

1000 – 1661 Portage Avenue Winnipeg, MB R3J 3T7 Tel: (204) 774-4344 Fax: (204) 774-0750 Toll Free (MB only) 1-877-774-4344

www.cpsm.mb.ca

MANITOBA OPIOID AGONIST THERAPY RECOMMENDED PRACTICE MANUAL

3.2 Recommendations for Methadone Induction, Titration, & Stabilization in the Treatment of Opioid Use Disorder

GENERAL CONSIDERATIONS

This chapter will outline recommendations for methadone induction for the treatment of opioid use disorder (OUD). Dose titration and key considerations through early to later stages of stabilization will also be discussed. While buprenorphine/naloxone is considered first-line therapy for the treatment of OUD, methadone is an evidence-based and effective alternative for many individuals, as discussed in other sections of this manual. Please refer to Recommendations for OUD for further guidance on treatment approaches.

The most common reason for death or non-fatal overdose from methadone treatment is overly aggressive prescribing/dose-titration during the first two weeks of treatment. The combination of overestimated cross-tolerance and underestimated serum-level accumulation of methadone is the main cause. After stabilization, the most common reason for significant complications is drugdrug interactions, typically with sedative/hypnotic medications and/or substances. Appropriate dosing during each phase of methadone treatment is therefore vital for patient safety.

Methadone doses are self-administered under the direct supervision of a pharmacist, approved prescriber, or nurse, until candidacy for a take-home dosing schedule is established.

The Centre for Addiction and Mental Health (CAMH) recommends that methadone be prescribed "in a way that balances the risk of adverse effects to the patient and people in their environment while optimizing the benefits, including retention in treatment and decreased health and quality-of-life harms related to substance use"¹.

Patient and community safety must remain at the forefront of treatment decisions when providing opioid agonist therapy (OAT), particularly with methadone treatment. Providers must ensure that patients receive adequate education regarding the risks involved, as care plans are negotiated and adjusted over time. Please see the Pharmacology of Methadone & Management of Adverse Effects for further details.

SPECIFIC CONSIDERATIONS

INITIATING OPIOID AGONIST THERAPY

Urgency of OAT Induction

Following the decision to initiate OAT, induction should be arranged urgently, ideally the same day or within 2-3 days of presentation. When access to OAT induction within this timeframe is not feasible due to patient, prescriber, geographic, or systemic factors, other interventions should be considered in the interim, including harm reduction strategies (e.g., clean supplies, naloxone), patient safety education, wound care, psychosocial support, and access to primary care and other forms of addiction treatment.

Providers involved in addiction treatment are encouraged to advocate for improved access to OAT in their region of practice.

Initial Assessment & Patient Education

Patients must undergo a comprehensive assessment including history and focused physical examination to establish the diagnosis of OUD before initiating OAT. Please see <u>Initiating OAT:</u>
Comprehensive Assessment, <u>Diagnosis</u>, <u>Informed Consent & Investigations</u> for detailed guidance on the assessment process.

Where immediately available, point-of-care urine drug screening should be performed. This is a useful clinical tool in the context of the initial assessment. Relevant lab work, including an STBBI screening, should also be ordered and completed as soon as practically feasible. While urine drug testing and other investigations are ideal on initial assessment or in early treatment, they should not delay access to timely treatment if OAT is indicated².

Consideration for methadone as an alternative to buprenorphine/naloxone may be appropriate in the presence of:

- Severe liver disease, such as advanced cirrhosis, that is causing problematic withdrawal symptoms (where activity of the naloxone component is enhanced due to reduced first pass effect).
- Previous failed treatment with buprenorphine/naloxone, severe side effects, or an allergy/intolerance to buprenorphine, naloxone, or to any ingredient in the formulation.

- Patient preference for methadone treatment, despite education regarding the enhanced safety and potential benefits of buprenorphine/naloxone.
- Very high opioid tolerance unlikely to stabilize on a partial opioid agonist.

Patients must be educated about the symptoms and signs of early opioid toxicity and overdose, and must be offered access to a naloxone kit at the time of induction.

Prescribers should also obtain and document informed consent for methadone treatment. The use of a written **Treatment Agreement** is strongly recommended. Informed consent and treatment agreements are also discussed in the <u>Comprehensive Assessment</u> chapter.

Clinical Stability & Treatment Goals

Prescribers should discuss and document the goals of treatment prior to induction and at regular intervals during follow-up. Both provider and patient-driven goals should be used to inform treatment decisions and support continued methadone prescribing.

