

# **Opioid Use Disorder: Diagnosis and Management in Primary Care**

Effective Date: June 1, 2018

# Scope

This guideline presents recommendations for the diagnosis and management of opioid use disorder (OUD) in primary care with a focus on induction and maintenance of buprenorphine/naloxone (Suboxone®) opioid agonist treatment (OAT) for adults and youth  $\geq 12$  years.

OUD can be effectively treated with buprenorphine/naloxone in primary care and is not contingent on having access to counselling or inpatient detox. Free online training and preceptorships with experienced buprenorphine/naloxone prescribers are available through the Provincial Opioid Addiction Treatment Support Program to all primary care practitioners in B.C. The goal of this guideline is to empower primary care practitioners to recognize and treat OUD with referral to specialist support such as the Rapid Access to Consultative Expertise (RACE) line when necessary, as with any other area of general practice. The provincial Addictions Medicine RACE line is available at 1-877-696-2131, Monday to Friday from 8 am to 5 pm.

Family practitioners are also encouraged to support patients who begin buprenorphine/naloxone in specialized addiction settings and then transfer to their family practitioner for long-term care (see long-term care section).

The intention of this guideline is not to suggest automatically transferring patients currently being treated for OUD with methadone to buprenorphine/naloxone; this requires careful consultation and discussion between patient and provider. This guideline does not provide guidance on opioid prescribing for pain and is not intended for patients taking opioid medication as prescribed for pain. For patients diagnosed with OUD who have complex chronic pain and/or other co-morbidities, consult with the RACE line. These patients will likely require individualized support beyond the scope of this guideline. Depending on the level of complexity, many patients with OUD and concurrent chronic pain can be successfully treated with buprenorphine/naloxone in primary care after consultation.

This guideline is a summary of the provincial Guideline for the Clinical Management of Opioid Use Disorder¹ developed by the BC Centre on Substance Use (BCCSU) and the BC Ministry of Health, available online at bccsu.ca. Appropriate use of this guideline benefits from reference to the provincial guideline. Despite the large size of the provincial guideline, readers will find that it is well organized to allow easy identification of key topics and useful guidance. Reviewing the full guideline will enhance one's ability to treat OUD.

# **Key Recommendations**

- Buprenorphine/naloxone (Suboxone®) is the recommended first-line treatment for OUD (also known as opioid addiction) in adults, and youth ≥ 12 years with moderate/severe opioid use disorder. Refer to *Appendix A: Opioid Use Disorder Diagnosis and Management Pathway* for a one-page overview.
- Withdrawal management (commonly known as detox) alone without long-term OAT or linkage to continuing care is not recommended. Dangers associated with detox withdrawal management alone include elevated rates of relapse, and risk behaviours after discharge which may lead to increased risk of HIV and HCV infection and overdose death, especially if there is no linkage to comprehensive and continuing addiction care.<sup>2–4</sup>







- Provide or recommend a take-home naloxone kit and other harm reduction supplies to patients who are at risk of overdose (see availability at towardtheheart.com).
- Requests for treatment for OUD should be treated with urgency; there is often a window where the patient is interested in discussing treatment. Delays in starting treatment increase risk of overdose and serious related harms, including death.
- Primary care practitioners and care teams are encouraged to take on addiction care as part of their practice, as they are well suited to diagnosing and treating OUD and supporting long-term recovery.
- OUD is a chronic, relapsing disease that benefits from a compassionate, patient-centred and non-judgemental approach. There are multiple, individual paths to treatment, stabilization, and recovery.
- Lack of access to counselling should NOT be a barrier to starting opioid agonist treatment. If available, and aligned with the patient's treatment goals, offer referrals to psychosocial treatment interventions and supports in conjunction with pharmacological treatment.
- If you are new to buprenorphine/naloxone prescribing, consider consultation with a local addiction medicine specialist or the provincial RACE line at 1-877-696-2131. New prescribers are encouraged to complete the online course that is part of the Provincial Opioid Addiction Treatment Support Program. This course offers modules on buprenorphine/naloxone that allow a new prescriber to quickly get up to speed. The Provincial Academic Detailing service offers a webinar-based session on buprenorphine/naloxone. Refer to the Associated Document: Resource Guide for Practitioners.
- Methadone is the recommended second-line opioid agonist treatment if induction with buprenorphine/naloxone is contraindicated or not preferred.
- Alternative, higher intensity treatment options are also available in BC for individuals who do not benefit from first- and second-line opioid agonist treatments, such as slow-release oral morphine and injectable opioid agonist treatment (refer to Guidance Document for Injectable Opioid Agonist Treatment), which can be prescribed by experienced addiction medicine practitioners.

# **Background**

Opioid Use Disorder (OUD) is a chronic relapsing illness characterized by problematic use of and addiction to opioids. OUD is associated with increased morbidity and mortality and is considered a major driver of the recent increases in overdose deaths that have led to BC's Public Health Emergency.¹ Furthermore, fentanyl and fentanyl-analogues in the illicit drug market have created a toxic drug supply in BC, which has significantly increased the risk of overdose death (also known as opioid poisoning). The number of overdose deaths has increased since the public emergency was declared in April 2016. In 2017, 1422 suspected overdose deaths were reported by the B.C. Coroners Service, an increase of 43% from 2016.⁵ However, when treated effectively, patients with OUD can achieve long-term, sustained recovery. Primary care practitioners can play a key role in providing safe, effective treatment and care that supports long-term recovery from OUD.⁶-8

Appendix B: Literature Review provides an overview of the evidence supporting the clinical management of OUD described in this guideline. Refer to the Guideline for the Clinical Management of Opioid Use Disorder for a detailed review of the evidence. Refer also to the Management of opioid use disorders: a national clinical practice guideline.9

"Withdrawal Management" has a specific meaning within the addiction medicine community. It describes the short-term process commonly known as detoxification or "detox" and does not simply refer to the management of withdrawal symptoms. Withdrawal management (inpatient or outpatient) often involves use of a short-term opioid agonist taper but does not include transition to stable, long-term opioid agonist treatment. In this guideline, "withdrawal management alone" refers to a short-term detox (days or weeks) typically administered in an inpatient or intensive outpatient program, which does not bridge to long-term continuing addiction treatment. Due to serious safety risks, including increased risk of relapse, and increased high risk behaviours that may lead to serious harms and overdose death, withdrawal management alone is not recommended.<sup>2-4</sup>

**Opioid Agonist Treatment** may also be called "opioid replacement therapy" or "opioid substitution therapy". Opioid agonist treatment includes the use of buprenorphine/naloxone, methadone, slow-release oral morphine and injectable hydromorphone and diacetylmorphine, and has been shown to be superior to withdrawal management alone.<sup>10,11</sup> It results in improved retention in treatment, sustained abstinence from opioid use and reduced risk of morbidity and mortality. The provincial *Guideline for the Clinical Management of Opioid Use Disorder* provides a detailed evidence review of opioid agonist treatment. Opioid agonist treatment can be part of the continuum or pathway of care that includes recovery.

