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

1.16 Discontinuing Treatment: Voluntary & Involuntary Withdrawal from Opioid Agonist Therapy

GENERAL CONSIDERATIONS

Opioid agonist therapy (OAT) is an effective and evidence-based treatment for opioid use disorder. OUD is a chronic medical condition that requires long-term treatment, and no recommendations exist to indicate a specific optimal treatment duration. However, it is encouraged and recommended that treatment continue for as long as desired by the patient to provide stability, functionality, and reduce harms.

During the course of treatment, OAT doses should be tapered and/or titrated up as needed and clinically indicated, to meet the needs of the individual in the context of their overall stability, other health conditions, and life circumstances. Where OAT doses higher than the typical range have been necessary for initial stabilization, it is encouraged to periodically trial a gradual small dose reduction to evaluate if stability can be maintained, while minimizing the side-effects and long-term medical complications of treatment.

For many individuals, the overall duration of treatment is an important question. Since OAT programs can be very intensive and demand a large commitment of time and resources from the patient, it is not uncommon for them to request withdrawal of treatment during their lifetime.

While withdrawal of treatment may occur for many reasons, it can typically be categorized as:

- **Voluntary and clinically reasonable**. A taper is requested and directed by a stable patient, in collaboration with the treatment team. In this context, the patient and provider agree that many treatment goals, including clinical stability, have been achieved and that a trial of tapering is a reasonable option.
- **Voluntary with clinical concerns**. A taper is requested by the patient before many important treatment goals are achieved, and/or before clinical stability is reached. The patient thus wishes to taper off of OAT but remains at high risk of relapse to non-prescribed opioid use and other harms.
- **Involuntary**. The patient is not requesting withdrawal from treatment, but given significant safety concerns (for the patient, treatment team, or the community), the treatment team determines that continuing OAT is either unsafe or inappropriate.

Whether voluntary or involuntary, it is important for OAT providers to have a good understanding of the benefits and risks of withdrawal of treatment and to develop practical strategies to support the patient and other members of the team throughout this process.

SPECIFIC CONSIDERATIONS

OAT is a long-term indefinite treatment. Patients who continue to benefit from OAT and do not wish to taper should not be pressured to do so.

When a taper is deemed appropriate, gradual tapering (over months to years) is preferred for safety and stability reasons. Often patients request more rapid tapering, and it is important that prescribers explain the dangers of rapid tapers to patients in language that is clear, yet compassionate and non-judgemental. Recognizing the overall burden of treatment is an important component of a balanced risk-benefit discussion. **Additionally, OAT providers must also recognize that the principle of patient autonomy dictates that prescribers cannot refuse to reduce a patient's OAT dose.**

Tapering the OAT dosage should ideally be undertaken as a *trial of weaning*. It is strongly recommended that the approach to tapering remain flexible to accommodate the patient's physical and psychosocial needs. This flexibility often serves to strengthen the therapeutic alliance, especially when the prescriber has concerns about the patient's readiness. Harm reduction strategies, including naloxone kits, should be revisited more regularly. **During or following a trial of tapering, patients who relapse to opioid use or who decompensate psychosocially or functionally should be encouraged to titrate back up to a stable dose**. These patients should be offered expedited access to resume and restabilize on OAT to prevent further serious adverse outcomes. Patients must never be penalized in any way for unsuccessful weaning.

VOLUNTARY TAPERING: WHEN CLINICALLY REASONABLE FOR A STABLE PATIENT

As with the treatment of other chronic diseases, the optimum benefits from OAT are not realized immediately and are often not seen for at least a year in treatment. Depending on the patient's pre-treatment circumstances, overall health, and severity of OUD, some patients may take longer to optimally benefit from treatment. In general, patients who have been on OAT for at least two to three years will have better outcomes when tapered than those who elect to taper after shorter durations in treatment. Therefore, to reduce the risk of relapse and other harms, patients should be encouraged to participate in OAT until stability is reached and important patient- and provider-driven treatment goals are achieved.

Evaluating a Request for Withdrawal of Treatment

A request to taper should be discussed collaboratively with the patient. The patient's motivation for the request and the KEY CONSIDERATIONS below should be explored.