While buprenorphine/naloxone often allows for rapid dose titration (see <u>Recommendations for Conventional Buprenorphine Induction</u>) methadone induction and titration MUST be approached slowly and cautiously. It may take several weeks to address opioid withdrawal effectively. It is important to be upfront with patients about this requirement and to discuss ways to cope with ongoing withdrawal and cravings, to maintain engagement in treatment.

However, unlike the conventional buprenorphine induction, methadone can be initiated without the prerequisite presence of opioid withdrawal. This may be preferential for some patients. The patient's dose should be titrated with a "start low and go slow" approach, based on regular clinical assessment, until initial dose stability is reached – see specific recommendations below.

A stable dose is achieved when opioid withdrawal is eliminated or adequately suppressed for 24 hours to allow patients to further engage in ongoing medical and psychosocial treatment. **The ultimate goal is to work toward clinical stability**, which is characterized by, but not limited to:

- Absence of opioid withdrawal symptoms and significantly reduced cravings
- Absence or significant reduction in illicit substance use (self-reported and supported by urine drug testing)
- Financial and/or employment stability
- Housing stability
- Improvements in self-care and wellness practices
- Strengthening of supportive relationships (and/or navigating difficult relationships)
- Improvements in mental and physical health

PREPARATION FOR INDUCTION

In most cases, methadone can be safely started in the community.

If concurrent use of sedative/hypnotic medications and/or substances are a concern, and/or if comorbid conditions could contribute to increased risk of respiratory depression or opioid toxicity during induction, further consultation with an addiction medicine specialist is recommended. Inpatient admission for induction and closer monitoring may be warranted, and further consideration of buprenorphine/naloxone may be required.

Collaboration with Pharmacy

Collaboration with the pharmacist is strongly encouraged prior to induction and should include the following:

- Verify the pharmacy provides OAT (with methadone). It is important to note that not all
 pharmacies in Manitoba dispense OAT, as specialized training is required. Thus, it is
 important to confirm that a pharmacy does dispense methadone prior to faxing an OAT
 prescription to that pharmacy.
- Communicate the plan. Sharing the plan for follow-up/titration and communicating an action plan if the patient misses any doses, appears intoxicated or unusually sedated, and/or receives sedating/psychoactive medication from a different prescriber during the induction phase is helpful for all those involved.
- Share special instructions. Specifying any special instructions for induction on the M3P prescription can be useful to prevent dosing errors and confusion.
- Provide comprehensive prescriber contact info. Supplying the pharmacy with method(s)
 to contact the prescriber/office outside of regular clinic hours is vital to ensuring that
 urgent clinical matters can be addressed quickly.

See Relationship with Pharmacy & Prescriptions for OAT for further recommendations.

THE EARLY STABILIZATION PHASE (0-2 WEEKS)

Methadone has a significant risk of morbidity and mortality during the early stabilization phase.

Since methadone has a highly variable elimination half-life of 22 to 48 hours and time to reach steady state can vary from 3 to 7 days, the clinical response can be difficult to predict. Additionally, methadone is a full agonist and has no ceiling effect. Thus, dose accumulation may lead to toxicity and serious harm if the induction dose is too high, or the dose is increased too quickly. A dose that is barely adequate on day one can be toxic after a few days at the same dose.

Clinical Assessment of Opioid Withdrawal

When clinically assessing opioid withdrawal, prescribers should consider using the Clinical Opiate Withdrawal Scale (COWS) to assess and document the severity of opioid withdrawal during methadone induction and titration (see **Appendix Z**). This helpful clinical tool utilizes objective and subjective measures of withdrawal and can assist in determining appropriate dosing during the early stabilization phase.

Of note, evidence of clinical opioid withdrawal is not necessarily required to start methadone if indicated, based on a thorough history including knowledge of the specific opioids (and other substances) consumed, their potency, duration of action, and urine drug screen results.

Conversely, if the patient appears sedated, somnolent, or intoxicated, methadone induction should be postponed until they can be reassessed to avoid opioid/multidrug toxicity or overdose.

Start Low & Go Slow

Methadone overdose can have an insidious onset. A patient appearing relatively alert during the day may succumb to an overdose during a nap or at night.

Early signs of toxicity include feeling tired or "nodding" during low stimulus activities, such as watching TV or attending a lecture in school. Ataxia, nausea/vomiting, slurred speech, euphoria, and slow or laboured breathing may be signs of progressive toxicity and require urgent medical attention. Careful prescribing, patient education, and intervention at the first sign of toxicity can reduce the risk of overdose. Again, patients must be offered access to a naloxone kit at the time of induction, and patients and their family/supports must be educated about the early signs of opioid toxicity. It is imperative that the dosing protocols below be followed to minimize the risks in early treatment.