Buprenorphine is safer than methadone with less risk of respiratory depression, fewer drug-drug interactions, and less risk of diversion or non-medical use. 11 Buprenorphine is a long-acting semi-synthetic partial opioid agonist that effectively alleviates opioid withdrawal symptoms and cravings without producing the same degree of euphoria associated with full agonist opioids like heroin, oxycodone and fentanyl. Buprenorphine's partial agonist activity results in a "ceiling effect" where increasing therapeutic doses do not cause increasing respiratory depression. Commonly observed side effects include headaches, pain, nausea, vomiting, hyperhidrosis, constipation, insomnia, vasodilation and over-sedation. These side effects are similar to but lower in intensity than side effects of full opioid receptor agonists (e.g., methadone). Buprenorphine can act synergistically with benzodiazepines, alcohol and/or other sedating medications to significantly increase risk of respiratory depression, overdose or death. Concurrent use of buprenorphine and benzodiazepines or other drugs that suppress the central nervous system requires careful medical management. Refer to Appendix C: Opioid Agonist Treatment Medication Table or product monograph for information on side effects and drug-drug interactions.

**Buprenorphine/naloxone (Suboxone®) is a 4:1 mixture of buprenorphine to naloxone** that is administered sublingually. The inclusion of naloxone prevents diversion for injection. When taken as directed by the sublingual route, the buprenorphine component has high bioavailability, while naloxone has very low bioavailability. If diversion for injection occurs, the naloxone component then has high bioavailability and causes rapid onset of withdrawal symptoms in opioid-dependent individuals.

Precipitated withdrawal is a sudden onset of severe withdrawal symptoms that occurs when the first dose of buprenorphine/naloxone (Suboxone®) is taken while other opioids are still present in the body. This can be avoided if patients are in moderate to severe withdrawal before the first dose of buprenorphine/naloxone is administered (i.e., the majority of opioids are out of their system). Precipitated withdrawal results from buprenorphine's high binding affinity and low activity at the opioid receptor. Buprenorphine rapidly binds to opioid receptors, replacing any other full opioid agonists present with a partial opioid agonist (i.e., partial or lower activation of the receptor) – essentially "precipitating" or immediately causing severe withdrawal. With appropriate addiction history taking and clinical assessment, the risk of precipitated withdrawal is reduced. There is minimal risk of precipitated withdrawal with subsequent doses of buprenorphine/naloxone. Refer to the *Guideline for the Clinical Management of Opioid Use Disorder* and/or Provincial Opioid Addiction Treatment Support Program for more information about precipitated withdrawal.

# Diagnosis

## Screening (Identification of Patients)

- Periodically ask all patients about their substance use as screening for substance use disorder:
  - "How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?" 12
    - o If answer is greater than zero for opioids, follow-up with DSM-5 OUD criteria.
- Treatment of opioid use disorder benefits from compassionate care and building a relationship with your patient. Individuals with OUD often face significant stigma and barriers to care.
- Offer a naloxone kit and other harm reduction supplies when it is discovered that a patient is using opioids for non-medical purposes. Naloxone kits are available for free for eligible patients, caregivers and practitioners. Intranasal naloxone kits are listed as a health benefit for First Nations and Indigenous peoples in BC. Refer to towardtheheart.com to find out where to access and how to distribute and educate patients about kits and other harm reduction supplies in your care setting.

# Diagnostic Criteria for Opioid Use Disorder (OUD)

Diagnose OUD using the DSM-5<sup>13</sup> diagnostic criteria outlined below. The presence of at least 2 of the criteria listed below indicates OUD, with the exception of patients who are taking opioids for chronic pain. Severity depends on the number of criteria present (MILD: 2 to 3 criteria, MODERATE: 4 to 5 criteria, SEVERE: 6 or more criteria).

Due to risk of overdose death when untreated, offer patients diagnosed with opioid use disorder (including youth) immediate induction of opioid agonist treatment, if suitable (refer to Management section below). There is often a "window" when patients are interested in discussing treatment. Delays in starting treatment increase risk of overdose. If possible, same day or next day treatment initiation is preferred.

- For "mild" OUD (individuals who meet 2–3 of the DSM-5 criteria), consider and discuss starting buprenorphine/naloxone treatment after assessing and discussing the risks and benefits.
- DSM-5 OUD criteria is not validated in youth. However, youth with significant impairment and high risk of overdose may be good candidates for opioid use disorder treatment including buprenorphine/naloxone treatment. (Refer to *Associated Document: BCCSU Youth Supplement* (available June 8th, 2018), for youth-specific criteria for starting OAT).
- If patients are unable or uninterested in starting treatment at this time, keep the door open for future treatment and begin building a rapport. Identify and address patient-centred goals. Follow up on patient goals regularly and consider motivational interviewing and harm reduction counselling.

# **Treatment Options**

Consider the advantages and disadvantages of alternative treatment options and take into account patient needs and preferences when tailoring a comprehensive treatment plan for each individual. Ask about past experiences with opioid agonist treatment, psychosocial interventions and recovery-oriented services, which may inform the approach to treatment. Connect patients with additional health system and community supports and services where appropriate and if aligned with patient treatment goals.

• Buprenorphine/naloxone (Suboxone®) is recommended first-line treatment in most cases.

# Table 1: The pros and cons of common treatment options for opioid use disorder

## **Buprenorphine/naloxone(Suboxone®):**

- Good safety profile: less risk of overdose
- · Milder side effects
- Easier to progress to take-home doses; generally can progress to take-home doses immediately at the discretion of the treating clinician once clinically stable and can safely store medication.
- Shorter time to achieve therapeutic dose
- Induction can be challenging and requires focused care
  - Time required to complete induction
  - Risk of precipitated withdrawal

#### Methadone

- May be preferred treatment for unstable individuals
- Consider when buprenorphine/naloxone is contraindicated or not-preferred.
- Generally requires daily witnessed ingestion
- Higher risk of overdose
- Increased risk of cardiac arrhythmias as a result of QTc prolongation
- Requires education and training via the Provincial Opioid Addiction Treatment Support Program available at bccsu.ca.

Refer to the provincial *Guideline for the Clinical Management of Opioid Use Disorder* and bccsu.ca for a detailed description of treatment options including OAT, slow release oral morphine, injectable OAT, psychosocial treatment interventions and recovery-oriented systems of care (Refer to *Appendix B: Literature Review*).

# Buprenorphine/naloxone (Suboxone®): First-Line Opioid Agonist Treatment

#### General Considerations

Family practice is well suited to treatment of OUD with buprenorphine/naloxone, including in rural and remote areas where specialized addiction services may be lacking and access to pharmacies for daily witnessing is limited. If questions arise, consider consultation with an addiction medicine specialist or a call to the RACE line. New buprenorphine/naloxone prescribers are encouraged to complete the online Provincial Opioid Addiction Treatment Support Program.

