 8 mg tablets).

Buprenorphine-naloxone dosing: Maintenance phase
Buprenorphine-naloxone has a ceiling effect. The Suboxone™ product monograph advises against administering doses in excess of 24 mg. Pharmacists may find literature recommending higher maximum daily doses. For example, an Australian policy document for addiction management identifies a maximum buprenorphine dose to be 32 mg daily, and it is possible that some addiction experts may prescribe such an “off-label” dose in special circumstances.

Doses of buprenorphine usually range from 8 to 12 mg per day during the maintenance phase. Patients may require one to three months to reach clinical stability on buprenorphine, even when they have achieved a maximum dose within the first few weeks. Following the induction period, some patients can be maintained on doses taken every other day. To accomplish this, the prescriber would double the regular daily dose and administer it every other day, the limitation being that the maximum daily dosage should not exceed 24 mg.

Switching from methadone to buprenorphine-naloxone
As the toxicity risk with methadone is a greater safety concern than toxicity resulting from buprenorphine-naloxone, prescribers should consider switching a patient’s therapy from methadone to buprenorphine-naloxone if:

- The patient is unable to tolerate the side effects of methadone.
- The patient is at risk of toxicity from methadone as a result of continued opioid or other illicit drug use.
- The patient is at risk of methadone toxicity as a result of non-compliance with attendance for witnessed doses.
- The patient is on other psychoactive or interacting medications

If a switch from methadone to buprenorphine-naloxone is warranted, consider the following dosing information:

- Prescribers should consider switching at an outpatient/community-based level for patients on a maximum of 30 mg per day of methadone in accordance with the product monograph for Suboxone™. Patients should have been on the same methadone dose for at least a week prior to switching. Patients on higher methadone doses are at a higher risk of severe withdrawal and switching attempts may be more appropriate within a monitored setting.
- Patients should commence buprenorphine-naloxone at least 24 hours after the last methadone dose since it can precipitate withdrawal symptoms (Note: Methadone has a variable half-life in individuals. Prescribers generally use a range of three to five days from the last methadone dose before initiating the first buprenorphine-naloxone dose).
- The Suboxone™ product monograph recommends the following induction dosing for patients initiating buprenorphine-naloxone treatment:
  - Patients should commence the dose 24 to 36 hours following the last dose of methadone.
  - Prescribers should consider a buprenorphine dose of 4 mg on day one with an additional 4 mg administered depending on the patient’s response.
  - The dose can be titrated upwards to as much as 8 mg by day two, and then increased to greater than 8 mg as necessary after the third day.
  - At dose initiation of buprenorphine-naloxone, prescribers should monitor the patient’s response one hour following sublingual dose administration to assess the severity of opioid withdrawal response and again at three hours to determine the response to the initial dose including an assessment as to whether an additional dose may be necessary.
- Addiction experts may vary in their management of the patient regarding the gap from the last opioid dose to the time of induction doses. They should initiate induction doses upon observation of moderate withdrawal symptoms; in some patients on methadone, this could take several days. Additionally, more aggressive induction doses with buprenorphine-naloxone have been used “off-label,” based on clinical experience.

Switching from buprenorphine-naloxone to methadone
Methadone has the primary advantage over buprenorphine-naloxone of having no ceiling effect. It can be titrated to higher doses with additional effect and is often a preferred agent for patients who are dependent on very high doses of opioids. Prescribers may consider switching a patient’s therapy from buprenorphine-naloxone to methadone if:

- The patient is unable to tolerate the side effects of buprenorphine-naloxone.
- The efficacy of buprenorphine-naloxone is inadequate at its maximal doses.

If a switch from buprenorphine-naloxone to methadone is warranted, prescribers should consider the following dosing information:
• The patient should be on a stable daily dose of buprenorphine-naloxone.
• Reducing the buprenorphine-naloxone dose to reach a dose of 8 mg before starting methadone may reduce its potential effect on methadone.
• Prescribers can initiate methadone 24 hours after the last dose of buprenorphine-naloxone.
• An initiation dose of methadone should not exceed 40 mg. The starting dose of methadone should be consistent with whether or not the buprenorphine-naloxone dose was low or high. The approach to titrating methadone is to start low and go slow.

7.2 Counselling and patient education
Pharmacists and pharmacy technicians involved in dispensing methadone and buprenorphine-naloxone must provide the patient with sufficient information to enable the patient to receive the intended benefit of the therapy and to optimize the safety of the drug to both the patient and the public.

The need for counselling may be ongoing as the prescriber adjusts doses and as the patient becomes ready for more information. Pharmacists must be able to assess the ability of their patient to understand the information provided, and wherever possible, should provide written instructions to allow the patient to absorb the information over time. Consider the literacy of the patient and provide appropriate literature that is clear and concise.

Keep in mind the following key components for counselling patients:

1. Counsel in a private area within a comfortable setting where the patient can sit down with the pharmacist counselling at the same eye level of the patient.
2. Schedule an appointment for counselling so that the patient prepares for the time commitment and can prepare their questions. This may also minimize interruptions from other areas of the pharmacy.
3. Use non-judgmental words and behaviour that demonstrate understanding of the patient’s circumstances. You may need to be assertive as well as compassionate.
4. Assess the patient’s current understanding of their treatment. This gives you an opportunity to determine literacy level, knowledge capacity, and evaluate the advice provided by other professionals or people associated with the patient.
5. Be ready to modify your counselling as necessary if you deem that there may be too much information provided at once. Be prepared with written information that the patient can take home to read or use written documents to organize and guide the discussion, highlighting key points with a highlighter or another writing implement to draw attention of these aspects when a patient reviews the information.

6. Document your encounter and record clinical impressions, concerns, assessments, and issues in the patient records that used by colleagues who may also be involved in the patient’s care. Highlight issues or information that may require reinforcement during the next encounter or during witnessed dosing as follow-up items.

Your initial counselling session should include the review and signing of the pharmacy–patient agreement, as this document should highlight some of the priority information and expectations for the patient and their caregivers.

Counselling topics may include, but are not limited to:

- Assessment and reinforcement of prior knowledge;
- Patient treatment goals;
- Patient’s rights and responsibilities;
- Pharmacist’s and the pharmacy’s rights and responsibilities;
- Procedural information for witnessed dosing;
- Information about the therapy to explain why and how it works in opioid dependence;
- Information about expected responses and potential side effects during induction versus during maintenance dosing;
- Information regarding safety and adverse effects;
- Dispelling myths and misconceptions that the patient may have about the treatment;
- Highlighting the importance of compliance and how missed, lost, spoiled, or vomited doses may be handled (in collaboration with the prescriber); and
- Counselling on pregnancy (as applicable).

Counselling tips for methadone maintenance therapy
Patients who are prescribed methadone maintenance therapy will require a comprehensive education and information session to ensure that they are fully aware of what they can expect when therapy begins, including some of the non-negotiable rules that must be adhered to once they have committed to treatment. This is not a drug for those who may have compliance issues as methadone can be extremely toxic in overdose. Most deaths from methadone occur during the induction period. Counselling before beginning methadone therapy is critical because of:

1. A delayed efficacy which can be uncomfortable or frustrating for a patient experiencing opioid withdrawal,
2. A requirement for careful and gradual titration, so patience is necessary,
3. The time commitment and possible daily transportation costs required by daily dosing,
4. The inherent risks and toxicities including fatality if patients take excessive doses, and
5. Specific requirements for storage and handling to enhance safety.

Due to the volume of important information that pharmacists
need to discuss with patients during the initial counselling session, prepare a check list for patients to take home and review. Do not worry about the potential for repetition of material already provided by other health professionals caring for the patient, since repetition positively reinforces the information. Pharmacists must ensure that they have made the patient aware of information pertaining to their own scope of practice.

An excellent and complete resource for patients is available from the Centre for Addiction and Mental Health in Toronto. Methadone Maintenance Treatment – Client Handbook is available to order or as a free download at http://www.camh.ca/en/education/about/camh_publications/Pages/methadone maintenance_clienthdbk.aspx.

Key counselling points
You can use the following points during patient counselling. Note that this list is not exhaustive. See Appendix 6 for a concise patient counselling sheet.

What is methadone?
Methadone is an opioid used to treat opioid dependence. It has been used to manage opioid addictions for more than 40 years. It is effective in treating opioid dependence because it does not make you feel high or low and it has a longer duration in your body so that once you are on a stable dose, you will be less likely to experience intense withdrawal side effects.

In fact, once you are on a stable dose, you may feel quite normal. This typical response to methadone is why it has been very successful to help people overcome the cravings and compulsive behaviours that occur when one becomes addicted to an opioid.

What should I expect when I start treatment with methadone?

- Only use methadone under the careful supervision of trained health professionals. A team with specialized training should ensure that your doses and responses to treatment are both effective and safe.

- Methadone is a safe drug when used appropriately, but it is also a drug that can be lethal. Never take extra doses on your own. Never accept doses from friends or others who take methadone. Never give your drug to others. Even a small dose can kill a child or an adult who has not taken opioids.

- Methadone is a drug that requires your patience and commitment. It can take several days to reach its full effect. A dose that seems to barely have an effect on the first day can become toxic by the third or fifth day. This is why your doctor will not make dose adjustments until you have been on the same dose for four days. The gradual dosing increases ordered by your doctor are for your safety. Most deaths from methadone occur from misuse in the first few weeks.

- Do not take additional doses or sedating drugs such as sleeping pills without checking with your doctor or pharmacist, even if you are experiencing withdrawal symptoms. It can be a rocky ride at the beginning, but most people will feel stable after two weeks, sometimes longer.

- You are supposed to feel normal on methadone, not high and not sleepy. Methadone levels in your system are more stable and don't fluctuate up and down, so you should eventually be more comfortable on methadone than on other opioids.

- You need to be aware of early warning signs of methadone toxicity. These may include symptoms such as falling asleep or decreased alertness, nodding off during the day, slurred speech, feeling unsteady and uncoordinated, feeling emotionally unstable, being forgetful, or appearing like you are drunk when you have not had any alcohol. If this occurs, it is a medical emergency and you should go to the hospital immediately. Do not feel embarrassed if it proves to be fine, as it is much safer to have these symptoms checked out. You should tell a close friend or family member about these symptoms so they can help you in the event that they notice symptoms. When methadone becomes toxic, you may lose your awareness of symptoms depending on the extent of the side effects, so it is important that someone you trust is also informed.