The following dosing protocol is strongly recommended:

- The initial dose should be between 10-30 mg of methadone per day for at least the first three days. Patients at higher risk for methadone toxicity (see section below) should start on no more than 5-20 mg^{1,2}.
- During the early stabilization phase for patients new to methadone, doses may be increased by up to 5 mg every 3-5 days, or by 10 mg increments every 7 or more days.
- During the early stabilization phase for patients new to methadone, providers may elect
 to prescribe a single dose increase of 10 mg after 5 days, but all subsequent 10 mg dose
 increases should occur no sooner than 7 days apart. Alternatively, a 5 mg dose increase
 may be considered 5 days after a 10 mg dose increase. Caution surrounding serial 10 mg
 dose increases is emphasized.

Daily Witnessed Ingestion

Doses are to be self-administered under the direct supervision of a pharmacist, approved prescriber, or nurse, until candidacy for a take-home dosing schedule is established. Please see Methadone Take-home (Carry) Dosing for detailed recommendations.

Note that if methadone is not already in a formulation that deters misuse/injection (e.g., cherry-flavored), then all doses must be diluted in a vehicle (e.g., Tang/juice) that does not lend itself to misuse/injection.

No take-home doses (carries) should generally be granted during the first two months of treatment. An exception may be granted for Sunday carries due to pharmacy closures, if the provider determines the benefits of uninterrupted daily dosing outweigh the risks of the carry. This may be particularly useful for rural or remote patients with limited pharmacy options and/or where patients must travel longer distances to access a pharmacy or nursing station.

Some OAT programs give weekend carries in similar contexts when there is no weekend pharmacy access and the patient demonstrates sufficient early stability, reliable behaviour, and can store the medication safely. However, when patients are deemed unstable and the risks of earlier carry doses are significant, the patient may have to forgo one or two doses per week if no pharmacy access is available on Saturdays and/or Sundays. The prescriber must document their risk assessment and rationale for such decisions.

Patients at Higher Risk for Methadone Toxicity

An initial dose of 5-20 mg with careful titration is recommended for the higher-risk patients described below¹. Consultation with an experienced OAT provider may be warranted and further consideration of buprenorphine/naloxone over methadone may be required. Please refer to Managing Polypharmacy, Benzodiazepines, Alcohol, & Polysubstance Use in OAT for detailed recommendations for managing some of these risks.

- Patients using benzodiazepines/Z-drugs are higher-risk. A thorough history of benzodiazepines/Z-drugs use is necessary. This includes use via prescribed and/or illicit sources. A strategy for benzodiazepine/Z-drug management (even for stable long-term prescriptions), including diagnosis of potential sedative-hypnotic use disorder, must be part of the overall treatment plan. See the polypharmacy chapter section MANAGING PRESCRIBED AND ILLICIT BENZODIAZEPINES & Z-DRUG USE for detailed guidance.
- Patients using other sedating/psychoactive medications. Patients using antipsychotic and sedating antidepressants are at higher risk, particularly if the sedating drug was started or increased within the last two months, or the dose is moderate or high.
- Patients struggling with alcohol use or Alcohol Use Disorder. Problematic alcohol use can be identified through an alcohol history and laboratory measures (GGT and MCV).

All patients should be advised to abstain from alcohol during early stabilization. If the patient is at significant risk for alcohol withdrawal, appropriate withdrawal management should be arranged. Consultation with an addiction medicine specialist may be helpful to review the treatment plan.

- Patients who are older (> 60 years) and have a respiratory illness. This includes patients with chronic illnesses such as COPD and acute illnesses such as pneumonia.
- Patients who are on drugs that inhibit/promote methadone metabolism. If a drug that
 inhibits metabolism is meant for short-term use only, the prescriber might recommend
 that the patient finish the course before prescribing methadone. Conversely, patients on
 medications that promote rapid methadone metabolism should avoid abrupt cessation of
 the medication.
- Patients with lower opioid tolerance (e.g., codeine use only, low-dose or low-potency opioid use, intermittent opioid use, or a recent period of abstinence due to incarceration or residential treatment). Tolerance is difficult to establish from history; therefore, if in doubt, it is safer to initiate methadone at a lower dose.
 - Urine drug testing (UDT) can be helpful in confirming the patient's self-reported use. Consideration must be given to select the type of UDT that will be most effective for the clinical context and history (e.g., point-of-care, street drug screen, or comprehensive). Initiate methadone at 5-10 mg for the recently abstinent with initial negative urine screening.
- Patients with low body mass (< 50 kg) may also require lower induction doses.