Buprenorphine/naloxone induction involves in-person or phone check-ins on the first day and periodic check-ins for the next few days, ideally by the prescriber, or member of the patient's care team (e.g., physician, nurse practitioner, nurse) and communication either in person or by phone (refer to Figure 1 below). Patients often find their withdrawal symptoms and cravings well managed by the end of the first or second day.

Patients may be started on buprenorphine/naloxone at their primary care setting or at home. If started in a specialized care setting (e.g., hospital, rapid access addiction clinic, public or private OAT clinic, withdrawal management facility), subsequent long-term management can be provided by a primary care practitioner. A list of opioid agonist treatment clinics can be found at bccsu.ca.

# The following populations may require specialist support, as they are beyond the scope of this guideline. Consult an addiction medicine specialist and/or contact the RACE line for:

- Pregnant individuals, those planning to become pregnant and breastfeeding mothers Refer to Associated Document: BCCSU Pregnancy Supplement;
- Patients with co-existing chronic pain or other complex co-morbidities;
- Patients currently taking methadone, slow-release oral morphine, or injectable OAT;
- Previous inductions with buprenorphine that were not successful;
- Youth Refer to Associated Document: BCCSU Youth Supplement (available June 8th, 2018);
- Patients with complex polysubstance use, especially youth.

# For additional practitioner and patient resources refer to

- Associated Document: Opioid Use Disorder: Resource Guide for Patients and Caregivers
- Associated Document: Opioid Use Disorder: Resource Guide for Practitioners
- Provincial Opioid Addiction Treatment Support Program Resources Page

**Figure 1: Overview of buprenorphine/naloxone induction** (for detailed guidance see below or refer to the *Guideline for the Clinical Management of Opioid Use Disorder*). See also the *Associated Document: Home Induction Patient Handout*.

### Screening

# Diagnosis of Opioid Use Disorder – DSM-5 criteria

## Harm Reduction – provide/recommend naloxone kit

## Preparing for buprenorphine/naloxone (bupl/nix) induction

- Explain how buprenorphine/naloxone works.
- · Discuss risk and benefits.
- Complete Assessment and Investigations.
- Complete treatment plan after shared decision-making.
- Review withdrawal assessment scales (Associated Document: COWS Clinical Opiate Withdrawal Scale or Associated Document: SOWS Subjective Opiate Withdrawal Scale discussed further below).
- Consider whether offering unobserved take-home doses for part of induction (i.e., "home induction") would be beneficial.
- Provide education and contact information if considering home induction for Day 1 or for first dose on Day 1.

#### Day 1

- Schedule 1st dose in the morning.
- Patient must be in moderate to severe withdrawal to begin induction. Assess withdrawal (COWS) and administer first dose (sublingual). Common dose is two 2 mg/0.5 mg bup/nlx tablets.
- Check for signs of precipitated withdrawal after first 30–60 min.
- Plan to have 1–2 additional office visits approximately 1–3 hours after each dose to check in and administer additional dose if needed until symptoms are managed.

# May incorporate home-based induction for first dose or all Day 1 doses: Consider what works best

- Patient assesses withdrawal (SOWS) and follows dosing instructions. Refer to Home Induction Patient Handout.
- Plan to check in by phone and provide contact information for after-hours advice if needed.
- It is recommended that the patient come in for an office visit the next day.

Max total Day 1 dose is 12 mg/3 mg bup/nix

#### Day 2

- Schedule 1st dose (total day 1 dose) in the morning.
- Reassess 1–3 hours later.
- If symptoms managed may not need any additional visits or doses until morning of Day 3.
- If symptoms not managed may require 1-2 additional office visits approximately 1-3 hours after each dose to check in and administer additional dose if needed until symptoms are managed. Common dose is two 2 mg/0.5 mg bup/nlx tablets.

#### May transition to home-based induction

- Plan to check in by phone.
- Consider asking patient to come for an office visit next day.

## Day 3

- Schedule 1<sup>st</sup> dose in the morning.
- If symptoms managed may not need any additional visits or doses until morning of Day 4.
- If symptoms not managed may require 1–2 additional office visits (approximately 1–3 hours after each dose until symptoms are managed).
- Consider transfer to daily dispensed doses at pharmacy or prescribing takehome doses (1–2 week supply).

Max total Day 2 dose is 16 mg/4 mg bup/nix

Day 3 onwards: maximum total daily dose is 24 mg/6 mg bup/nix

#### **End of first week**

Aim to achieve a stable once-daily dose of buprenorphine/naloxone that will sustain the patient 24 hours with no withdrawal symptoms and no medication-related intoxication or sedation by the end of the first week. Once a stable dose is achieved, patient can be transferred to receive daily dispensed doses at a community pharmacy, or prescribed take-home doses (1–2 week supply), at the discretion of the treating clinician.

# Assessment for buprenorphine/naloxone induction It is imperative to establish the following prior to induction:

• Assess for common contraindications to buprenorphine/naloxone induction: allergy to components of buprenorphine/naloxone; severe respiratory distress; *delirium tremens*; acute alcohol intoxication; and severe liver insufficiency.

- o Note: Liver enzyme tests are recommended (see below) but not required to start treatment due to the increased risk of overdose and death associated with delaying treatment, compared to the relatively low risk of liver toxicity. Severe liver dysfunction can be determined by history and physical exam. If suspicion for severe liver disease is high, consider reviewing with the RACE line. Consider risks and benefits of initiating treatment for patients with liver enzymes > 3–5 times normal upper limit.
- Review substance use history (if not already completed): including other substance use and substance use disorders (e.g. alcohol, stimulants (cocaine, methamphetamine), benzodiazepines, and other sedating medications). Identify past treatment history with buprenorphine/naloxone, other opioid agonist treatment, withdrawal management, psychosocial treatment interventions (e.g., alcohol/drug counselling, mutual support groups) and recovery-oriented approaches (e.g., residential treatment).
- Identify concurrent substance use including alcohol, benzodiazepines, and other sedating medications: Because other central nervous system (CNS) depressants increase risk of respiratory depression, buprenorphine/naloxone doses may require adjustment. Consult with a specialist or call the RACE line. Complete a PharmaNet review. If you do not yet have PharmaNet, call a pharmacist for a review. For guidance on access to PharmaNet refer to: http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/system-access/medical-practice-access-to-pharmanet.
- For women of childbearing age, offer point-of-care urine pregnancy test Refer to Associated Document: BCCSU Pregnancy Supplement.