- Take the drug in the morning so that you are awake when its effects are at their peak. This will help you to be able to notice and monitor side effects from therapy at a time when you are awake.

- You may experience cravings or symptoms of withdrawal during the induction or initiation phase of therapy as we adjust the methadone to the right dose for your needs. Report these each day to your pharmacist and/or your doctor (depending on what their doctor has instructed them about when to seek their help).

Pharmacists can provide the patient with a print-out that lists some of the signs and symptoms of withdrawal (see Appendix 2). You can also provide a copy of the patient information sheet for methadone highlighting side effects and symptoms of toxicity.

Counselling to motivate

- By seeking the help of a doctor and acknowledging your opioid addiction, you have taken the first step to overcoming your illness.

- There are many benefits of persisting with methadone maintenance therapy.
  - Methadone can help you to feel more normal physiologically and psychologically so that you have a chance to gain control of your life. It can help
you to overcome some of the chaotic behaviours associated with addiction.

- Death from opioid dependency is common. Methadone therapy can decrease your likelihood of harm from the risks associated with opioid abuse.
- By following the advice of your doctor and those monitoring your care, you are helping yourself and those who care about and who want you to get your health and your life back.
- Addiction is costly, both financially and socially. Overcoming substance abuse will give you a chance to use your money for other things and get your life back on track.

- Methadone maintenance treatment has had over 40 years of success. You may have your own reasons for trying this strategy, and the fact that you have sought the help of a doctor shows that you are looking for something that can help you.

Counselling about patient commitments

- Arrive for regular daily witnessed dosing at the scheduled time agreed.
- Phone if you are running late or need to change the time of your arrival.
- If the pharmacy is closed on certain days, we will make arrangements for you to obtain your doses during days when the pharmacy is closed. This may involve weekend take-home doses if deemed safe, or arranging to have another pharmacy provide you the doses on those days.
- You should not be using opioids or other drugs of abuse when you are on methadone.
- You may be required to take random urine tests ordered by your doctor. In some cases, I [the pharmacist] may be reminding you of this. If you do not show up for the test, your dose may be held since these tests help to monitor your progress and keep you safe while on therapy. Let your doctor/program service provider know if you have a special reason for not being able to provide a requested sample.

Counselling about patient safety

- Do not take someone else’s methadone treatment as taking even a small additional dose can be fatal. Also, never share methadone with anyone.
- Do not drive or operate machinery during the initiation phase of methadone maintenance treatment and during periods of dose adjustment.
- I [the pharmacist] will check that you are not intoxicated with any substance before dispensing your methadone dose. We may ask you to provide a urine sample for testing or to take a breathalyzer test. This is required for your personal safety since the combination of methadone with other sedating or depressant drugs can make methadone more toxic and the mixing of these in the body can be lethal.
- Do not use methadone with other drugs that are known to depress the central nervous system as this can cause more side effects and toxicity. These include sleeping pills, alcohol, marijuana, heroin, narcotic pain killers, over-the-counter sedatives, and natural health products like St. John’s Wort.
- Methadone can sometimes affect your heart rhythm. Your doctor will monitor your heart using an electrocardiogram (ECG) to try to carefully monitor and determine any effect the drug may have on the heart.
- If you become pregnant, notify your doctor immediately so he/she can assess the situation and minimize risks and dose and monitor the methadone in such a way to minimize risks to the developing fetus.
- Those who do not intend to become pregnant while on methadone should protect themselves using up to two methods of reliable birth control.

Counselling tips for maintenance carries

- Once you are stable on a methadone dose for about two to three months, your doctor may permit you to take home some doses. You may find this to be more convenient.
- Methadone can be a very toxic drug when used by someone who has never taken it. Even small doses can kill a child, and it can be lethal to those who have never taken opioids.
- Take-home doses are a privilege. You are responsible for storing the doses so that others cannot accidentally ingest them.
- Keep the bottles in the locked or secured box provided to you from the pharmacy. Store the box in the refrigerator when you arrive home. You must keep all carry bottles and return the empty bottles back to the pharmacy for proper disposal.
- I [the pharmacist] may ask you to come in with your carries during the carry period to ensure you are taking your drug properly and to make sure you are not experiencing side effects.
- You must follow the exact instructions and ingest the entire contents of each bottle as a single dose.
- If you are not able to manage your take-home doses, your doctor may put you back on regular daily
Counselling tips for buprenorphine-naloxone therapy
When first meeting with a patient beginning buprenorphine-naloxone therapy, pharmacists should outline the expectations and obligations of the patient towards the pharmacy and its staff as well as other members of his or her addiction management health care team. Emphasize aspects that can impact the safety of the patient and the medication, as well as some of the non-negotiable rules that the patient must adhere to once he or she has committed to treatment.

Buprenorphine-naloxone is an alternative to methadone which, by the nature of its pharmacology, is less toxic in overdose. It has a ceiling effect of both its efficacy and toxicity from respiratory depression. Although there are few reported deaths from buprenorphine-naloxone administered in the absence of other CNS depressants, concurrent use of this drug with depressant substances like alcohol or benzodiazepines can be dangerous, even fatal.

As with methadone, initial dosing of buprenorphine-naloxone relies on patient commitment to daily dosing which can require both a time commitment to travel to the location for the daily witnessed ingestion and possibly a daily transportation cost to reach the pharmacy if the patient does not live within walking distance.

During the counselling session, pharmacists can prepare by organizing a checklist of items to discuss and written take-home materials that the patient can review and reference. Don’t worry about the potential for repetition of material already provided, since repetition can positively reinforce the information. Be sure to make the patient aware of information pertaining to your own scope of practice.

Key counselling points
You can use the following points during patient counselling. Refer to the Suboxone™ product monograph for a complete patient counselling sheet.

What is buprenorphine?
Buprenorphine is an opioid used as substitution therapy to treat opioid dependency. It has been available in Canada since 2007 as an alternative to methadone maintenance treatment. The tablet that we dispense in Canada is combined with another drug called naloxone.

Buprenorphine does not make you feel high and it does not cause intense withdrawal symptoms towards the end of the day because it has a long duration in your body, which eliminates it gradually and slowly. Once you are on a stabilized dose, you may feel quite normal. This typical response to buprenorphine has made it a successful drug to help people overcome the cravings and compulsiveness that can occur with opioid dependence.

What is the purpose of the naloxone in the buprenorphine tablet?
Naloxone is added to the buprenorphine tablet to prevent people with addictions from abusing the drug by making it into a form that can be injected into the body. The naloxone actually doesn’t have any action in your body because it doesn’t get into the blood stream when you are taking it sublingually (under the tongue) or orally. When you inject naloxone into the body, it can cause you to become very sick if you are taking an opioid such as buprenorphine or another opioid (e.g., heroin, oxycodone, morphine). The naloxone will “knock” the opioids already in your system off their receptors, causing withdrawal symptoms. In fact, hospitals use naloxone injection to treat narcotic overdose.

What should I expect when I start treatment with buprenorphine?
- Only use buprenorphine under the careful supervision of trained health professionals.
- [If they have been on another opioid before starting buprenorphine] Your doctor and I [the pharmacist] will start your first buprenorphine-naloxone dose after the opioid in your body has started wearing off and when you start experiencing withdrawal symptoms as the drug clears from your system. These withdrawal symptoms typically start 12 hours after the last dose of opioid. Having both buprenorphine and another opioid in your body at the same time can lead to more severe withdrawal symptoms.
- Your doctor will gradually increase your buprenorphine dose over a period of a few days or over a week. Typically, patients will reach the maximum dose of buprenorphine-naloxone within the first or second week of treatment.
- You are supposed to feel normal on buprenorphine-naloxone, not high and not sleepy. Buprenorphine levels in your system are more stable and don't fluctuate up and down, so you should eventually be more comfortable on buprenorphine than on other opioids. In the initiation phase, some people may experience a headache, dizziness, nausea, and sedation if the dose is increased too quickly. Let your doctor know if these symptoms occur.
- You may experience cravings or symptoms of withdrawal during the induction or initiation phase of therapy as we adjust the buprenorphine to the right dose for your needs. Report these to your pharmacist and/or your doctor (depending on what their doctor has instructed them about when to seek their help).

Pharmacists should provide a print-out that lists some of the sign and symptoms of opioid withdrawal (See Appendix 2).
You should provide a copy of a patient information sheet for buprenorphine highlighting side effects and symptoms of toxicity. This can be the patient information section available from the manufacturer’s product monograph.

**How to take buprenorphine-naloxone**

- Buprenorphine-naloxone is a sublingual tablet. This means that you take the drug by placing it under your tongue and waiting for it to dissolve. It can take from one to ten minutes to dissolve.

- Take the drug in the morning so that you are awake when its effects are at their peak. This will help you to be able to notice and monitor side effects from therapy at a time when you are awake.

- If your daily dose consists of multiple tablets of buprenorphine-naloxone, you should dissolve the tablets under your tongue simultaneously. Carefully break the tablets into halves so they dissolve more quickly under the tongue. If this is not possible, you should take the required number of tablets for your dose one immediately after the other to gain the most benefit of the higher dose.

- Your doctor may try alternating day dosing after the first week or two of therapy. You may appreciate this because it means you will only have to come to the pharmacy for witnessed dose ingestion every other day. If you think this is more confusing for you to organize, let me or your doctor know so that we can adjust the dosing schedule to your preference.

**Counselling to motivate**

- By seeking the help of a doctor and acknowledging your opioid addiction, you have taken the first step to overcoming your illness.

- There are many benefits of persisting with your therapy:  
  - Buprenorphine can help you to feel more normal physiological and psychologically so that you have a chance to gain control of your life. It can help you to overcome some of the chaotic behaviours associated with addiction.
  - Death from opioid dependency is common. Buprenorphine is a replacement therapy that can decrease your likelihood of harm from such behaviours.
  - By following the advice of your doctor and those monitoring your care, you are helping yourself and those who you care about and who want you to get better.
  - Addiction is costly, both financially and socially. Overcoming substance abuse will give you a chance to put your money towards other things and get your life back on track.

**Counselling about patient commitments**

- Arrive for regular daily witnessed dosing at the scheduled time.

- Phone if you are running late or need to change the time of your arrival.

- If the pharmacy is closed on certain days, we will make arrangements for you to obtain your doses during these days. This may involve weekend take-home doses if your prescriber deems it safe, or arranging to have another pharmacy provide you the doses on those days.

- Do not use opioids or other drugs of abuse when you are on buprenorphine-naloxone.