KEY CONSIDERATIONS: QUESTIONS TO EVALUATE A TAPER REQUEST

1) How long has the patient been abstinent from non-prescribed opioids and/or other mood-altering substances, as per the patient's treatment goals around abstinence? The longer the period of stability, the higher the likelihood of success with a taper.
2) How stable is the patient's mental and physical health?
3) Does the patient have stable housing?
4) Does the patient have a stable source of income?
5) Has the patient developed healthy and non-chemical coping skills?
6) Has the patient developed supportive relationships (particularly with others who do not use drugs)? Do they still have contact/inappropriate involvement with dealers or criminal organizations? Do they still associate or live with others who use drugs regularly?
7) Does the patient have a concurrent chronic pain condition that may complicate withdrawal of treatment? Should other pain management strategies be explored or optimized prior to initiating withdrawal of treatment?
8) Has the patient attempted withdrawal of treatment in the past? What did they learn from that experience that could help them in this attempt?
9) Is the patient able and willing to attend more frequent follow-up appointments during the tapering process, to facilitate appropriate monitoring and dose adjustment?

It is important to understand what is driving the desire to stop treatment. Some of the patient's concerns may be amenable to medical management (e.g., side-effects, re-evaluating take-home dosing schedules), education, and/or reassurance. Providers may want to ask about finances, difficulties with transport, family responsibilities, and work schedules.

Explore any misconceptions about the need to withdraw, for example, due to a pending incarceration. Patients may also be subject to stigma and judgements from family or friends, employers, or even other care providers. These concerns must be explored in a sensitive manner.

Preparing for Withdrawal of Treatment

Once the decision is made to start an OAT taper, the initial tapering plan should be discussed with the patient. This plan must include relapse prevention strategies, including practical instructions on how the patient can access a dose increase in between follow-up appointments.

Providers should also incorporate the following into the tapering plan:

- **Individualize the tapering plan for each patient**. The plan may include a dose reduction schedule for patients with previous tapering experience, who can anticipate what to expect over time. For patients tapering for the first time, in-person assessment is often a good idea after an initial small dose reduction. Discuss how the change felt for the patient. This discussion will inform decisions about the size and intervals of future dose reductions, as needed.
- **Inform the pharmacy about the plan to taper**. The pharmacist can be another source of support for tapering patients. They can also notify prescribers of any concerns and can offer feedback on how the patient is coping with the change.
- **Include more frequent reassessment appointments in the plan**. Patients who are ready to taper are often seeing their provider every three months, given their long-term stability. It is important to advise the patient that a taper will likely require more frequent appointments to evaluate progress and the need to modify the tapering plan.
- **Prepare the patient for potential difficulties associated with tapering**, namely anxiety, craving, withdrawal symptoms, and decreased overall distress tolerance. The risk of relapse must be discussed. Discuss strategies to proactively manage these challenges. Ideally, patients should be guided to taper at a pace that minimizes these symptoms. Patients should be able to perform all their previous activities of daily living while tapering slowly over time, to decrease the risk of decompensation.
- **Reassure the patient that flexibility with dose adjustments during the taper is standard care**, i.e., it is reasonable to return to the previous dosage or to hold the taper at a certain dose for an extended period, as needed, if tapering becomes too challenging. Encourage the patient to proactively discuss life issues that may require their taper to be adjusted or paused to maintain stability.
- **Offer supportive resources during the process** and discuss if engaging in additional counselling or support groups would be helpful, especially if the patient benefitted from such supports in early treatment.

General Tapering Recommendations

In general, it is recommended that the OAT dose be lowered by no more than 5-10% of the total remaining dosage per month, to minimize cravings and reduce the risk of destabilization.

When low doses of OAT have been achieved (i.e., ≤ 10 mg buprenorphine and ≤ 30 mg methadone), the rate of taper may be slowed even further to optimize successful weaning.

Voluntary withdrawal can be suspended at any time with the option of titration back to a stable dosage.

For patients who are unsuccessful tapering off OAT, or dissatisfied with their quality of life while tapering, other ways of simplifying treatment without stopping OAT should be discussed. These options may include alternate day dosing, buprenorphine extended-release subcutaneous injections (Sublocade®) or the buprenorphine subdermal implant (Probuphine®).