# The following may be completed subsequent to induction:

- Targeted physical exam and mental health assessment
- Laboratory tests (if not already completed):
  - o Liver tests for screening for potential liver disease (ALT, GGT)
  - o Complete blood count
  - o Creatinine for kidney function

- o HIV and hepatitis B, C serology,
- o Syphilis, gonorrhea, and chlamydia testing;
- o Tuberculosis (assess clinical factors and order appropriate testing if indicated).
- Urine drug testing at point of care, if available, otherwise at laboratory. In the current public health emergency, it is recommended that fentanyl always be requested or included in the point-of-care test. Refer to Associated Document: Frequently Asked Questions: Buprenorphine/Naloxone Treatment.
  - o **Point-of-Care urine drug testing.** Most point-of-care urine drug tests do not include specific tests for fentanyl, oxycodone, and hydromorphone in their standard opioid panel. Ensure fentanyl and buprenorphine strips are ordered in addition to standard urine drug tests or part of a customized panel. Refer to *Associated Document: Frequently Asked Questions: Buprenorphine/Naloxone Treatment* for information of how to order and use point-of-care urine drug tests.
  - o **Laboratory-based urine drug testing:** a urine drug screen, as currently defined by the BC Medical Services Plan (MSP), covers methadone/methadone metabolite, opiates, benzodiazepines, cocaine/cocaine metabolite and amphetamine. Fentanyl and additional types of synthetic opioids (for example buprenorphine, oxycodone, hydromorphone) must be specifically requisitioned.
  - o A urine drug test that is positive for opioids typically confirms the use of the indicated drug or drug class, but false positive results can occur due to cross-reactivity for both point-of-care and laboratory-based immunoassays. Tests may be negative if patient is currently abstinent but false negatives may occur. If in doubt, consider a call to a colleague, the RACE line or local laboratory.
  - o Only consider confirmatory testing in cases where results would alter treatment plan.

## ▶ Planning and preparation for induction of buprenorphine/naloxone

1. Consider whether induction will be entirely office-based or incorporate home-based induction.

Typically, buprenorphine/naloxone induction is office-based with the first dose scheduled to take place under supervision at clinician's office at a morning appointment, followed by 1–3 scheduled follow-up appointments over the first 3 days. Refer to *Associated Document: Frequently Asked Questions: Buprenorphine/Naloxone Treatment* for examples of prescriptions for first three days of buprenorphine/naloxone. Patients may pick up their Day 1 prescription and bring it to the office for witnessed ingestion by a primary care team member after assessment of withdrawal.

Emerging research suggests unobserved or 'home' induction is comparable to office-based induction in terms of safety, patient retention in continued treatment, and reduction in opioid use.<sup>7, 14–16</sup> Home induction may also be appropriate for youth who have a reliable caregiver present to provide support during induction.

It is recommended that the provider have some experience and comfort with buprenorphine/naloxone induction before recommending a home induction. Performing two office-based trials, before offering home induction as an option to patients, may be sufficient.

The core principles of induction are the same whether it is entirely office-based or incorporates home induction as part of the overall buprenorphine/naloxone treatment induction pathway. Providers and patients may benefit from a flexible approach to buprenorphine/naloxone induction. Some patients may require every induction dose to be witnessed by the practitioner. Others may benefit from having the first dose unobserved and then checking in the office later on Day 1, while others may be comfortable with self-managing all of Day 1, followed by an office visit on Day 2. Others may have initial doses witnessed and then transfer to unobserved home dosing. A combination of these pathways may be created to suit patient, caregiver and practitioner preferences.

Patients may benefit from home induction if they have:

- · Ability to safely store medication;
- A reliable caregiver at home who can monitor and help if needed (especially youth);
- · Previous experience with buprenorphine/naloxone; or
- Barriers to office attendance.

For home induction, primary care practitioners should provide the following:

- Practitioner contact information including out of hours advice if needed.
- Written instructions for home induction dosing and timing that has been carefully reviewed with patient and caregiver (if applicable) in advance.
- Schedule regular follow-up by phone or in office.

Refer to Associated Document: Home Induction Patient Handout.

# 2. Emphasize to the patient that a successful induction depends upon having moderate to severe withdrawal symptoms prior to first dose.

Signs of active withdrawal include very bad flu-like symptoms, runny nose, nausea, vomiting, diarrhaea, chills or sweating, goose bumps, bone and muscle aches, stomach cramps, restlessness, yawning, enlarged pupils, shaking or tremors, anxiety, irritability, and a strong desire to use opioids.

If a buprenorphine/naloxone induction is started before a patient is in moderate to severe withdrawal, they will experience a sudden buprenorphine-induced 'precipitated withdrawal', which is much more severe than typical withdrawal, where onset of withdrawal symptoms is gradual. Experiencing a severe, precipitated withdrawal may discourage patients and/or providers from further attempts to use buprenorphine/naloxone.

Ask about the patient's prior experience with withdrawal symptoms. The Clinical Opiate Withdrawal Scale (COWS, practitioner-led assessment) or Subjective Opiate Withdrawal Scale (SOWS, patient self-assessment) can be used to assess extent of withdrawal symptoms and guide induction dosing. Patients may already be familiar with what level of withdrawal they need to be in for successful induction.

For pharmaceutical grade opioids, the length of time from their last dose to onset of moderate to severe withdrawal may be predictable. For example, for pharmaceutical grade opioids, it typically takes 12–16 hours for short-acting opioids (heroin, morphine, hydrocodone, immediate-release oxycodone); 17–24 hours for intermediate-acting opioids (slow-release oral morphine, controlled-release hydromorphone, sustained released oxycodone; and 30–48 hours for long-acting opioids (methadone) before an individual starts to experience moderate withdrawal. While these estimates may be helpful to keep in mind, they may be an underestimate if illicit opioids are contaminated with unknown substances.

In reality, it is unknown which illicit opioids are currently available on the street and how these illicit opioids are metabolized, as there can be considerable variation in drug metabolism between individuals. Anecdotally, addictions medicine specialists in BC have observed precipitated withdrawal occurring even 24 hours or greater after last illicit opioid use due to contamination

of drugs with illicit fentanyl analogues. Therefore, it is important to do the symptom assessment (COWS) and rely on the physical symptoms of withdrawal as well as to ask the patient about their experiences with withdrawal.

Withdrawal symptoms in youth may not correspond to COWS and SOWS criteria and therefore may require individualized clinical assessments. Consider calling the RACE line.