- You may be required to take weekly urine tests ordered by your doctor. In some cases, I may remind you of this. If you do not show up for the test, your buprenorphine dose may be held since these tests help to monitor your progress and are necessary to keep you safe while on therapy. Let your doctor know if you have a special reason for not being able to provide a requested test.

**Counselling about patient safety**

- Do not take someone else’s buprenorphine and do not share your medication with anyone.

- Do not drive or operate machinery during the initiation phase and during periods of dose adjustment.

- During witnessed dosing, we will check that you are not intoxicated with any substance before dispensing the buprenorphine dose. We may ask you to provide a urine sample for testing or to take a breathalyzer test. This is required for your personal safety.

- Do not use buprenorphine with other drugs that are known to depress the central nervous system without the advice of your doctor and pharmacist as these medications can cause more side effects and toxicity. These include sleeping pills, alcohol, marijuana, heroin, narcotic pain killers, over-the-counter sedatives, and natural health products like St. John's Wort. Inform your doctor if you are on any of these drugs or products.

- Buprenorphine-naloxone may pose risks to a fetus, especially during certain phases of pregnancy. Those on buprenorphine-naloxone should protect themselves from pregnancy by using two reliable methods of birth control. If you become pregnant, notify your doctor and pharmacist immediately. The doctor will determine if you require a change in therapy.

- If you wish to become pregnant while being treated for opioid dependence disorder, arrange an appointment to discuss this with your doctor.
**Counselling tips for maintenance carries of buprenorphine-naloxone**

- Once you are stable on buprenorphine for about two to three months, your doctor may permit you to take home some doses to take on your own. When your doctor will make this decision can vary depending on your progress with the treatment.

- Take home doses are a privilege. You are responsible for storing the doses so that others cannot accidentally ingest them.

- I may ask you to come in during the carry period to ensure you are taking your drug properly and to make sure you are not experiencing side effects.

- You must take the buprenorphine exactly as prescribed.

- If you are not able to manage your doses at home, your doctor may put you back on regular daily witnessed administration so you will retain your progress on the therapy.

### 7.3 Monitoring

Pharmacists are directly involved in the monitoring of medication-assisted treatment for opioid dependence. Monitoring activities considered a priority for pharmacists are generally those to optimize the response and outcomes to therapy—in particular, activities to evaluate the efficacy and safety of the treatment and the patient’s compliance to the therapy. Additionally, pharmacists are entrusted with judging if the patient may pose a risk to the public through their use of methadone or buprenorphine-naloxone, especially in decisions for allowing take-home doses.

Below are some of the monitoring activities performed by pharmacists and the pharmacy team.

#### Initial assessment

- Monitor for patient’s understanding of their treatment, along with their attitude, commitment, and ability to comply with the treatment prescribed.

- Monitor that the patient is indeed the person for which the prescribed therapy is intended by checking valid photo identification.

- Monitor for symptoms or evidence of intoxication to determine if you should dispense the dose.
  - Intoxication from opioids: Pinpoint pupils, drowsiness, itchiness and scratching, slow heart rate, low blood pressure.
  - Intoxication from alcohol: Slurred speech, imbalance while walking, uncoordinated movements, drop in blood pressure, alcohol smell on breath.
  - Intoxication from benzodiazepines: Sedated, drooling, low blood pressure, loss of muscle coordination, slurred speech.
  - Intoxication from stimulants like amphetamines: Dilated pupils, hyperactivity, rapid heart rate, tremor, high blood pressure.

- Monitor for symptoms of opioid withdrawal to determine when to start therapy with buprenorphine-naloxone.

- Monitor daily response to administered doses, including symptoms of withdrawal, symptoms of intoxication from the treatment that may require stoppage of the medication or an adjustment of the dose, proper administration of ingested doses, drug interactions with other concurrent therapies, and use of other opioids or illicit drugs.

- Monitor laboratory findings, including creatinine and renal function tests, liver function tests for various enzymes, urine tests and drug screens, and blood tests of drug levels.

- Monitor for diversion. Diversion is minimized by the following activities:
  - The requirement for daily witnessed ingestion;
  - Mixing the drug in a crystalline drink or juice
  - Supervising ingestion between carries;
  - Random monitoring during the carry period;
  - Ensuring the patient has swallowed the dose by engaging in conversation with the patient following dose administration or having the patient show you that the tablet has disappeared from under their tongue;
  - Checking the patient identification each time;
  - Verifying that the prescription and prescriber are authentic;
  - Ensuring all dosing cups do not leave the pharmacy;
  - Storing methadone and buprenorphine-naloxone in a secured and locked cupboard or room;
  - Promptly reporting lost or stolen doses;
  - Ensuring that the patient returns all used carry bottles with intact labelling;
  - Monitoring for patterns and frequency of missed, lost, spoiled doses and having a policy of non-replacement; and
  - Random requests for urine testing.

#### Monitoring tools

- Urine toxicology tests.

- Blood tests to monitor drug levels, liver function, infection, electrolyte imbalances.

- Breathalyzer to monitor for alcohol levels in intoxication and differentiate from intoxication from other substances.
Urine Toxicology Testing

Urine Toxicology Testing (UTT) is used to monitor the stability, safety and benefit of the treatment, to ensure that the patient is taking the carried doses, and to test if the patient is using any proscribed drugs. The prescriber or program service provider is responsible for scheduling the tests and follow up; however, some programs may ask pharmacies to communicate the timing of the tests. Additionally, pharmacies have the option to collect the samples for testing on behalf of the prescriber and program.

Although Alberta pharmacists are permitted to order such tests if it is within their scope of training to be able to assess the results, duplication of testing is discouraged. Pharmacists should collaborate with the prescriber or program before initiating testing on their own for medication-assisted treatment of opioid dependence.

If you feel strongly that UTT is required for a patient, work with the prescriber/program service provider to identify your concerns and have the test ordered consistently from the prescriber/program service provider. Tests should be performed randomly and the patient must not be given more than 24 hours notice prior to testing unless otherwise stipulated. The sample should be obtained privately; however, the patient should remain on the premises to ensure that the sample has not been tampered with and that it actually came from the patient.

Frequency of urine testing will depend on individual patient needs as determined by response to treatment and progress. If a patient does not show up when testing is required, or if the prescriber is concerned with the results of the test, the prescriber may ask the pharmacist to withhold the dose.
**8.0 Patient rights and care in special situations**

**Patient privacy**
Awareness of privacy concerns is imperative when serving those receiving medication-assisted therapy for opioid dependence. There is a stigma surrounding those with addictions, and the community is generally not supportive of treatment centres and pharmacies servicing such patients due to concerns about the impact of these services on property values and the likelihood of exposure of their children and family to those with addiction.

Pharmacists and pharmacy staff must be sure to provide services in a private area and must keep the patient’s confidential information private. You must receive written consent from the patient before sharing any information with family or caregivers. An initial two-way or three-way agreement can ensure an understanding of the parameters around which pharmacists and other health professionals involved in the patient’s care will share information.

**Transfer of care**
If a patient voluntarily or involuntarily requires a transfer of care, it is the obligation of the pharmacy and delegated staff to assist the patient and to maintain continuity of care. This may require the provision of records and transfer of patient information to the new care provider or assistance in seeking a new provider if the patient relocates to a new city, province, or country.

Note that only licensed dealers with appropriate permits are authorized to import or export narcotics across international borders; patients transferring out of country will have to secure a prescriber and submit themselves to the rules and regulations for their treatment within their new country.

A pharmacist is not required to provide carry doses if he/she deems it unsafe for both the patient and the public. Advanced planning is the patient’s responsibility if the patient initiates the transfer of care decision.

**Voluntary patient discontinuation of treatment**
If a patient wishes to discontinue methadone, you must respect their decision. Make the patient aware of the consequences and risk of relapse to illicit drug use. Inform other members of the health care team of the patient’s decision and status. The prescriber will need to prescribe the taper schedule for the individual. Abrupt discontinuation is discouraged to prevent severe withdrawal symptoms that may last up to two weeks. Medications for symptoms of withdrawal may be considered and these can include such agents as clonidine, loperamide, non-steroidal anti-inflammatory pain medications, and dimenhydrinate. Pharmacy staff should continue to support the patient until the patient-pharmacy relationship is terminated.

**Involuntary discontinuation of treatment**
The pharmacy should establish the ground rules for termination of services at the outset of therapy. This can be part of the patient-service provider agreement. If discontinuation of pharmacy services is necessary, the pharmacist must assist the patient in receiving care from another pharmacy to ensure continuity of care. The pharmacist must also inform the other members of the treatment team.

A typical schedule for involuntary withdrawal is as follows: a 10% reduction of the daily dose per day, or 1 mg per day, whichever is greater. This results in complete cessation within 30 days for any dose under 150 mg, and within 40 days for any dose less than 500 mg. The initiating physician may use pharmacotherapy in the final one to two weeks of the decrease to relieve withdrawal symptoms.

**Incarceration**
Methadone maintenance or buprenorphine-naloxone treatment should continue if a patient is incarcerated. Methadone programs are often available in provincial correctional facilities, remand centres, and federal prisons.

Pharmacies providing medication-assisted treatment services that become aware of the incarceration of a patient should notify the patient’s prescriber or program to facilitate a seamless and coordinated transition of care. Where possible, a healthcare professional within the patient’s circle of care should relay the message; this should be someone who is knowledgeable about the patient’s clinical circumstances and needs.

While most correctional facilities and remand centres have their own processes and resources for managing patients on medication-assisted therapies for opioid dependence, including procedures for notification of the patient’s community prescriber/program and the provision of ongoing treatment within the facility itself, pharmacies providing services to these individuals have a responsibility to perform their own due diligence in this process. Additionally, pharmacies that had serviced these patients may be a resource to the facility, especially as it relates to confirming the details of the patient’s most recent doses, progress, and compliance to treatment. Communication and collaboration between the facility, the prescriber/program, and the pharmacy are also important to ensure a smooth transition of care upon the patient’s release from incarceration, if ongoing treatment is necessary.

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If a patient voluntarily or involuntarily requires a transfer of care, it is the obligation of the pharmacy and delegated staff to assist the patient and to maintain continuity of care. This may require the provision of records and transfer of patient information to the new care provider or assistance in seeking a new provider if the patient relocates to a new city, province, or country.