STRONG RECOMMENDATION: REMINDER TO DISPENSE WITH OAT

Typically, all psychoactive/sedating medications should be dispensed with OAT, i.e., on the same schedule as OAT. Communicating with the patient's pharmacy about the plan for managing these medications is essential. Controlled dispensing instructions, such as "dispense as per OAT schedule", must be written on all relevant prescriptions. Please see the Managing Polypharmacy in OAT chapter for further medication safety recommendations.

Patients with High Tolerance of Potent Opioids

Specific guidance for methadone titration in patients with high tolerance of high-potency opioids (e.g., injecting or smoking primarily illicitly sourced fentanyl) is evolving. Please revisit this section for updates. While a more conservative approach to methadone titration is recommended for most patients, a subset of patients using primarily high-potency opioids may require more aggressive titration to stabilize effectively and for treatment retention, either alone or in combination with slow-release oral morphine (SROM).

See <u>Alternative Treatment Approaches for OUD Including SROM (Kadian®)</u> for detailed guidance. Consultation with an addiction medicine specialist should be sought to best support these patients.

CAMH guideline, <u>Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid</u>
Use Disorder, recommends the following approach¹:

- Conduct a risk-benefit assessment for patients with high tolerance of high potency opioids for whom slower titration could jeopardize retention in treatment.
- Prescribe an initial methadone dose of 5-30 mg. Then increase the dose by 5-15 mg every 3-5 days (as necessary) **for patients who both:**
 - a) Have high tolerance of high-potency opioids from daily use and have UDT confirmation of recent opioid use, and
 - b) Do not have risk factors for excessive CNS depression (i.e., patients who do not fall into one or more of the higher-risk patient categories listed above).
- Consider using a limited duration of SROM for outpatients, or immediate release oral
 morphine for inpatients, to manage emergent withdrawal while titrating the methadone
 dose to reach a clinically therapeutic outcome (i.e., 24 hours without any withdrawal or
 need for supplemental morphine).
- Exercise extreme caution if you are considering rapid and high dose titration (increasing
 the methadone dose by more than 10 mg at a time in a period under 5 days). Consult
 with a colleague who has experience with rapid and high dose titration.
- Monitor the patient closely, with direct assessment before each dose increase and assurance that they have a reliable family member/support person available for frequent contact and check-ins, for early detection of methadone toxicity.

It is paramount to reassess patients frequently during the first two weeks of treatment – they are at the highest risk of fatal overdose during this period. Discuss this risk and strategies to reduce it (e.g., use only small amounts of additional opioids, do not use alone, have a naloxone kit available). Document these discussions and reassess the patient with every subsequent dose increase.

Additional Resources – META-PHI Recommendations

It is important to note that these recommendations are more aggressive. Caution is advised.

- Methadone treatment for people who use fentanyl: Recommendations
- Methadone treatment for patients who use fentanyl: Plain language summary

Reducing Risk During the Early Stabilization Phase

The steps described below can help to reduce risk during the early stabilization phase.

- No new prescriptions for sedative drugs. Avoid prescribing any new sedating drugs during the early stabilization phase. Patients should also be advised to avoid alcohol and overthe-counter sedating drugs.
 - The risks and benefits of prescribing non-opioid medications for symptomatic withdrawal management must be carefully considered while methadone is being titrated (see **Appendix AA**). Regularly scheduled acetaminophen and ibuprofen may be sufficient. Use extra caution when prescribing symptomatic management medications with sedating properties in the context of methadone care.
- Missed doses. During the early stabilization phase, patients should be on the same dose
 for three to four consecutive days with no missed doses before a dose increase. If a
 patient misses three or more doses consecutively in this phase, they should resume at the
 initial dose (as per the dosing protocols above) for at least three consecutive days.
- General advice to the patient and their family/supports. Explain to the patient that it
 takes several weeks to reach the optimal dose of methadone, and that it is dangerous to
 try to relieve withdrawal symptoms with benzodiazepines, alcohol, opioids, illicit
 methadone, or other drugs. Advise the patient to limit their driving or use of machinery
 after a dose increase, particularly in the first few hours after dosing. Advise the patient to
 take their methadone dose in the morning, if possible, since the risk of overdose is
 increased at night.
 - During the early stabilization phase patients and their families/supports (with patient consent) should be educated about methadone toxicity, appropriate actions to take at the first signs of toxicity, and provided naloxone kits and training. A patient information guide may be used for this purpose (see The Pharmacology of Methadone Appendix Y for an example).
- Explain the risks of diverted methadone. Even a single dose of methadone can be fatal to both children and adults. Patients are responsible for the safe storage of their methadone. Prescribers must advise patients that it is dangerous and illegal to sell or give methadone to anyone, even in small doses or done with good intentions.