- Refer to Associated Document: COWS Clinical Opiate Withdrawal Scale
- Refer to Associated Document: SOWS Subjective Opiate Withdrawal Scale
- Refer to Associated Document: BCCSU Youth Supplement (available June 8th, 2018)
- Consider completing a patient treatment agreement and consent form. Refer to *Associated Document:*Buprenorphine/Naloxone Treatment Agreement Forms and BCCSU Patient Agreement for Take Home Dosing Form for examples.
- **3.** Provide the appropriate prescriptions for office or home-based buprenorphine naloxone induction.
  - Refer to Associated Document: Frequently Asked Questions: Buprenorphine/Naloxone Treatment for an example.
  - Refer to Appendix C: Opioid Agonist Treatment Medication Table

# Induction of Buprenorphine/Naloxone

- ▶ Day 1 of Induction [Maximum Day 1 total dose is 12 mg/3 mg buprenorphine/naloxone]
  - 1. Immediately prior to first dose, assess withdrawal using COWS or SOWS: Patient must be in moderate to severe withdrawal (COWS ≥ 12 or SOWS ≥ 17) with no signs of alcohol intoxication. Dosing or titration may be adjusted or reduced for patients who are actively using alcohol, benzodiazepines, or other sedating medications, due to increased overdose risk.
  - 2. 1st Dose: For the majority of patients, begin office or home induction with two 2 mg/0.5 mg buprenorphine/naloxone tablets taken sublingually. It is imperative that the patient take the medication sublingually. Place under the tongue and allow to dissolve (medication may take up to 10 minutes to completely dissolve), without swallowing, eating, drinking or smoking. Consider adjusting dosage if withdrawal is very severe (COWS ≥ 24), up to 6 mg/1.5 mg buprenorphine/naloxone. If the patient is currently abstinent, consider lowering dose to 2 mg/0.5 mg buprenorphine/naloxone.

For youth, there is limited information on dosing. It is recommended that clinicians use an individualized and step-wise approach in order to determine the optimal dose for each patient. The induction recommendations included here and in the full guideline, when paired with clinical judgement, can be followed for youth. Refer to *Associated Document: BCCSU Youth Supplement* (available June 8th, 2018).

- 3. Check in 30-60 minutes after the 1st dose for precipitated withdrawal.
  If patient is experiencing precipitated withdrawal in office or at home: Discuss options and obtain informed consent to stop or continue induction depending on severity, patient preference and provider experience. Offer support and encourage patients to continue induction. It is important to note that precipitated withdrawal is not a life-threatening situation and does not generally require emergency department visits.
  - If decision is to continue induction despite precipitated withdrawal, administer 2 mg/0.5 mg buprenorphine/ naloxone every 1–2 hours until withdrawal symptoms resolve, up to the Day 1 max of 12 mg/3mg buprenorphine/ naloxone. If symptoms persist, consider non-opioid symptomatic treatment for withdrawal (clonidine, oral antiemetics, antidiarrheals, NSAIDs, acetaminophen).
  - **If decision is to stop induction**, reassure the patient that symptoms will pass and consider offering non-opioid symptomatic treatment for withdrawal (clonidine, oral anti-emetics, antidiarrheals, NSAIDs, acetaminophen). Refer to the *Guideline for the Clinical Management of Opioid Use Disorder* or seek specialist support (e.g., call the RACE line).
  - If prescribing clonidine for short term symptomatic relief, instruct patients to take 0.1–0.2 mg every 4 hours as needed for < 12 hours. Refer to *Appendix C: Opioid Agonist Treatment Medication Table*.
- 4. Check in 1–2 more times, 1–3 hours apart until withdrawal symptoms are relieved.
  - When withdrawal symptoms are adequately relieved, induction for Day 1 is complete. Consider prescribing one or two 2 mg/0.5 mg buprenorphine/naloxone tablets as take-home doses to treat withdrawal symptoms that may occur later.

- If withdrawal symptoms are not adequately relieved, administer additional one to two 2 mg/0.5 mg buprenorphine/naloxone tablets every 1–3 hours, to a maximum Day 1 total of 12 mg/3 mg buprenorphine/naloxone. If patient has not yet reached maximum Day 1 total, consider prescribing one or two 2 mg/0.5 mg buprenorphine/naloxone tablets as take-home doses for withdrawal that may occur later.
- In rare cases, if symptoms persist, consider non-opioid symptomatic treatment for withdrawal (clonidine, oral anti-emetics, antidiarrheals, NSAIDs, acetaminophen). Refer to *Appendix C: Opioid Agonist Treatment Medication Table* for clonidine dosing information
- **5. Calculate the total dose taken throughout the day**. Patients following home induction instructions should be noting the total dose (number of tablets). The total dose taken on Day 1 is the Day 2 starting dose.
- **6.** Arrange for the patient to come to the office, ideally early in the morning, for their first Day 2 dose or call to check in if patient is following home induction instructions.
- **Day 2 of Induction** [Maximum Day 2 total dose is 16 mg/4 mg buprenorphine/naloxone]
  - 1. Meet the patient in office or check in by phone (ideally in the morning).
    - If withdrawal symptoms are adequately relieved, administer the Day 1 total dose (sublingually, all at one time).
    - If withdrawal symptoms are not adequately relieved, administer the Day 1 total dose and an additional two 2 mg/0.5 mg buprenorphine/naloxone tablets (taken sublingually, all at one time).
    - If needed, administer additional doses of 2 mg/0.5 mg buprenorphine/naloxone tablets every 1–3 hours to a maximum Day 2 total of 16 mg/4 mg buprenorphine/naloxone.
  - **2. Optional:** Check in one or two more times if needed (1–3 hours between check-ins).
    - When withdrawal symptoms are adequately relieved, induction for Day 2 is complete.
    - If withdrawal symptoms are not adequately relieved, administer additional one to two 2 mg/0.5 mg buprenorphine/naloxone tablets every 1–3 hours, to a maximum Day 2 total of 16 mg/4 mg buprenorphine/naloxone.
    - In rare cases, if symptoms persist, consider non-opioid symptomatic treatment for withdrawal.
- **Day 3 onwards** [Maximum total daily dose is 24 mg/6 mg buprenorphine/naloxone]
  - 1. Each day (ideally in the morning) meet patient in office or check-in by phone.
    - If no withdrawal symptoms were present the previous day, administer the previous day's daily total, plus an additional one to two 2 mg/0.5 mg buprenorphine/naloxone tablets to a final range of 12 mg/3 mg 16 mg/4 mg buprenorphine/naloxone.
    - If patient is feeling sedated, total dose can be titrated down to reduce undesirable side effects.
    - If withdrawal symptoms, craving, or illicit opioid use persists, increase dose by one to two 2 mg/0.5 mg buprenorphine/naloxone tablets every 1–3 hours as needed to maximum dose of 24 mg/6 mg buprenorphine/naloxone per day.
  - 2. Aim to achieve an optimal stable once-daily dose of 12 mg/3 mg to 16 mg/4mg buprenorphine/naloxone that will sustain the patient for 24 hours with no withdrawal symptoms and no medication-related intoxication or sedation by the end of the first week (maximum total daily dose after day 2 is 24 mg/6 mg buprenorphine/naloxone per day).
  - 3. Prescribe optimal once-daily dose and arrange for a follow-up appointment the next week. Daily dispensed buprenorphine/naloxone is not witnessed unless specifically requested by prescriber. Consider prescribing take-home doses at the discretion of the prescribing clinician provided patient is clinically stable and has access to safe-storage for medication (see below for more information).
  - **4. For individuals not benefiting from buprenorphine/naloxone**, consider transition to methadone or other alternative treatment options. Refer to specialist and see also the *Guideline for the Clinical Management of Opioid Use Disorder* for detailed methadone transition and management strategies.