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While most correctional facilities and remand centres have their own processes and resources for managing patients on medication-assisted therapies for opioid dependence, including procedures for notification of the patient’s community prescriber/program and the provision of ongoing treatment within the facility itself, pharmacies providing services to these individuals have a responsibility to perform their own due diligence in this process. Additionally, pharmacies that had serviced these patients may be a resource to the facility, especially as it relates to confirming the details of the patient’s most recent doses, progress, and compliance to treatment. Communication and collaboration between the facility, the prescriber/program, and the pharmacy are also important to ensure a smooth transition of care upon the patient’s release from incarceration, if ongoing treatment is necessary.
Hospitalization

Pharmacies involved in delivering medication-assisted treatment services that become aware of the hospitalization of a patient must notify the patient’s prescriber/program to facilitate a seamless and coordinated transition of care. Where possible, a healthcare professional within the patient’s circle of care should relay the message; this should be someone who is knowledgeable of the patient’s clinical circumstances and needs.

All healthcare professionals who prescribe or dispense medication-assisted treatments for opioid dependence should be aware of the regulatory requirements and standards of practice that govern the prescribing and dispensing of such treatments. All prescribers require an exemption from the Office of Controlled Substances (OCS) in order to prescribe methadone. The Office of Controlled Substances may grant hospital prescribers a temporary exemption to prescribe doses while the individual remains an inpatient. It is the pharmacist’s responsibility to ensure that an exemption has been granted to the prescriber prior to dispensing methadone. Pharmacists and pharmacy technicians must also be aware of and adhere to the regulatory requirements and guidelines for the prescribing and dispensing of buprenorphine-naloxone.

The processes and options to ensure continuity of treatment during hospitalization may vary depending on the hospital’s resources and its internal policies and procedures with regard to narcotics and use of a patient’s own medications. Community pharmacies and prescribers that provide medication-assisted treatment for opioid dependence can collaborate with hospitals to provide continuity of treatment where gaps exist and this may include the provision and transfer of interim doses at the time of admission. The patient’s caregivers at the hospital and in the community should also collaborate to ensure continuity of care and treatment at the time of hospital discharge.
9.0 Methadone for analgesia

Methadone for the treatment of pain requires that the prescriber has a methadone for pain/analgesia exemption from Health Canada. The use of methadone to treat chronic pain is common since it is an effective analgesic with a longer half-life and duration of action than other opioids. When methadone is prescribed for analgesia, it is sometimes ordered more than once daily. Methadone tablets are usually considered for self-administration; those using methadone solely for pain do not require witnessed dose ingestion. Dispensing is typical to how other oral narcotics are dispensed, labelled, and administered.

Pharmacists can provide similar counselling to patients about how to take methadone and the dangers to children or the public. You can affix warning labels similar to those used in methadone maintenance.

If a patient requires methadone for both opioid dependence and pain, it is in the best interest of the patient and the public to treat the prescription as methadone maintenance and to follow the rules, regulations, and exemptions for dispensing methadone maintenance treatment. If the prescriber does not have an exemption, the pharmacist should make every effort to collaborate on the recommended approach and suggest a clinic or potential prescriber. The safety of the patient must take priority, and the prescriber can consider a different therapy as appropriate. You are under no obligation to fill a prescription if you are not comfortable with the prescriber’s decisions or have concerns for patient safety based on the decisions. Clearly document your concerns and communication with the prescriber and retain the records.
10.0 Important numbers and contact information

Provincial and federal regulators

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<tr>
<th>Alberta College of Pharmacy</th>
<th>T: 780-990-0321</th>
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<tr>
<td>1100-8215 112 St. NW</td>
<td>TF: 1-877-227-3838</td>
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<tr>
<td>Edmonton, AB T6G 2C8</td>
<td>F: 780-990-0328</td>
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<tr>
<td>Web: abpharmacy.ca</td>
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<th>College of Physicians &amp; Surgeons of Alberta</th>
<th>T: 780-423-4764</th>
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<td>2700-10020 100 St. NW</td>
<td>TF: 1-800-561-3899</td>
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<tr>
<td>Edmonton, AB T5J 0N3</td>
<td>F: 780-420-0651</td>
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<tr>
<td>Web: <a href="http://www.cpsa.ab.ca">www.cpsa.ab.ca</a></td>
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<th>Office of Controlled Substances, Health Canada</th>
<th>T: 613-946-5139</th>
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<tr>
<td></td>
<td>TF: 1-866-358-0453</td>
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<td>(Health professionals’ dedicated methadone line)</td>
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<td>E: <a href="mailto:exemption@hc-sc.gc.ca">exemption@hc-sc.gc.ca</a></td>
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Alberta methadone clinics

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Recommended reading

Alberta College of Pharmacy. (2011) *Standards of Practice for Pharmacists and Pharmacy Technicians*. Edmonton: Alberta College of Pharmacy, 1 July 2011. PDF. 
<https://abpharmacy.ca/nPharmacistResources/StandardsofPractice.aspx>

Alberta College of Pharmacy. *Standards for the Operation of Licensed Pharmacies*. Edmonton: Alberta College of Pharmacy, 1 July 2011. PDF. 
<https://abpharmacy.ca/nPharmacistResources/StandardsofPractice.aspx>


Glossary

**Breathalyzer test** – A test to determine a patient’s blood alcohol levels. It is available in some methadone clinics and pharmacies that dispense methadone, and is used to determine or validate suspected intoxication from alcohol.

**Carries** – Take-home doses of a medication-assisted treatment such as methadone or buprenorphine-naloxone (authorized by the prescriber) that are dispensed by the pharmacy and taken by the patient without supervision.

**Chronic pain** – Pain persisting for more than six months.

**Initiation phase** – Also called the “induction phase,” this represents the start of therapy and initial doses of a medication-assisted treatment. It is considered to be the phase where the patient is at the greatest risk of clinical instability as doses are tried, observed, and gradually increased or adjusted based on the patient’s response. Patients may experience craving, withdrawal, or symptoms of toxicity from their therapy during this phase of “dose finding.”

Stability is determined by the positive changes in the patient’s actions, disposition, and well-being and can also be seen in their response to the treatment when they are less likely to experience withdrawal and craving.

**Maintenance phase** – This is the phase where the dose and response of medication-assisted treatment for opioid dependence remains clinically stable. Patients are in the period of stability. It is a phase where the prescriber may consider carries if he or she deems it appropriate, taking patient and community safety into consideration.

**Opiate** – A naturally occurring or semi-synthetic compound derived from the opium poppy (*Papaver somnifer*).

**Opioid** – A compound having actions or properties similar to opiates. Heroin, morphine, hydromorphone, codeine, fentanyl, methadone, and buprenorphine are all opioids.

**Proscribed substance** – A substance that is considered contraindicated during substitution treatment and that may include both legitimate or illicit drugs and substances.

**Serum methadone levels** – A blood test to determine the methadone concentrations in the plasma. The peak level is obtained three to four hours following ingestion and the trough level is the level taken prior to the next dose. This is not a routine test in Alberta.
Works cited


## Appendices

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Appendix 1: Defining substance dependence

The diagnostic criteria for substance dependence come from the Diagnostic and Statistical Manual of Mental Disorders from the American Psychiatric Association, 2000. This definition is the one accepted by the majority of guidance documents across Canada and is reproduced for you below, with permission from its publishers.

DSM-IV-TR Criteria for Substance Dependence

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

1. **Tolerance** as defined by either of the following:
   a. a need for markedly increased amounts of the substance to achieve intoxication or desired effect,
   or
   b. markedly diminished effect with continued use of the same amount of the substance.

2. **Withdrawal**, as manifested by either of the following:
   c. the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for withdrawal from the specific substances), or
   d. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.

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

6. There is a persistent desire or unsuccessful efforts to cut down or control substance use.

7. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects.

8. Important social, occupational, or recreational activities are given up or reduced because of substance use.

9. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

Specify if:

- **With physiological dependence**: evidence of tolerance or withdrawal (i.e., either item 1 or 2 is present)
- **Without physiological dependence**: no evidence of tolerance or withdrawal (i.e., neither item 1 or 2 is present)
## Appendix 2.1: Comparison of methadone and buprenorphine-naloxone