Taper Considerations for Buprenorphine/naloxone

Given that the buprenorphine/naloxone lowest dosage in tablets and film is 2 mg/0.5 mg, many patients on buprenorphine may find the step-downs towards the end of tapering difficult, especially below 10 mg daily.

Many patients tolerate a buprenorphine/naloxone taper better when reducing by 1 mg at a time, particularly below 10 mg daily. Consider splitting a 2 mg tab or cutting a 2 mg film in half (i.e., taking approximately 1 mg of the 2 mg tablet/film daily). When splitting a 2 mg tablet or film, the remaining half should be stored in an enclosed container and protected from moisture until it is used at the next scheduled dosing time. Avoid splitting tablets or film in advance. These measures will help protect the integrity of the tablet or film used for splitting. Off-label utilization of a buprenorphine transdermal patch (Butrans®) is also an option for stable patients who struggle with further tapering once they reach 2 mg or 1 mg of buprenorphine/naloxone daily.

It is important to discuss such tapering strategies with the pharmacy in advance of sending a prescription requiring tablet or film splitting. This will ensure everyone is on the same page and consistent instructions and support are given to the patient by all members of the team.

Taper Considerations for Sublocade

Currently, no clear evidence exists to guide clinical decision making for patients who are stable on Sublocade® when they request to stop treatment. The injectable depot version of buprenorphine has a half-life of 43 to 60 days. Considering the long half-life, withdrawal symptoms and signs may be delayed. Furthermore, “model simulations indicate that steady state buprenorphine plasma concentrations decrease slowly over time following the last injection and could remain at therapeutic levels for up to 2 to 5 months, depending on the dosage administered (100 or 300 mg, respectively)”[1].

Practical experience, however, indicates that some patients may experience withdrawal symptoms much sooner after stopping treatment, especially if they were prone to early withdrawal symptoms when they presented late for routinely scheduled monthly injections or if they never felt entirely stable on their routine Sublocade® regimen. These patients may have been receiving Sublocade® at more frequent intervals, or at higher doses than indicated by the product monograph to facilitate clinical stability.

Patients who elect to discontinue treatment with Sublocade® should thus be monitored for symptoms and signs of withdrawal for several months. If acceptable and accessible to the patient, providers may consider low dose transmucosal buprenorphine, if needed, to treat withdrawal after discontinuing Sublocade®.

Frequent Assessment of Stability & Safety

During the taper, reassess stability more frequently to ensure patient and community safety by:

- Re-evaluating take-home dose schedules more often,
- Adjusting follow-up appointment frequency as appropriate, and in partnership with the patient,
- Screening for relapse at each appointment and in between as needed, including urine drug testing (UDT), and
- Continually reviewing and adjusting the tapering plan and other treatment goals.

In some cases, it may be useful to collaborate with the community pharmacy if the provider has specific concerns about instability during the taper. The pharmacist is in a unique position to report any behavior or activity that could warrant attention at the next reassessment.

Importantly, **documentation of these issues is critical** to support clinical decision making and to facilitate appropriate episodic care by other OAT team members or other healthcare providers.

VOLUNTARY TAPERING: WHERE CLINICAL CONCERNS OR INSTABILITY EXIST

Some patients choose to taper OAT despite its benefits. Patients may also request a taper early in treatment or before meaningful clinical stability is reached, and/or major treatment goals are achieved.

When the potential harms of a taper outweigh the potential benefits, the tapering process may put the patient at high risk of relapse and other serious harms. The OAT prescriber must explore the patient's motivation for tapering, educate them about the potential harms, and clarify any misconceptions. The prescriber may recommend the continuation of OAT using the same medication or by exploring simplifications of treatment. Details of this discussion and education should be documented in the patient record.

However, if despite this discussion the patient still insists on withdrawing from OAT, the patient and prescriber should prepare a plan for a *trial of weaning*, taking into consideration the relevant risks.

Harm reduction strategies should be offered proactively throughout the process, and especially if relapse occurs. Education on safer use techniques, sterile drug consumption equipment, and take-home naloxone kits should be offered regularly. Patients who relapse to opioids and become unstable, or who change their decision to wean at any point, should be encouraged to continue OAT in some form and ideally return to a stable dose.