Treatment agreements are useful to clearly outline risks and delineate expectations.

UDT Negative for Opioids

Of note, if urine testing *does not* detect opioids upon intake, this does not preclude a patient from starting OAT if clinically indicated. There may be clinical reasons for this, such as recent abstinence, or failure of the test to reliably detect certain opioids.

However, if patients report recent abstinence and initial UDT results are negative for opioids – but OAT is indicated based on a reliable history – then buprenorphine/naloxone induction is strongly recommended over methadone. Methadone could be considered in some circumstances (e.g., patient choice, severe liver impairment), but titration must be approached with caution. The initial methadone dose should be 5-10 mg, titrated upwards in increments of 5 mg or less, every five or more days, with careful assessment of withdrawal symptoms and sedation.

THE LATE STABILIZATION PHASE (2-6 WEEKS)

Frequent Reassessment Early in Treatment

Ideally, the patient should be reassessed frequently during the first few weeks/months of treatment, until they achieve reasonable relief of withdrawal symptoms and cravings, in the absence of sedation or toxicity, for a complete 24-hour period following their dose. The OAT prescriber, or a member of the treatment team who possesses the necessary knowledge, skills, and clinical judgement, should ideally see the patient weekly to assess and adjust their dose, in collaboration with the prescriber.

All dose adjustments require an assessment. These assessments can be completed using a combination of in-person and virtual visits. On-camera assessment is preferable with virtual visits, if available. Avoid automatic dosage adjustments on the prescription.

Ongoing Titration

Most patients in the late stabilization phase are taking between 50-80 mg of methadone.

Throughout the early to late stabilization phase, the patient may experience incomplete relief of withdrawal symptoms. They may continue to use other opioids. **Discuss the use of other opioids or non-prescribed substances candidly with patients, with a non-judgmental, non-punitive approach. Revisit harm-reduction strategies as needed**. The emphasis should be on using safely, if needed, while cutting back on amounts/frequency of use, as the methadone dose accumulates.

During this period, dose adjustments are usually in the **3-5 mg range every 3-7 days**, depending on the severity, onset, and duration of the patient's withdrawal symptoms. Careful assessment of withdrawal symptoms is essential, with continued use of the COWS (**Appendix Z**).

MAINTEANCE PHASE (6 WEEKS +)

By this time, most patients have substantially reduced opioid use, they are largely tolerant to methadone, and experience no withdrawal symptoms for most of the day. They may occasionally ask for dose increases because of episodic subjective withdrawal symptoms, opioid cravings, or a relapse to opioids. During the maintenance phase, or if the dose is 80 mg or higher, dose adjustments are **typically between 3-5 mg every 3-7 days**.

Stable Daily Dose

The optimal methadone dose will mostly eliminate withdrawal symptoms, block opioid-induced euphoria, and reduce cravings without sedation or other signs of toxicity. UDT should be negative for opioids most of the time (see <u>Recommendations for the Use of UDT</u> for further guidance).

With experience, prescribers can typically establish a stable dose for many patients within two to eight weeks of initiating methadone. The stable dosage range for most methadone patients is 50-120 mg, however the focus should be on clinical indicators of stability, not the dose.

Patients who use high-potency opioids (e.g., fentanyl) regularly, may require higher overall doses for stability.

Given the high degree of variability in methadone pharmacokinetics and metabolism, "the optimum methadone dose can vary significantly between patients, necessitating careful, individualized dose titration as opposed to standardized dosing regimens"².

See <u>Ongoing Care</u> for more detailed recommendations around methadone dosing, specifically the sections on *Higher Methadone Doses (Above 120 mg)*, *Methadone Split Doses, Rapid Metabolism & Serum Levels*, and ECG MONITORING FOR PROLONGED QTc.