<table>
<thead>
<tr>
<th>Action</th>
<th>Methadone maintenance therapy</th>
<th>Buprenorphine-naloxone treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Full opioid agonist with actions at the µ (mu) opioid receptor.</td>
<td>• Partial opioid agonist with agonist effects at the µ (mu) opioid receptor and antagonist effects at the kappa opioid receptor.</td>
<td></td>
</tr>
<tr>
<td>• No ceiling effect.</td>
<td>• Ceiling effect.</td>
<td></td>
</tr>
<tr>
<td>• Dose continues to accumulate over many days.</td>
<td>• Longer half-life than methadone so may be dosed every other day once stabilized.</td>
<td></td>
</tr>
<tr>
<td>• Onset of action: 3 hours</td>
<td>• Onset of action: 30 to 60 minutes</td>
<td></td>
</tr>
<tr>
<td>• Peak effects: 2 to 4 hours</td>
<td>• Peak effects: 1 to 4 hours</td>
<td></td>
</tr>
<tr>
<td>• Elimination half-life: 25 hours (5 to 130 hours)</td>
<td>• Elimination half-life: 37 hours (20 to 72 hours)</td>
<td></td>
</tr>
<tr>
<td>• Steady state: 2 to 9 days</td>
<td>• Steady state: 7 to 10 days</td>
<td></td>
</tr>
<tr>
<td>Pharmacology</td>
<td>• Available as a 10 mg/ml oral concentrate in a red, cherry-flavoured hypertonic syrup and as a dye-free, sugar-free, unflavoured clear concentrate. The two formulations allow for patient preferences in taste, and can accommodate for those with dye allergies.</td>
<td>• Available in two strengths of sublingual tablets that are not scored. Dose range less flexible, ranging from 2 mg to 24 mg daily.</td>
</tr>
<tr>
<td>Administration and availability</td>
<td>• Titration to desired response is possible over a wide range of doses.</td>
<td>• Witnessed dosing can be prolonged. Sublingual tablet dissolves in two to ten minutes.</td>
</tr>
<tr>
<td>Advantages</td>
<td>• No ceiling effects. Better efficacy profile in those addicted to higher doses of opioid.</td>
<td>• Better safety profile. Has a ceiling effect on respiratory depression so is safer in overdose compared to methadone.</td>
</tr>
<tr>
<td></td>
<td>• Flexible dosing.</td>
<td>• Partial agonist, therefore lower abuse potential.</td>
</tr>
<tr>
<td></td>
<td>• Reimbursed by Alberta’s provincial health plan.</td>
<td>• Easier to prescribe. Dosing guide is simple.</td>
</tr>
<tr>
<td></td>
<td>• Long history of use and clinical experience with this opioid. Many resources for guidance on proper use.</td>
<td>• Access to prescribers of this drug is greater</td>
</tr>
<tr>
<td></td>
<td>• Prescribed by trained prescribers of MMT due to regulatory requirements.</td>
<td>• Enhanced convenience, as it may allow for an increased number of carry doses due to reduced overdose risk.</td>
</tr>
<tr>
<td></td>
<td>• Considered a safer option to buprenorphine-naloxone in pregnancy.</td>
<td>• Rapid escalation to the maximal dose.</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>• Titration to response may take longer than buprenorphine-naloxone and drug poses a greater danger of toxicity from improper use during the initiation phase.</td>
<td>• Longer half-life means possibly more moderate withdrawal symptoms when weaning someone completely off treatment. May be a choice for those with a good prognosis to be off opioids with time.</td>
</tr>
<tr>
<td></td>
<td>• Level of respiratory depression or sedation does not have a ceiling effect and therefore may be fatal in overdose.</td>
<td>• Lower prevalence of drug interactions than methadone.</td>
</tr>
<tr>
<td></td>
<td>• Access is limited by availability and location of prescribers who meet federal and provincial requirements to prescribe MMT.</td>
<td>• Less toxic. Carry doses poses less danger to the public.</td>
</tr>
<tr>
<td></td>
<td>• Efficacy is limited by its ceiling effect. May be inadequate to control withdrawal symptoms in those dependent on higher doses of opioids. Maximum dose is 24 mg.</td>
<td>• Efficacy is limited by its ceiling effect. May be inadequate to control withdrawal symptoms in those dependent on higher doses of opioids. Maximum dose is 24 mg.</td>
</tr>
<tr>
<td></td>
<td>• Generally more expensive than methadone</td>
<td>• Generally more expensive than methadone</td>
</tr>
<tr>
<td></td>
<td>• At greater risk of misuse by untrained prescribers.</td>
<td>• At greater risk of misuse by untrained prescribers.</td>
</tr>
<tr>
<td></td>
<td>• Newer drug for addiction. Limited experience with use and/or long term safety.</td>
<td>• Newer drug for addiction. Limited experience with use and/or long term safety.</td>
</tr>
</tbody>
</table>
| | • Not recommended in pregnancy due to the }
<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>Methadone maintenance therapy</th>
<th>Buprenorphine-naloxone treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• More clinically significant drug interactions with an increased need for</td>
<td>• Requires routine ECG and monitoring.</td>
<td>• Not recommended for use while breastfeeding.</td>
</tr>
<tr>
<td>close monitoring and appropriate prescribing.</td>
<td>• Greater toxicity to children and those who are opioid naïve and as such, carry doses may pose</td>
<td></td>
</tr>
<tr>
<td>• Requires routine ECG and monitoring.</td>
<td>a greater danger to the public and require close monitoring and communication for proper storage.</td>
<td></td>
</tr>
<tr>
<td>• Greater toxicity to children and those who are opioid naïve and as such,</td>
<td>• Difficult to wean completely off.</td>
<td></td>
</tr>
<tr>
<td>carry doses may pose a greater danger to the public and require close</td>
<td></td>
<td></td>
</tr>
<tr>
<td>monitoring and communication for proper storage.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Difficult to wean completely off.</td>
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</table>
Appendix 2.2: Opioid withdrawal symptoms

What causes opioid withdrawal symptoms?
Your body has chemicals and receptors that are in balance. Natural endorphins play a role in reducing pain and bringing a sense of well-being to your body. Opioids (e.g., heroin, oxycodone, methadone) are substances that look and act similar to the natural endorphins that are produced by your body. When you use opioids regularly, your body does not produce as many natural endorphins. When you suddenly stop taking opioids, your body does not have a chance to adjust, and this sudden imbalance of the “endorphin-like” substances in your body can cause you to feel quite sick.

When do withdrawal symptoms start?
The start of withdrawal symptoms usually depends on how quickly your body eliminates the opioid that you have become dependent on. Symptoms occur when enough of the opioid leaves your system to cause an imbalance. For those addicted to heroin and oxycodone, symptoms may appear as early as 12 hours after the last dose and may be at their worst in 36 to 72 hours. For methadone, withdrawal symptoms generally don’t appear until after 24 hours and will peak at 72 hours to 96 hours.

Heroin or oxycodone withdrawal may last for seven to ten days, and methadone withdrawal symptoms can persist for up to two weeks. There are medications available that can help relieve some symptoms.

Are withdrawal symptoms the same for all drugs?
No. The withdrawal symptoms for alcohol and sleeping pills can differ from that of opioids. There may be some symptoms that are the same, but there are some that you only see with some types of addictions. The nature of the withdrawal symptoms are based on what chemicals are suppressed by the addictive substance and the type of symptoms created by the actions of the opposing natural chemicals that are in balance within your body. For instance, hallucinations and seizures in someone without a seizure history are not seen in opioid withdrawal.

Can you die from opioid withdrawal?
Opioid withdrawal, while quite uncomfortable, generally does not lead directly to life-threatening symptoms. An individual’s tolerance to the symptoms can be affected by their other health conditions or circumstances that may put them at risk.

Common symptoms of opioid withdrawal

<table>
<thead>
<tr>
<th>Severe flu-like symptoms</th>
<th>Stomach cramps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Runny nose</td>
<td>Achy bones and joints</td>
</tr>
<tr>
<td>Sneezing</td>
<td>Goosebumps</td>
</tr>
<tr>
<td>Yawning</td>
<td>Rapid heart rate</td>
</tr>
<tr>
<td>Tearing eyes</td>
<td>Muscle cramps and twitches</td>
</tr>
<tr>
<td>Chills and hot flashes</td>
<td>Tremor</td>
</tr>
<tr>
<td>Dilated pupils</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>Sweating</td>
</tr>
<tr>
<td>Nausea</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Irritability</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>High blood pressure</td>
</tr>
</tbody>
</table>
Appendix 3.1: Pharmacy-patient agreement for medication-assisted opioid dependence treatment services

This is an agreement for services provided for opioid dependence treatment involving
☐ methadone maintenance therapy  ☐ buprenorphine-naloxone
between
Patient name

and
Pharmacy name

As your pharmacy provider of medication-assisted opioid dependence treatment services, we are committed to your success to overcome your opioid dependency. This agreement highlights our mutual expectations while you are using our pharmacy services.

Your pharmacy agrees to provide you with:

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

As the patient on the medication-assisted opioid dependence treatment, I agree to:

1. Take methadone or buprenorphine-naloxone as treatment for my opioid dependence. I will take it as prescribed by my doctor. I will let my doctor and/or pharmacist know if I am experiencing any withdrawal effects or any side effects from the treatment.

2. Keep my regular daily meeting with my pharmacy to receive my daily dose. I will make every effort to be punctual and reliable and I will call the pharmacy if I am going to be late.

3. Bring and show my photo ID each time I visit my pharmacy for my daily dose.

4. The pharmacy calling my doctor if they have any concerns about my safety on the treatment(s).

5. The pharmacy calling my doctor if a dose is missed, lost, stolen, and/or partially administered.

6. Call the local police as well as my pharmacist if I lose a dose or if a dose in my possession is stolen, as the drug may be dangerous to the community.

7. Inform any other doctor, dentist, or pharmacy that I am on medication-assisted opioid dependence treatment. I will also inform my pharmacy and my doctor of any other drugs (prescription and non-prescription), natural health products, and vitamins that I take as I realize that some treatments may interact with my opioid dependence treatment and cause harm to me. My doctor may be more aware of this issue than a doctor not trained in this specialized treatment.

8. Notify my pharmacy and doctor if I become pregnant so they can consult and adjust my treatment as needed.

9. Take urine tests or other tests required to monitor progress and safety on medication-assisted opioid dependence treatment as directed by my doctor or pharmacist.

10. Be polite and respectful while on the premises of the pharmacy. I agree that I will not be disruptive, violent, abusive, or threaten or cause harm to anyone or to any property. I acknowledge that bad behaviour may result in the termination of my services from the pharmacy. Also, some offences may be brought to the attention of law enforcement as determined by provincial and federal legislation.
As the patient on the medication-assisted opioid dependence treatment, I am aware that:

1. The pharmacy will not provide me with my daily dose if I arrive intoxicated or with other symptoms where taking the dose may be harmful to me.

2. If I am not compliant with my daily doses, my treatment may have to stop as it can pose a danger to me to have inconsistent dosing.

3. Medication-assisted opioid dependence treatment may cause drowsiness, especially at the initiation of therapy and when doses are adjusted. I agree not to drive or operate machinery that requires my alertness when I am being initiated on therapy (typically the first two weeks) or when I am having doses adjusted or if I am having treatment effects that are making me sleepy and not alert.

4. Taking narcotics, sleeping pills, alcohol, or other sedating substances may interact with medication-assisted opioid dependence treatment to cause overdose, coma, or even death. I will not take other medications unless prescribed by either my medication-assisted opioid dependence treatment or pain doctor or my family doctor (if different).

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

_____________________________  ____________________________
Patient signature  Date

_____________________________  ____________________________
Pharmacy witness signature  Date

Appendix 3.1: Pharmacy-patient agreement for medication-assisted opioid dependence treatment services
Appendix 3.2: Prescriber-pharmacy-patient three-way agreement for methadone maintenance therapy

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

Methadone is a medication that is generally taken long-term and will require your commitment and responsibility to take the drug only as prescribed. A pharmacist will determine if it is safe for you to take your daily dose and then watch you as you ingest the dose. Observation of daily doses will continue until your doctor considers that you may be ready to try take-home doses. Some patients may never be considered for take-home doses if their personal safety and the safety of the community are of concern.

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

This agreement is between:

Your pharmacy and its staff

Your prescriber

You, our patient

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

Your pharmacy agrees to provide you with:

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

Your doctor agrees to provide you with the following:

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

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

1. Take methadone as treatment for my opioid dependence. I will take it as prescribed by my doctor. I will let my doctor and/or pharmacist know if I am experiencing any withdrawal effects or any side effects from the treatment.

2. Keep my appointments with my doctor. I know that my doses of methadone will only be prescribed if my doctor can monitor my response and progress. I know that my appointments are especially important in the initiation phase of therapy until I am stabilized on methadone because the first few weeks of therapy is a time when patients can be harmed by therapy. If I do not keep my appointments, my doctor may no longer be able to...
prescribe the drug to me.