INVOLUNTARY WITHDRAWAL OF OAT TREATMENT

Clinical decision making while providing OAT can be challenging at times. Deciding to involuntarily withdraw a patient from treatment is an example of a potentially difficult treatment decision. It is thus important to have a thorough understanding of the issues that may make ongoing treatment unsafe or inappropriate, and to have a practical approach to involuntary withdrawal of treatment.

Treatment agreements can be revisited with patients to review behavioural and safety expectations throughout the course of treatment and particularly as concerns arise that may warrant withdrawal of treatment. See the Comprehensive Assessment chapter for more information on treatment agreements.

In general, involuntary withdrawal of treatment is indicated when the OAT prescriber, in collaboration with the treatment team, determines that **ongoing treatment poses a serious risk to the patient, a member of the treatment team (including pharmacy staff), or the community.**

Once a decision is made to withdraw treatment on an involuntary basis, alternative treatment options, including a referral to another OAT treatment program/provider must be considered and offered to the patient, if available.

Concerns That May Warrant Involuntary Withdrawal

Examples of behavior or circumstances that may warrant involuntary withdrawal of treatment include:

- **Evidence of repeated failure to ingest dispensed OAT doses**. This includes witnessed and/or take-home doses. This may constitute sufficient grounds for immediate dose reduction or cessation of OAT. Dose reduction is appropriate if the patient is not consuming their full dose or if they are potentially diverting one or more doses. Such a **dose reduction is intended to protect against overdose** when take-home doses are converted to witnessed doses and/or when the patient resumes consuming their full witnessed dose on a daily basis.

Discussion around these behaviors is always warranted to ensure that legitimate patient concerns are addressed. Explore the patient's potential reason for this behaviour.

For example, were they feeling unwell, sedated, or experiencing side effects on their prescribed dose? Are they wanting to taper, are they being pressured to divert doses, or selling doses for extra income? This should be discussed sensitively and non-judgementally with patients, while explaining the risks in clear language. This includes the risk of being discharged from care via involuntary withdrawal, especially if the issue is medication diversion.

Again, it may be useful to review the OAT treatment agreement with the patient and increase supervision during administration. The pharmacy team must be included in the clinical discussion and plan moving forward, as they are on the front lines of dosing safety and can help observe for clinical sedation.

- **Conclusive evidence of diversion of prescribed OAT doses**. This constitutes sufficient grounds for an involuntary taper to zero or immediate cessation of OAT. Alternatively, increased supervision and strict witnessed dosing seven days per week, with no option for take-home dosing (for any reason) may be considered, if deemed appropriate by the treatment team. If the latter option is chosen but the behavior continues, OAT must be discontinued. Instituting a dose reduction (as above) can again protect against overdose while the treatment team considers the situation and decides on a longer-term plan.

  Evidence of methadone and/or slow-release oral morphine (SROM) diversion is typically considered a much greater safety risk to the public, and thus results in involuntary withdrawal of treatment more often.

  Diversion of buprenorphine/naloxone still constitutes a concern, and may be grounds for a written request from the prescriber to the pharmacist to crush all buprenorphine doses prior to witnessed self-administration. This practice is not routinely recommended and should be reserved for exceptional circumstances. If there are ongoing concerns despite this measure, treatment should be discontinued.

- **Physical or verbal threats to any member of the OAT care team, including pharmacy staff**. Such behavior constitutes sufficient grounds for immediate cessation of OAT. In some cases, an involuntary taper to zero may be attempted, along with a more intensive behaviour agreement, prior to opting for immediate cessation of treatment.

- **Ongoing disruptive behaviour in clinic or at the pharmacy**. This may also constitute sufficient grounds for cessation of OAT. In some cases, a trial of weaning or a more intensive behavioural treatment agreement may be an interim measure.

- **Continued, heavy use of non-prescribed, sedative/hypnotic medications, including benzodiazepines/Z-drugs, OTC medications and/or alcohol**, may constitute a serious enough safety concern to justify cessation of OAT. A careful risk-benefit assessment, including the patient's response to options for treatment intensification, should help determine whether treatment should be continued or stopped.