# Long-term care (maintenance)

## Follow-up with regular scheduled office visits

- Initially every 1–2 weeks or as needed, with longer intervals once stabilized. Assess treatment effectiveness and side effects or withdrawal symptoms and reassess treatment plan:
  - o "How are your cravings?" "Have you had any withdrawal symptoms?" "Have you used any opioids?" "Are there any other substances that you are using at this time (specifically ask about sedating agents e.g., alcohol, benzodiazepines, etc)?" "How are you sleeping?" "How is your mood/anxiety?" "How are things at home?"
- Relapse is common and should not be seen as a failing. OUD is a chronic, relapsing condition. As in other chronic diseases, treatment strategies should be adjusted. Patients should not be asked to leave treatment if they relapse. It is critical to provide patients with non-judgemental support and encouragement in achieving their goals.
- PharmaNet should be checked to corroborate treatment adherence or missed doses.
- Generally, patients can receive take-home dosing immediately, provided medications can be safely stored, unless daily dispensed doses (generally at pharmacy) would be preferable for a particular patient at the discretion of the treating clinician.
- Patients typically achieve optimal dosing within 7–10 days of treatment (often sooner).
- Patients can be maintained on buprenorphine/naloxone for years.
- Refer to the *Guideline for the Clinical Management of Opioid Use Disorder* for detailed guidance regarding long-term maintenance, including guidance about tapering buprenorphine/naloxone after careful consideration of the risks.
- Patients do not need to be tapered off buprenorphine/naloxone for surgery or management of acute pain. Short acting opioids can be used successfully perioperatively and in setting of acute pain while patient is maintained on their dose of buprenorphine/naloxone. Call the RACE line for more information.

# Consider take-home doses for clinically stable patients at stable doses

Take-home dosing should be considered for all patients once clinically stable and able to safely store medication. Quick transition to take-home dosing has been shown to improve treatment adherence and retention.<sup>17,18</sup> Consider the impact of providing or limiting take-home dosing on treatment adherence or loss to care. Consider the impact of providing or limiting take-home dosing on treatment adherence or loss to care. Refer to the *Guideline for the Clinical Management of Opioid Use Disorder* for information about take-home dosing. The rationale for not prescribing take-home doses should be carefully documented in the medical record.

It is recommended that the prescriber and patient complete an agreement form for receiving take-home dosing which can be documented alongside the patient's medical records. Provide a copy to the patient. Refer to BCCSU Patient Agreement for Take Home Dosing Form.

## Considerations for safely maintaining a patient on take-home buprenorphine naloxone:

- It is recommended that buprenorphine/naloxone be prescribed as a 1–2 week supply in blister-packs.
- It is recommended that practitioners continually monitor for signs of relapse to opioid use, use of sedating agents (e.g., alcohol, benzodiazepines, etc.), social instability, and diversion.
- Practitioners may request random urine drug tests and random pill counts to reduce risk of diversion. Currently, 4 random pill counts and 4 random urine drug tests (24 hour notice) in the first year of treatment is recommended for patients who are prescribed take-home doses.

#### The following are considerations for follow-up and reassessment:

- Self-reported or other indication of non-medical opioid use.
- Missed appointments and/or missed doses, or repeated reports of lost, spilled, stolen or vomited doses.
- Requests to increase a previously stable dose.
- Unable to attend the clinic for random urine drug tests (see below).
- Unable to attend the clinic for random pill counts or evidence of tampering with blister-pack.

Evidence of other non-medical opioid use and/or other substance use should prompt reassessment of treatment plan, but not automatic discontinuation of take-home doses. Before take-home prescriptions are discontinued, the prescriber

must balance the risks of destabilizing patients by enforcing daily dispensing of medication. Daily witnessing of medication has not been shown to improve outcomes and is a recognized barrier for treatment engagement. In addition, the buprenorphine/naloxone formulation was created to facilitate take-home dosing and make treatment more attractive to patients due to its safety profile and lower risk of diversion.

Evidence of diversion (e.g., urine drug test negative for buprenorphine) should prompt immediate reassessment of treatment plan, and, in most cases, discontinuation of take-home dosing with consideration of dose reduction upon re-introduction of daily dispensing and supervised ingestion if doses have been missed (see Table 2, below). Patients should not be asked to leave treatment. It is critical to provide patients with non-judgemental support and encouragement in achieving their goals.

# Complete periodic urine drug testing (4 random tests recommended for the first year for patients prescribed take-home doses)

General indications for requesting urine drug testing:

- To assess adherence to buprenorphine/naloxone treatment.
- To validate self-reported use of opioids or other substances.
- To detect use of other substances which may affect safety (e.g., benzodiazepines).
- To evaluate treatment response and outcomes (i.e., abstinence from heroin or other opioids).
- In the current public health emergency, it is recommended that fentanyl always be requested or included in the point-of-care test.

Complete urine drug testing at point of care if available, otherwise at laboratory. See above description of urine drug testing and refer to Associated Document: Frequently Asked Questions: Buprenorphine/Naloxone Treatment and Appendix 2 in the Guideline for the Clinical Management of Opioid Use Disorder.

#### Missed Doses

- If 5 or fewer daily consecutive doses are missed, resume the previous dose.
- If 6 or more daily consecutive doses are missed, a loss of tolerance to buprenorphine may have occurred and patients may require re-stabilization. Refer to Table 2 below.
- If it has been greater than 6 days and the patient has relapsed to non-medical opioid use, consider consultation with an addiction specialist or the RACE line about whether a re-induction is required
- Note the dispensing pharmacy will cancel the prescription after ≥ 6 days of missed doses as per College of Pharmacists of British Columbia policy.<sup>20</sup>

Table 2: Missed dose adjustment schedule (doses listed are mg/mg buprenorphine/naloxone)

Dose	Number of missed days	Suggested Dose Adjustment		
2 mg/0.5 mg - 4 mg/1 mg	≥ 6 days	No change		
6 mg/1.5 mg - 8 mg/2 mg	≥ 6 days	Restart at 4 mg/1mg		
> 8 mg/2mg	6–7 days	Restart at 8 mg/2 mg		
> 8 mg/2mg	≥ 7 days	Restart at 4 mg/1mg		

# **Alternative Treatment Options for OUD**

#### Methadone

# Methadone is recommended for opioid agonist treatment if induction with buprenorphine/naloxone is challenging or not preferred

- As of May 19th 2018, a federal exemption (through section 56 of the *Controlled Drugs and Substances Act*) will no longer be required to prescribe methadone.
- To be eligible to prescribe methadone, BC practitioners are required to complete education and training via the Provincial Opioid Addiction Treatment Support Program, available at bccsu.ca
- Primary care practitioners providing care to individuals with OUD are encouraged to consider taking the Provincial Opioid

Addiction Treatment Support Program, alternatively patients can be referred to a local specialist in methadone treatment.