3. Keep my regular daily meeting with my pharmacy to receive my daily methadone dose. I will make every effort to be punctual and reliable and I will call the pharmacy if I am going to be late. If I am not compliant with my daily doses, I am aware that my methadone treatment may have to stop as it can pose a danger to me to have inconsistent dosing with methadone.

4. Bring and show my photo ID each time I visit my pharmacy for my daily dose.

5. The pharmacy calling my doctor if they have any concerns about my safety on the treatment(s).

6. The pharmacy calling my doctor if a dose is missed, lost, stolen, and/or partially administered.

7. Call the local police, as well as my pharmacist and my doctor, if I lose a dose or if a dose in my possession is stolen, as the drug may be dangerous to the community.

8. Inform any other doctor, dentist, or pharmacy that I am on methadone treatment. I will also inform my pharmacy and methadone maintenance doctor of any other medication that I am prescribed as I realize that some treatments may interact with methadone and cause harm to me. My methadone doctor may be more aware of this issue than a doctor not trained in this specialized treatment.

9. Keep both my doctor and pharmacist informed of all the drugs (prescription and non-prescription) that I am taking, including natural health products and vitamins.

10. Take urine tests or other tests required to monitor progress and safety on methadone treatment as directed by my doctor or pharmacist.

11. Be polite and respectful while on the premises of the pharmacy. I agree that I will not be disruptive, violent, abusive, or threaten or cause harm to anyone or to any property. I acknowledge that bad behaviour may result in the termination of my services from the pharmacy. Also, some offences may be brought to the attention of law enforcement as determined by provincial and federal legislation.

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

1. The pharmacy will not provide me with my daily methadone dose if I arrive intoxicated or with other symptoms where taking the methadone dose may be harmful to me.

2. Methadone may cause drowsiness, especially at the initiation of therapy and when doses are adjusted. I agree not to drive or operate machinery that requires my alertness when I am being initiated on therapy (typically the first two weeks) or when I am having doses adjusted or if I am having treatment effects that are making me sleepy and not alert.

3. Taking narcotics, sleeping pills, alcohol, or other sedating substances may interact with methadone to cause overdose, coma, or even death. I will not take other medications unless prescribed by either my methadone or pain doctor or my family doctor (if different).

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

______________________________________________________________
Patient signature

______________________________________________________________
Date

______________________________________________________________
Pharmacy representative signature

______________________________________________________________
Date

______________________________________________________________
Prescriber signature

______________________________________________________________
Date

Appendix 3.2: Prescriber-pharmacy-patient three-way agreement for methadone maintenance therapy
Appendix 3.3: Prescriber-pharmacy-patient three-way agreement for buprenorphine-naloxone therapy

Your prescriber prescribed therapy with buprenorphine-naloxone treatment for your opioid dependence disorder. Our pharmacy will provide the services for buprenorphine treatment.

Buprenorphine is a medication that is generally taken long-term that will require your commitment and responsibility to take the drug only as prescribed by your doctor. It is usually administered in the presence of a pharmacist or trained health professional who, for your personal safety and well-being, will be required to determine if it is safe for you to take your daily dose and then watch you as the medication is administered. Observation of daily doses will continue until your doctor considers that you may be safe to try take-home doses. Some patients may never be considered for take-home doses if their personal safety and the safety to the community are of concern.

Your doctor and pharmacist will be working together to support your success with therapy and, as such, they may consult each other, your family doctor (as applicable), or other members of your treatment team, if issues and concerns arise as you progress with your treatment. You are also welcome to consult your doctor or pharmacist as needed if you have issues and concerns regarding your condition or your treatment.

This agreement is between:

Your pharmacy and its staff

Your prescriber

You, our patient

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

Your pharmacy agrees to provide you with:

• Professional, non-judgmental services that recognize your rights to respect and personal dignity.

• Access to trained professionals who are competent in buprenorphine-naloxone therapy to answer your questions and concerns about your treatment(s).

• Professional expertise, skills, and knowledge about your treatment that will always have your best health interests in mind for decisions that are made.

• Privacy and confidentiality with your private and health information. Your private information will only be shared with your consent or unless we are required by law.

• Ongoing monitoring of your response and progress with methadone while you remain under the pharmacy’s care.

Your doctor agrees to provide you with the following:

• Professional, non-judgmental, services that recognize your rights to respect and personal dignity.

• Professional expertise, skills, and knowledge about your treatment that will always have your best health interests in mind for decisions that are made.

• Regularly scheduled appointments offered at a frequency that is deemed necessary for your personal health and safety and that is based on your progress and needs while on methadone treatment.

• Ongoing monitoring of your response and progress with methadone while you remain in his or her care.

• Privacy and confidentiality with your private and health information. Your private information will only be shared with your consent or unless required by law.

As the patient on the buprenorphine-naloxone treatment, I agree to:

1. Take buprenorphine-naloxone as treatment for my opioid dependence. I will take it as prescribed by my doctor. I will let my doctor and/or pharmacist know if I am experiencing any withdrawal effects or any side effects from the treatment.

2. Keep my appointments with my doctor. I know that my doses of buprenorphine-naloxone will only be prescribed if my doctor can monitor my response and
progress. I know that my appointments are especially important in the initiation phase of therapy until I am stabilized on buprenorphine-naloxone because the first few weeks of therapy is a time when patients can be harmed by therapy. If I do not keep my appointments, my doctor may no longer be able to prescribe the drug to me.

3. Keep my regular daily meeting with my pharmacy to receive my daily buprenorphine-naloxone dose. I will make every effort to be punctual and reliable and I will call the pharmacy if I am going to be late. If I am not compliant with my daily doses, I am aware that my buprenorphine-naloxone treatment may have to stop as it can pose a danger to me to have inconsistent dosing with buprenorphine-naloxone.

4. Bring and show my photo ID each time I visit my pharmacy for my daily dose.

5. The pharmacy calling my doctor they have any concerns about my safety on the treatment(s).

6. The pharmacy calling my doctor if a dose is missed, lost, stolen, and/or partially administered.

7. Call the local police, as well as my pharmacist and my doctor, if I lose a dose or if a dose in my possession is stolen.

8. Inform any other doctor, dentist, or pharmacy that I am on buprenorphine-naloxone treatment. I will also inform my pharmacy and doctor of any other medication that I am prescribed as I realize that some treatments may interact with buprenorphine-naloxone and cause harm to me. My buprenorphine-naloxone doctor may be more aware of this issue than a doctor not trained in this specialized treatment.

9. Keep both my doctor and pharmacist informed of all the drugs (prescription and non-prescription) that I am taking, including natural health products and vitamins.

10. Take urine tests or other tests required to monitor progress and safety on buprenorphine-naloxone treatment as directed by my doctor or pharmacist.

11. Be polite and respectful while on the premises of the pharmacy. I agree that I will not be disruptive, violent, abusive, or threaten or cause harm to anyone or to any property. I acknowledge that bad behaviour may result in the termination of my services from the pharmacy. Also, some offences may be brought to the attention of law enforcement as determined by provincial and federal legislation.

---

**As the patient on the buprenorphine-naloxone treatment, I am aware that:**

1. The pharmacy will not provide me with my daily buprenorphine-naloxone dose if I arrive intoxicated or with other symptoms where taking the buprenorphine-naloxone dose may be harmful to me.

2. Buprenorphine-naloxone may cause drowsiness, especially at the initiation of therapy and when doses are adjusted. I agree not to drive or operate machinery that requires my alertness when I am being initiated on therapy (typically the first two weeks) or when I am having doses adjusted or if I am having treatment effects that are making me sleepy and not alert.

3. Taking narcotics, sleeping pills, alcohol, or other sedating substances may interact with buprenorphine-naloxone to cause overdose, coma, or even death. I will not take other medications unless prescribed by either my buprenorphine-naloxone or my pain doctor (if different).

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

---

Patient signature

Date

Pharmacy representative signature

Date

Prescriber signature

Date
Appendix 3.4: Agreement and consent for take-home doses of methadone

Your doctor has authorized us to provide you with take-home doses (carries) of methadone that you can take yourself on selected days as indicated on each single-dose bottle.

I agree to the take-home (carry) doses of methadone that my physician has prescribed for me. I understand and agree to the following responsibilities:

1. I will pick up my carries in person and will show my valid identification to the pharmacy staff or pharmacist when I pick up the take-home doses.

2. I will store my carries in the locked or secured box in which they are dispensed by the pharmacist. The pharmacist will inform me of the proper place to store my carries (e.g., refrigerator for diluted carries or at room temperature in a locked cupboard if I receive undiluted carries).

3. I will store and take the methadone in such a way that it cannot be accidentally ingested by anyone.

4. I will take the dose as prescribed by my doctor and on the ingestion date that is specified on the label of each bottle. I understand that each bottle contains one full diluted dose and that I am to follow the labelled instructions.

5. I will save all my bottles with their original labels left intact and bring them back to the pharmacy for the pharmacist to check that I have taken my medication and for proper disposal of the bottles.

6. I am aware that for my personal safety, my pharmacist may call me to come in for a random check during the carry period. The pharmacist may ask me to bring in all my full and empty bottles at such a time. I am aware that my doctor agrees with this decision and I will comply with the request.

7. I am aware that my pharmacy will not replace lost, stolen, spoiled, spilled, or vomited doses, and I will abide by this policy.

8. I will call my doctor or my pharmacist if I have any withdrawal symptoms or side effects.

9. I am aware of the side effects of methadone that are considered medical emergencies and I will go immediately to the hospital emergency room if I experience any of these side effects.

10. I am aware that for my personal safety and for the safety of the public, take-home doses of methadone can only continue if I am responsible with the medication and if I remain clinically stable on the drug.