Considerations for Low Maintenance Doses (Below 50 mg)

Some patients stabilize at lower than average doses. Low maintenance doses may be suitable for some patients, such as those with lower opioid tolerance (e.g., codeine use only, low-dose or low-potency opioid use, intermittent opioid use, or a recent period of abstinence) or those at higher risk for methadone toxicity. Again, buprenorphine/naloxone would be the preferential treatment for these patients and should be offered/discussed as appropriate.

Doses below 50 mg are generally less effective than higher doses at reducing high-potency opioid use and retaining patients in treatment². Again, the focus with patients should be on clinical indicators of stability, not the dose.

Ongoing Follow Up

At each follow-up visit, review as needed and document the patient's dosage, withdrawal symptoms and cravings if present, ongoing substance use, missed doses, adverse effects, and relevant markers of clinical stability.

See <u>Ongoing Care</u> for detailed guidance on ASSESSING CLINICAL STABILITY and issues commonly encountered during the course of treatment. See <u>Methadone Take-home (Carry) Dosing</u> for detailed guidance on the provision of carries.

Periodically discuss the goals of treatment and adjuncts such as harm reduction strategies and psychosocial supports.

If indicators of clinical stability do not improve as expected during OAT treatment, consider whether continued prescribing is appropriate and aligns with the patient's and prescriber's goals. See <u>Discontinuing Treatment</u> for guidance on managing safety concerns in unstable patients and recommendations around withdrawal of treatment.

References

- 1. Centre for Addiction and Mental Health (CAMH). Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder. CAMH; 2021. Available at: https://www.camh.ca/-/media/files/professionals/canadian-opioid-use-disorder-guideline2021-pdf.pdf
- Provincial Opioid Use Disorder Treatment Guideline Committee. A Guideline for the Clinical Management of Opioid Use Disorder. British Columbia Centre on Substance Use (BCCSU) and BC Ministry of Health; 2017. Available at: https://www.bccsu.ca/care-guidance-publications/

Appendix Z²



CLINICAL OPIATE WITHDRAWAL SCALE¹

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Patient's name:	Date and Time:/::
Reason for assessment:	
Resting Pulse Rate beats/minute Measured after patient is sitting or lying for one minute 0 pulse rate 80 or below 1 pulse rate 81–100 2 pulse rate 101–120 4 pulse rate greater than 120	GI Upset over last ½ hour 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating over past ½ hour not accounted for by room temperature or patient activity 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	Tremor observation of outstretched hands 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness observation during assessment 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	Yawning observation during assessment 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil Size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	Anxiety or Irritability 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint Aches If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored onot present mild diffuse discomfort patient reports severe diffuse aching of joints/muscles patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh Skin 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny Nose or Tearing Not accounted for by cold symptoms or allergies 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score The total score is the sum of all 11 items. Initials of person completing assessment:

1. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (cows). J Psychoactive Drugs. 2003;35(2):253-259.

More information: www.bccsu.ca





Score: 5-12 = mild; 13-24: moderate; 25-36 = moderately severe; more than 36 = severe withdrawal





^{2.} From https://www.bccsu.ca/wp-content/uploads/2017/08/Clinical-Opiate-Withdrawal-Scale.pdf

Appendix AA

NON-OPIOID MEDICATION FOR SYMPTOMATIC MANAGEMENT OF OPIOID WITHDRAWAL

The following non-opioid medications may be useful to treat symptoms of opioid withdrawal.

Prescribers should exercise caution with all sedating medications during OAT induction, as they may interfere with the assessment of withdrawal severity and increase the risk of fatal overdose. In the absence of precipitated withdrawal (in the context of buprenorphine induction), many prescribers prefer to avoid these medications entirely during induction.

- Acetaminophen 500-1000 mg PO Q4-6h PRN for muscle pain (to a maximum dose of 4000 mg in 24 hours, or as appropriate based on known liver function/impairment).
- Ibuprofen 400 mg PO Q6-8H PRN for muscle pain.
- Ondansetron 4 mg PO Q6H PRN for nausea.
- Loperamide 4 mg PO PRN for diarrhea, then 2 mg PO after each loose stool, up to a maximum of 16 mg in 24 hrs.
- Trazodone 50-100 mg PO QHS PRN for insomnia.
- Quetiapine 25-50 mg PO QHS PRN for anxiety/insomnia.
- Clonidine 0.1 mg PO QHS PRN for opioid withdrawal symptoms and insomnia.
 Clonidine can be titrated up to 0.2 mg PO BID for severe withdrawal, but caution is advised due to the potential risks of sedation, hypotension, and diversion.