• Refer to *Guideline for the Clinical Management of Opioid Use Disorder* for detailed methadone induction and continuing care strategies, which are out of the scope of this summary guideline.

# Slow-release oral morphine and injectable OAT

- Higher intensity treatment options are available for patients who have been unsuccessful with first-line (buprenorphine/naloxone) and second-line (methadone) treatment options, such as OAT with slow-release oral morphine (prescribed as once-daily witnessed doses) and injectable OAT with medications such as hydromorphone and diacetylmorphine.
- Prescription of slow-release oral morphine or injectable OAT medications requires specialized addiction medicine training and is outside the scope of this guideline.
- Consult with an experienced prescriber in your area, or the RACE line.
- Refer to the online Provincial Opioid Addiction Treatment Support Program available at bccsu.ca.
- For more information about injectable OAT refer to the Guidance Document for Injectable Opioid Agonist Treatment.

# "Withdrawal management alone" (also known as detox) without supporting long-term addiction treatment is not recommended.

The terms "withdrawal management", "withdrawal management alone" and "detox" can have multiple meanings for the general public and experts, which can lead to confusion. In this guideline, the term "withdrawal management" refers to a short-term detox or opioid agonist taper that takes place over days or weeks (not months). "Withdrawal management alone" refers to situations where short-term detox or opioid agonist taper is administered without a plan for long-term opioid agonist treatment.

- Dangers associated with "withdrawal management alone" include elevated rates of relapse, and increased high risk behaviours that may lead to HIV and HCV infection, and overdose death after discharge if there is no linkage to comprehensive, continuing care.
- Risk of overdose and death increases after a reduction or the cessation of opioids because of lower tolerance to opioids.
- Treatment options should always be discussed with the patient, however the safest and most effective treatment option is long-term OAT.
- If patient requests withdrawal management against medical advice, slow (months, not days), outpatient withdrawal management with supporting long-term addiction and recovery-oriented treatment is recommended after discussion of risks (refer to Associated Document: Withdrawal Management Safety Bulletin). This can be done in the primary care setting as an outpatient.
- The primary care setting offers a supportive patient-practitioner relationship, continuity of care and less risk of loss to follow-up. Refer to the provincial *Guideline for the Clinical Management of Opioid Use Disorder* and consult RACE line as needed.

# **Additional Supports**

### ▶ Psychosocial Treatment Interventions and Supports

Lack of availability to psychosocial treatment interventions and supports should not be a barrier to care and medication should not be contingent on patient willingness to engage in counselling or other supports. If available, and aligned with the patient's treatment goals, offer psychosocial treatment interventions and supports in conjunction with pharmacological treatment.

#### ▶ Harm Reduction: Take-home naloxone kits and other harm reduction education

Provide or recommend a take-home naloxone kit to all patients at risk of overdose. Information and referral to take-home naloxone programs and other harm reduction services, if appropriate (e.g., safe inhalation supplies, safe sex supplies), should be routinely offered as part of standard care for OUD. Additionally, patients with ongoing injection drug use can be referred to needle distribution and harm reduction supply sites, as well as supervised consumption and overdose prevention sites, where available.

Practitioners, patients and caregivers can access free naloxone kits and harm reduction supplies (refer to towardtheheart.com) which are also available for purchase at most pharmacies. First Nations Health Authority clients can access intramuscular and intranasal naloxone kits for free at any pharmacy.

For more information on accessing free naloxone kits and educational information and high quality videos describing how to administer naloxone for patients, caregivers and health care providers, refer to the BC Centre for Disease Control's website: towardtheheart.com.

## ▶ Trauma-Informed Practice and Adverse Childhood Experiences (ACEs)

Treatment of OUD benefits a compassionate, patient-centred and non-judgemental approach and consideration of the principles of trauma-informed practice. Consider asking patients about past trauma using the Adverse Childhood Experiences questionnaire available at collaborativetoolbox.ca. Family practitioners who use the questionnaire often find that many patients are open to being asked about past trauma. Conversations about adverse childhood experiences may provide an opportunity to offer additional supports. The Provincial Opioid Addiction Treatment Support Program available at bccsu.ca, includes a module on trauma-informed practice in the context of treating patients with OUD. Practitioners may also refer to the collaborativetoolbox.ca for information and resources about trauma-informed practice and adverse childhood experiences.

## Recovery Oriented Care

Primary care providers are encouraged to incorporate and use language that promotes recovery in their practice. Those seeking recovery require understanding and support, as well as referrals to appropriate services and programs to achieve their individual goals. Recovery-oriented care includes ensuring respect of the patient's autonomy and individuality (both as partners in determining treatment modalities and throughout their recovery), emphasizing skills and strengths, and avoiding reinforcement of authoritarian models of care provision<sup>21</sup>. Additionally, and as appropriate, primary care teams are encouraged to work with patients to develop long-term, personalized, strengths-based recovery plans regardless of the severity, complexity, and duration of their substance use.

# **Considerations for Youth**

Buprenorphine/naloxone is recommended as the first-line treatment for adolescents and young adults (12 to 24 years of age) with moderate to severe OUD where indicated and appropriate. Buprenorphine/naloxone is approved for people over 18 years of age. For youth, the benefits associated with treating OUD outweigh the risks. It is recommended that practitioners document informed consent and rationale for treatment.

Practitioners are encouraged to develop a relationship with youth and promote screening and early intervention for substance use disorders in this population. It is recommended that all youth be screened for co-occurring mental health disorders, when appropriate. Youth benefit from age- and developmentally-appropriate, youth-oriented substance use care as well as continuity of care as they enter young adulthood

- Be aware of the need for confidentiality, trust and issues related to information sharing for young people.
- Refer to Associated Document: BCCSU Youth Supplement (available June 8th, 2018)

## Resources

# Appendices

- Appendix A: Opioid Use Disorder Diagnosis
- Appendix B: Literature Review
- Appendix C: Opioid Agonist Treatment Medication Table

# Associated Documents

Resource guides:

- Resource Guide for Practitioners
- Resource Guide for Patients and Caregivers

Withdrawal Scales available at bccsu.ca:

- COWS Clinical Opiate Withdrawal Scale
- SOWS Subjective Opiate Withdrawal Scale

Treatment agreement forms available at bccsu.ca:

- BCCSU Buprenorphine/Naloxone Treatment Agreement Form
- BCCSU Patient Agreement for Take Home Dosing Form

Patient Handout for starting Buprenorphine/Naloxone Home Induction:

Home Induction Patient Handout
 Original concept based on a patient handout produced Dr. Joshua Lee.<sup>22</sup>