Patient signature

Date

Witness signature

Date

Important information

Methadone is a very powerful medication. Even small doses can harm or kill a child. Methadone can also be fatal to an adult if accidentally ingested. You are responsible for properly securing and storing your methadone so that others cannot be harmed from an accidental exposure.
Appendix 4.1: Patient record of drug administration

<table>
<thead>
<tr>
<th>Date</th>
<th>Time of ingestion</th>
<th>Drug (Methadone or Suboxone)</th>
<th>Dose ingested</th>
<th>Witnessed by (initials)</th>
<th># of carries</th>
<th>Date carry received</th>
<th>Patient signature</th>
<th>Notes (# of carry bottles returned)</th>
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### Appendix 4.2: Dilution record

**Special instructions:**
Label with 14 day expiration from date of dilution. Keep refrigerated.

<table>
<thead>
<tr>
<th>Staff name (please print)</th>
<th>Initials (for file)</th>
<th>Staff name (please print)</th>
<th>Initials (for file)</th>
<th>Special instructions</th>
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<tbody>
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<table>
<thead>
<tr>
<th>Date prepared</th>
<th>Prescription #</th>
<th>Prescribed methadone dose</th>
<th>Quantity used</th>
<th>Ingredient name</th>
<th>Lot #</th>
<th>Expiry date</th>
<th>Beyond-use date of diluted cherry</th>
<th>Prepared by</th>
<th>Checked by</th>
<th>Number of doses prepared</th>
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**Label instructions:**
- Label with 14 day expiration from date of dilution.
- Keep refrigerated.
Appendix 5.1: Checklist of things to do when receiving a methadone prescription

- Ensure the prescription is on a triplicate prescription form.
- Confirm the purpose of the methadone (dependence or analgesia).
- Confirm that the prescriber has an exemption to prescribe methadone for the use ordered on the prescription.

If you cannot confirm all three of these points, do not fill the prescription.

If the prescription is for methadone maintenance treatment:
- Confirm the patient’s identification.
  - Require a valid document with photo identification.
  - Make a copy of the identification to affix to the patient’s file and ask staff to confirm identity before every witnessed ingestion.

Before providing the first dose, you must:
- Explain the drug and pharmacy services and expectations to the patient.
- Have the patient sign a two-way or three-way agreement before initiating treatment.
- Provide the patient with a copy of the agreement.
  - If it is a three-way agreement, provide them with a preliminary copy until you are able to obtain the physician’s signature on the document. Check in advance that MMT prescribers in your area to are satisfied with the agreement’s wording and agree to receive and sign it.
- Start a patient profile and take a patient medication and health history to identify things you should know to optimize efficacy and safety while on treatment. Record information about drug allergies, other medications, alcohol use, smoking history, other health problems (e.g., any cardiac disease or heart problems, any problems with sleep, mental wellness), important contacts in case of emergency, and special instructions.
- Document your consultation with the patient and/or with their caregivers.
- Monitor patient for signs and symptoms of intoxication from other substances such as alcohol, sedatives, stimulants, or opioids. You can ask the patient if they have taken any of these substances and the time that they were last used.
- When you are satisfied that the patient meets the conditions to initiate treatment, you can have the dose dispensed and provide it to the patient for ingestion.

- Document the witnessed ingestion on the appropriate form which includes date, dose, time of administration and person who witnessed the ingestion. All witnessed doses should have the observer’s signature or initials distinctly identified on the document.
- Have the patient wait for about five minutes before they leave the pharmacy. Document any pertinent details for other staff who may be serving the same client.
- Remind the patient of store hours and the next scheduled dosing time and date.
Appendix 5.2: Pharmacist-prescriber faxed communication

Pharmacy name: ____________________________________________

Pharmacist: _______________________________________________

Date: ____________________________  Time: _______________________

Pharmacy phone #: __________________________  Pharmacy fax #: _______________________

Dear Dr. ____________________________________________________:

For your records, please note that your patient, ____________________________,
is taking ____________________________ for opioid dependence treatment.

The following problems have occurred:

☐ Missed his/her dose on (date): _____________________________

☐ Vomited his/her dose on (date): _____________________________

☐ Witnessed by pharmacist
☐ Witnessed by another health care professional
☐ Vomiting not witnessed

☐ Reported a lost or stolen dose on _____________________________

We require a prescription to clarify the dose of ongoing treatment.

The last dose of ____________________________ was ____________________.
It was ingested on the following date: ____________________________.

☐ This dose was witnessed by a pharmacist
☐ This dose was not witnessed by a pharmacist

Please fax us a triplicate prescription indicating the ongoing treatment dosage.

Sincerely,
Appendix 6: Methadone patient information sheet

What is methadone?
Methadone is an opioid that is used to treat your opioid dependence. It has been used to manage opioid addictions for more than 40 years. It is effective in treating opioid dependence because methadone generally does not make you feel high and once you are on a stable dose, it is unlikely to cause intense withdrawal side effects over a 24 hour period because it has a longer duration in your body than other opioids. In fact, once you are stabilized on a dose, you may feel quite normal.

What should I expect when I start treatment with methadone?
- Methadone should only be used under the careful supervision of trained health professionals. It is a safe drug when used appropriately but it is also a drug that can be very toxic. Methadone can be lethal in overdose.

- Methadone is a drug that requires your patience and commitment. It can take several days to reach its full effect. A dose that seems to barely have an effect on the first day can become toxic by the third or fifth day. This is why dose adjustments are rarely made until you have been on the same dose for four days. The gradual dose increases ordered by your doctor are for your safety. Most deaths occurring from methadone occur during the first few weeks of starting therapy. You need to be aware of the signs that the methadone is working, and be able to distinguish these from side effects and from symptoms of methadone toxicity. If you experience side effects, alert your doctor or pharmacist. If you experience symptoms that are associated with methadone toxicity, go to a hospital—this requires immediate attention.

- To optimize safety, you will receive daily witnessed doses of methadone from your pharmacy when you first start methadone. Your methadone dose will be mixed in a flavoured drink such as Tang™ and you will ingest the dose in front of the pharmacist.

- You are supposed to feel normal on methadone, not high, and not sleepy. Methadone levels in your system are more stable and don’t fluctuate up and down like that of other opioids, so you should eventually be more comfortable on methadone than on other opioids.

- It usually takes two to six weeks to stabilize on methadone maintenance treatment.

Safety tips
- Do not drive or operate machinery during the initiation phase of methadone maintenance treatment and during periods of dose adjustment.

- Never take extra doses on your own. Never accept doses from friends or others who take methadone.

- Never give your drug to others. Store the medication appropriately. Even a small dose can harm or kill a child or an adult who has not taken opioids.

- Methadone can be toxic in combination with benzodiazepines, alcohol, or other central nervous system depressants. Make sure your doctor and pharmacist are aware of everything you take including all prescription drugs, natural health products, vitamins, and non-prescription drugs.

- Tell a trusted friend or house mate about some of the symptoms of methadone toxicity so that they can help to keep an eye on you until you become stabilized on therapy. This is especially important during the first two weeks of treatment. They should know that toxicity to methadone is a medical emergency requiring an immediate trip to the hospital. If toxicity does occur, it is possible that you may not have the alertness to be self-aware of the symptoms, so it is good to have a friend as a “back-up” to assist you.

- It is safer and preferable to take your methadone dose in the morning so that side effects are more appropriately noticed and can be monitored when you are awake. The risks from excessive doses are greater if they occur overnight as they are likely to be missed.

- If you become pregnant, notify your doctor immediately so they can assess the situation and minimize risks to the developing fetus by dosing and monitoring your treatment.

- Those who do not intend to become pregnant while on methadone should protect themselves using up to two methods of reliable birth control.

Side effects from methadone
Most common: Light-headedness, nausea, dizziness, sedation, vomiting, sweating, constipation, sexual dysfunction, dry mouth, dry eyes and nose, and changes to sleep patterns.
You may experience cravings or symptoms of withdrawal during the induction or initiation phase of therapy as your methadone is adjusted to the right dose for your body and needs. Report any symptoms to the pharmacist each day and/or your doctor.

**When to seek immediate medical attention**

Be aware of the early signs of methadone toxicity such as falling asleep or decreased alertness, nodding off during the day, slurred speech, clumsiness or unsteadiness, feeling emotionally unstable, being forgetful, or appearing like you are drunk. If any of these side effects occur, it is a medical emergency and you need to go to a hospital immediately.

**Your pharmacy’s hours of service are:**

Monday

Tuesday

Wednesday

Thursday

Friday

Saturday

Sunday

Closed on: ___________________________________________________________________

Your daily methadone dosing time is scheduled for:

___________________________________________________________________________

- Arrive for regular daily witnessed dosing at the scheduled time agreed. ________________
- Phone if you are running late or need to change the time of your arrival. (Phone #: )
- If your pharmacy is closed on certain days, an arrangement will be made for you to obtain your doses during days when the pharmacy is closed.
Appendix 7: Process flow: Dispensing medication-assisted treatment for opioid dependence

- Receive prescription on a triplicate prescription form.
- Confirm prescription authenticity and prescriber exemptions.
- Confirm patient’s identification (photo identification is preferable).
- Gather information from the patient and document patient agreement when initiating treatments. For ongoing treatment, update patient profile as needed.
- Check for appropriateness, accuracy, and drug therapy problems before dispensing or releasing a dose.
- Ensure the patient does not have symptoms of intoxication.
- If satisfied with all issues, dispense dose(s).
- Witness the ingestion and ensure that the patient takes the dose properly.
- Document every witnessed dose or every missed dose.
- Document to ensure there is an audit trail for compounding, dispensing, administering, and cognitive service activities.

- Ensure prescription meets all standard prescription requirements in Alberta, including those in the Pharmacy and Drug Act, Controlled Drugs and Substances Act, Alberta College of Pharmacy Standards of Practice for Pharmacists and Pharmacy Technicians, Narcotic Control Regulations, and the Triplicate Prescription Program.
- Determine if the methadone is for dependence, analgesia, or both.
- Confirm that the physician has an exemption to prescribe methadone for the clinical circumstance requested.
- Confirm that the physician meets the training requirements for initiating or maintaining methadone and/or buprenorphine-naloxone with the College of Physicians & Surgeons of Alberta.
- To check for exemptions, contact CPSA at 1-800-561-3899 or the Office of Controlled Substances, Health Canada at 1-613-946-5139, or email exemption@hc-sc.gc.ca.

- Take a patient history. Record drug allergies, concomitant drugs and conditions, opioid use, sedatives, alcohol, smoking, substances of abuse, and emergency contacts.
- Counsel the patient about the prescribed treatment.
- Review and sign a two- or three-way agreement.

- Monitor the patient for withdrawal from opioids.
- Monitor the patient for toxicity from opioids or other substances of abuse. Check for pinpoint pupils, altered speech or gait, and alcohol or marijuana odours.

- Administer the methadone to the patient. You may administer Methadose™ undiluted if using the cherry-flavoured red syrup. If using the sugar-free, dye-free solution, dilute it in a suitable crystalline drink.
- When diluting Methadose™, use the dilution record to record the date of dilution, the lot number and expiry dates of both the Methadose™ and the diluent, the signatures of persons diluting and checking, and the use-by date.
- Administer buprenorphine-naloxone sublingually. Multiple tablets are optimized if taken all at once. Split tablets in half to facilitate dissolution.