  Patients who repeatedly seek sedating prescription medications from prescribers other than their designated treatment providers (as also outlined in the treatment agreement) may also be at sufficient risk to warrant involuntary withdrawal of treatment.

- **Repeated failure to attend appointments**, including the minimum requirement for in-person assessment as deemed appropriate by the treatment team, may constitute sufficient grounds for involuntary withdrawal of treatment. Appropriate initial responses to repeated missed appointments should include the 1) removal of any take-home doses, 2) slow involuntary tapers of undesirable sedating prescription medications, and eventually 3) a taper of the OAT medication to zero.

Process for Involuntary Withdrawal

During the involuntary withdrawal of treatment process, the following steps should be considered:

1) **The decision to involuntarily withdraw treatment should be discussed as a treatment team**. These discussions are crucial to build consensus and maintain team morale, as different team members may have different thresholds for what constitutes unacceptable behavior. When strong therapeutic relationships exist between the patient and certain members of the team, it is important to keep in mind that all team members have a right to be heard and feel safe at work.

2) **Ensure that pharmacy staff are notified about the clinical decision to involuntarily withdraw treatment**. Provide the pharmacy with enough information to determine if they wish to be involved in the involuntary withdrawal process. This is especially relevant if the behavior occurred in the pharmacy or within the immediate vicinity of the pharmacy. It may be necessary to switch the patient to an alternative pharmacy if the plan involves an involuntary taper over time.

3) **Inform the patient of the decision to involuntarily withdraw treatment using clear language**. Set clear expectations and boundaries around what is expected of the patient moving forward (in terms of clinic/pharmacy attendance, consequences of further inappropriate behavior, etc.). Discuss details of the tapering schedule and provide the patient with a written copy if requested. Document the team's decision, rationale for the decision, the plan moving forward, and the discussion with the patient, including the patient's response to the plan, in the medical record.

4) **Provide the patient an option to transfer to another OAT prescriber or program**, if appropriate and possible. Provide appropriate collateral information to the new prescriber or program regarding the circumstances around the transfer of care.

5) **Reinforce that safety is key for all involved**. Patients exhibiting verbally abusive or threatening behaviour may have their OAT rapidly tapered or simply discontinued if the prescriber has concerns regarding the safety of clinic staff, pharmacy staff, other patients, or the public (for instance individuals accessing the same area/building where the pharmacy or clinic is located).

6) **Consider safety in aspects of dispensing and witnessed dosing**. If the patient was not regularly ingesting their prescribed dose, there may be a need to lower the dose and observe the patient for a period after dosing (i.e., in clinic or in pharmacy) to monitor for sedation or opioid toxicity.

7) **A typical schedule for involuntary tapering is generally quicker than a voluntary taper** and may involve a 5-10% reduction of the remaining daily dose per day, or per week, depending on the patient's level of cooperation and the severity of the perceived risk.

8) **During involuntary tapering all doses must be daily witnessed doses with no take-home doses permitted**. This means that if the patient has no pharmacy access on a given day, that dose will not be dispensed to the patient.

Returning to OAT After Involuntary Withdrawal

Patients who are involuntarily withdrawn from treatment may be considered for return to treatment at a future date, especially in regions where other OAT prescribers/clinics are not available. This is a decision that the prescriber must make case by case, along with the treatment team, considering the circumstances at the time of involuntary withdrawal and the circumstances when the patient wishes to resume treatment.

A minimum waiting period of three to six months should be considered before resuming treatment in the same program. **This reinforces the message that unacceptable behavior will not be tolerated and that the safety of clinic and pharmacy staff is non-negotiable**. During the second half of the waiting period, it may be beneficial for the patient to meet with program counselling staff, if available and deemed safe, to discuss what went wrong leading up to the involuntary withdrawal and to assess the patient's insight and readiness to commit to behavioral expectations upon their return. Prescribers are not obligated to resume treating patients who have been involuntarily withdrawn if significant safety concerns or behavioural problems persist, or if the program is no longer accepting new patients (e.g., the program has reached capacity).

References

1. INDIVIOR. *Prescribing Information: Sublocade® (buprenorphine extended-release) injection, for subcutaneous use*. https://www.sublocade.com/Content/pdf/prescribing-information.pdf. Accessed January 10, 2023.