- Record the observed daily administration on patient’s drug administration record. Include the date, time, dose, and signature of the person who witnessed the dose. Document pertinent observations, notes, and concerns. Confirm prescription authenticity and prescriber exemptions.

Carry requirements:
- Receive triplicate prescription from prescriber.
- Ensure patient has signed a carry agreement.
- Dispense with required instructions on each dose.
- Send home in a locked or secured box.
- Include instructions to patients to prevent harm to self or others.
- Schedule interim witnessed ingestion as necessary.
- Ensure that the patient returns all used bottles with original intact labeling.
- Record dispensing and have patient acknowledge receipt of carries through signature.
Summary of Standards: Medication-assisted treatment for opioid dependence disorders

1. Comply with provincial and federal rules and regulations.

2. Collaborate with prescribers and other healthcare professionals involved in the patient’s care.

3. Establish and maintain professional relationships with patients.

4. Assess the appropriateness of each prescription.

5. Identify, consider, assess, and take appropriate action on drug therapy problems before providing a treatment.

6. Confirm the identity of each patient before dispensing, releasing, or administering a prescription.

7. Follow proper procedures for dispensing and compounding, including determining the authenticity of prescriptions.

8. Use appropriate labeling and packaging.

9. Document appropriately to ensure that an audit trail of all the people and processes involved in dispensing and administering the final process can be identified.

10. When administering a drug, optimize the environment, comfort, and privacy of the patient.

11. Ensure that proper emergency procedures are available.

12. Create and maintain patient records.

13. Optimize the potential for the patient to receive the intended benefit of therapy.


1Standards of Practice for Pharmacists and Pharmacy Technicians.

Disclaimer: This document is intended to highlight the work flow and processes involved in dispensing methadone and other substitution therapies to manage opioid addition. Health professionals are advised to use their professional judgment and to consult available literature when dispensing or counseling patients and other health professionals about these therapies. This document should not replace sound professional judgment.
Addendum: Compounding methadone

Background
In Alberta, methadone should only be compounded in exceptional circumstances. Commercially manufactured methadone is available in the following formulations:

1. Methadose™ is available for use for opioid dependence.
2. Metadol™ is available for analgesia.

Health Canada provides the following guidance regarding compounding:

- Methadone should only be compounded if there is a specific therapeutic need or a shortage of a commercially available product, and should not be done solely for economic reasons that benefit the involved healthcare professionals.

- The compounded product must provide a customized therapeutic solution to improve patient care without duplicating an approved drug product.

Addendum to ODT Guidelines: Compounding methadone

Practice standards and responsibilities

Standards
Pharmacists and pharmacy technicians who compound methadone must comply with the following standards and responsibilities:

• Compliance with Health Canada’s policy on manufacturing and compounding drug products in Canada.
• Be aware of changes to the laws that govern their practice and adjust their practices to ensure compliance with the changes. (S1.2, S1.3)
• Pharmacists and pharmacy technicians dispensing a Schedule 1 drug must ensure that they fill the prescription correctly, that they use appropriate dispensing procedures, that they properly package and label the drug, and that they perform a final check. (S7)
• Pharmacists and pharmacy technicians must compound according to a written compounding formula and a written preparation process. (S10)
• Pharmacists and pharmacy technicians must assign compounded products a beyond-use date and ensure that the products are not to be used after this date. (S10)
• A pharmacist or pharmacy technician who repackages drugs must take appropriate steps to protect patient safety. (S21)
• Pharmacists and pharmacy technicians must create and maintain appropriate patient records for dispensing and administration. (S18)
• Records must demonstrate an audit trail of staff involved in each process in the preparation, dispensing, and administration of the final product. (S7, S10, S21)
• Pharmacists must ensure that those whom they supervise act within the limits of their profession or training. (S20)

Responsibilities
• Pharmacists and pharmacy technicians must use proper equipment for compounding. Measuring devices must meet error allowances for weights and measures during the preparation of stock solutions and carries.
• For health reasons and risk mitigation, pharmacists and pharmacy technicians must not reuse carry bottles.
• In light of the potential of toxicity and lethality from errors involving methadone, pharmacies should organize their compounding areas and processes to optimize safety to staff and patients.
• The beyond-use date assigned to products must recognize the ingredients and the compounding processes. Pharmacies choosing to use beyond-use dates in excess of 14 days should provide support for stability and sterility from guidelines, published literature, or laboratory batch testing.
• A second qualified staff member should double check all preparations.
• Pharmacy staff should label and store all equipment used for compounding methadone separately from other equipment.
• Pharmacy staff should clearly identify methadone stock solutions, preferably using bottles, colours, or stickers that distinguish the preparation.
• There must be a working refrigerator on the premises to store prepared carries or other compounded methadone products. Pharmacy staff must monitor and routinely record the refrigerator temperature to maintain the cold chain.
• Pharmacists and pharmacy technicians involved in compounding methadone must remain responsible for the delivery of all components of activities that fall under the standards and expectations of their regulated profession.

Formulating methadone stock solutions
Pharmacists and pharmacy technicians are both authorized to compound and prepare methadone. Staff compounding methadone must be competent in the processes and use of equipment to compound the stock solution.

• Prepare methadone stock solution within a clean and organized environment following work processes that minimize the risk of error and mix-ups with other pharmaceuticals.
• Ensure that equipment or devices used to prepare the stock solution meet compounding standards for accuracy of measuring devices (e.g., glass graduated cylinders and oral syringes with marked volumes).
• If possible, pharmacies should label measuring equipment used to prepare methadone compounds and keep this equipment separate for the sole purpose of compounding methadone. If this is not possible, all equipment used must be properly washed and cleaned before reuse to prevent cross-contamination with other preparations.
• If possible, pharmacies should prepare only one standard concentration of methadone stock solution.
most common to their patient population to minimize the risk of error. Common strengths include 1 mg/ml, 5 mg/ml, and 10 mg/ml.

- Label the stock solution distinctly. The label should include:
  - The ingredients and concentration of the solution (e.g., methadone 10 mg/ml stock solution in distilled water), and
  - The expiry date or use-by date of the solution.

Note: If it is difficult to label the bottle distinctly, pharmacies can also use a distinct bottle.

- To avoid mix-ups, store compounded solutions in a separate area away from other solutions. Label and identify the compounded solution in such a way that it is visibly distinct from other solutions. This may include a distinct bottle with appropriate labeling. A boldly marked label and a poison sticker should be included in the labeling of the methadone solution.

The pharmacy must keep a bulk compounding log and record the following information for each prepared solution:

- Date prepared;
- Assigned batch number;
- Names (printed legibly) and signatures of personnel involved in preparing and/or checking the preparation;
- Name, quantity, lot numbers, and expiry dates of ingredients used to prepare the stock solution (e.g., methadone, distilled or bacteriostatic water, preservatives etc.);
- Concentration of the final solution;
- Volume of the final solution; and
- Expiry date or beyond-use date.

Stability of methadone
Methadone in powder form is very stable. Methadone has a long stability when distilled water is used as the diluent in preparing the stock solution. However, without a preservative, the shelf-life of methadone prepared in distilled water may be shortened; monitor for bacterial growth.

In spite of the excellent stability of methadone in distilled water, there can be variability in the compounding environment, processes, and techniques that can deviate from the conditions within a testing environment where published stability and sterility studies have originated.

Many factors can impact the sterility of the final product. Pharmacists and pharmacy technicians should base the stability and sterility of stock solutions on current evidence and consideration of pharmaceutical principles of compounding.

Attention has shifted to acknowledging the possibility of growth of bacteria or other pathogenic organisms within the prepared formulation. Therefore, the current recommendation is to discard stock solution prepared without a preservative after 14 days. This includes solutions prepared with distilled water.

For pharmacies choosing to prepare formulations with a preservative, methylparaben 0.5g/L or propylparaben 0.2 g/L are both appropriate preservatives with which to prepare stock solution.

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

Dispensing compounded methadone
Unless otherwise indicated by the prescriber, pharmacists must dispense all compounded methadone in a diluted juice or crystalline drink deemed compatible with the methadone. If the prescriber directs the pharmacist to deviate from this standard, the prescriber must provide and document a clear rationale on the prescription.

- Dilute the prescribed dose in approximately 100 ml of a coloured, flavoured vehicle such as Tang™ crystalline drink or Kool-Aid™. Plain water is not acceptable. Dilution in a 100 ml volume of flavoured drink will:
  - Mask the bitter taste of methadone,
  - Prevent abuse by injection due to the sugar content and exipients in the crystalline drink or juice, and
  - Discourage diversion.

- Dispensing guidelines within many provincial jurisdictions have identified the duration of stability of methadone in various diluents from a collection of past literature; however, the available literature has not addressed the issue of sterility which includes the likelihood of bacterial growth of the prepared solution stored under refrigerated or unrefrigerated conditions.

- To avoid the potential for mix-ups during dosing, formulations further diluted for administration should not be prepared far in advance. Additionally, given the variability in the compounding environment and processes, consider the aspect of bacterial growth within the prepared formulation.

Diluents

1. Methadone formulations that are prepared in advance for carries or witnessed dosing may use the examples of diluents listed in the table below. If stored under refrigeration, the preparation should be used within 14 days of compounding. If the product is prepared in
Allen’s Apple Juice, discard it after seven days if stored under refrigeration.¹

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

3. Pharmacies may consider stability and sterility tests of their prepared formulations to support decisions to extend expiry dates beyond the guidance provided in this document. Pharmacies are encouraged to use reputable sources and to maintain records of their findings.

Table 1: Methadone stability in various diluents for carries

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


¹ Metadol™ product monograph (March 2009).
# Bulk compounding record

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<tr>
<th>Name and concentration:</th>
<th>Special instructions:</th>
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| Storage instructions & expiry: | |
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<th>Initials (for file)</th>
<th>Staff name (please print)</th>
<th>Initials (for file)</th>
<th>Special instructions</th>
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<table>
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<th>Quantity used</th>
<th>Ingredient name</th>
<th>Lot #</th>
<th>Expiry date</th>
<th>Final strength</th>
<th>Final volume</th>
<th>Beyond-use date</th>
<th>Prepared by</th>
<th>Checked by</th>
<th>Notes</th>
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Addendum to ODT Guidelines: Compounding methadone