BCCSU Supplements and information sheets available at bccsu.ca:

- BCCSU Youth supplement (available June 8th, 2018)
- BCCSU Pregnancy Supplement
- BCCSU Frequently Asked Questions: Buprenorphine/Naloxone Treatment
- BCCSU Withdrawal Management Safety Bulletin

# Billing Codes for opioid agonist treatment (OAT):

For more information, refer to the MSC Payment Schedule available at gov.bc.ca: MSP Payment Schedule

### • P13013 Assessment for Induction of Opioid Agonist Treatment (OAT) for Opioid Use Disorder (\$42.65)

- o Initial assessment requires complete medical history, substance use history and appropriate targeted physical examination. If assessment and induction are done on the same day, withdrawal assessment using COWS or SOWS and administration of first dose of OAT included per 15 minutes or greater portion thereof. Can be billed for up to 4 units per day.
- o Payable to a maximum of 4 units per patient/per day/per intended induction.
- o Payable only to the physician who intends to provide or share management of the patient's OAT induction for opioid use disorder.
- o Start and end times must be entered in both the billing claim and the patient's chart.
- o No other visit fees billable same day except 13014, 14018 and 14077.
- o 13014, 14018 and 14077 payable in addition to 13013 only when not performed concurrently.
- o Payable for assessment for change of OAT with induction to a different medication.
- o May not be repeated within 30 days by the same physician.
- o This service payable only for physician time spent on patient assessment (and on administration of first dose of OAT if provided same day).

#### • P13014 Management of OAT Induction for Opioid Use Disorder (\$20.00)

This fee is payable for individual interactions with the patient during the first three days of OAT induction for opioid use disorder within the limits described in the following notes

- o Billable in addition to 13013 or a same day visit fee (in-person, telephone or video conference) with a physician when not performed concurrently.
- o Billable up to 3 times on day of first dose of OAT.
- o Billable up to 2 times on day 2 of OAT induction.
- o Billable once only on day 3 of OAT induction.
- o May be provided in-person, by telephone, or by video conference.
- o May be billed when delegated to a nurse (LPN, RN, NP) employed within the eligible physician practice.
- o Start time must be entered in both the billing claim and patient's chart.
- P00039 Management of Maintenance OAT for Opioid Use Disorder (\$23.42/week)
- P15039 Point of Care urine drug screen testing for opioid agonist treatment (\$12.53)
- General Practice Services Committee (GPSC) fees that support treatment of opioid use disorder: http://www.gpscbc.ca/news/gpsc/opioid-treatment-and-management-practice-resources

### Abbreviations

- ALT Alanine aminotransferase
- ALP alkaline phosphatase
- COWS Clinical Opiate Withdrawal Scale
- · GGT gamma-glutamyl transpeptidase
- INR International Normalized Ratio
- SOWS Subjective Opiate Withdrawal Scale

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This guideline is based on scientific evidence current as of the effective date. The guideline was developed by the Guidelines and Protocols Advisory Committee and the British Columbia Centre on Substance Use, based on the provincial *Guideline for the Clinical Management of Opioid Use Disorder* (2017), approved by Doctors of BC and adopted by the Medical Services Commission.

### THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

## The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- · recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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## Disclaimer

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions.** If you need medical advice, please contact a health care professional.

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**Guidelines & Protocols Advisory Committee** 

# **Appendix A: Opioid Use Disorder Diagnosis and Management Pathway**

#### **Addiction Medicine Consult**

Contact local specialist or RACE line: 604-682-2344 Toll-free 1-877-696-2131 www.raceconnect.ca

\* For detailed guidance refer to Guideline for the Clinical Management of Opioid Use Disorder

# Screening

"How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?"

More than zero for opioids?

**Diagnosis of Opioid Use Disorder** DSM-5 Diagnostic croteria

YES everyone at risk should have a naloxone kit

Lack of access to counselling **should not be considered a barrier** to beginning treatment for opioid use disorder.

#### Ongoing high-risk drug use?

 Discuss risks and harm reduction (naloxone kit, drug checking, safe injection, harm reduction supplies, overdose prevention), and follow up

If no opioid use, screen for other substance use disorders using DSM-5 criteria

- e.g. alcohol, stimulants, benzodiazepines
- contact RACE line and refer to bccsu.ca

#### **Discuss pros/cons of Common Treatment Options**

#### 1. Buprenorphine/naloxone (bup/nlx)

- · Good safety profile: less risk of overdose
- · Milder side effects
- Easier to progress to take-home doses; generally can progress to take-home doses immediately at the discretion of the treating clinician once clinically stable and can safely store medication.
- Induction can be challenging and requires focussed care
  - Time required to complete induction
  - Risk of precipitated withdrawal

#### 2. Methadone

NO

- · May be preferred treatment for unstable individuals
- Consider when buprenorphine/naloxone is contraindicated or not-preferred.
- · Requires daily witnessed ingestion
- Higher risk of overdose
- Requires education and training to prescribe via the Provincial Opioid Addiction Treatment Support Program, available at bccsu.ca

# 1

#### **Recommended 1st line treatment**

# Buprenorphine/Naloxone (Suboxone®) Opioid Agonist Treatment

#### Assessment and Investigations Preparing for Induction

# • Treating opioid use disorder benefits from a supportive, empathetic, open-door approach.

- Assess addiction history and co-morbidities.
- Assess concurrent medications (review Pharmanet).
   If concurrent alcohol, benzodiazepines, sedatives-consult RACE line.
- · Review contraindications.

Allergy to drug components, severe liver dysfunction, severe respiratory distress, *delirium tremens*, acute alcohol intoxication.

- Offer an office-based urine pregnancy test. If positive, consult RACE line.
- Complete the following within the first week if not already.
  - Targeted physical and mental health assessment.
  - Laboratory tests.
  - Urine drug test, include test for fentanyl.
- Provide education and discuss the following with the patient and caregiver (if appropriate).
  - How bup/nlx works.
  - Home and office induction.
  - Precipitated withdrawal and how it can be avoided by being in withdrawal for 1st dose on Day 1.
  - Withdrawal assessment tools: COWS (office) and SOWS (home).
  - Review treatment plan.

# Induction: Patient must be in withdrawal for 1st dose on Day 1 (COWS ≥ 12) or (SOWS ≥ 17)

#### Office Based Induction

 Ask patient to come to office, in withdrawal. Patient will stay and/or check-in several times throughout Day 1. Doses are witnessed in office unless practitioner determines it is appropriate for patient to take-home.

#### • Home Induction (if appropriate)

- Provide contact info where patient/caregiver can reach you including after-hours advice if needed
- Provide instructions about timing and doses
- Patient self-assesses withdrawal using SOWS and takes dose at home. Youth require supervision by a responsible adult.
- Ask patient to call after they have taken 1st dose.

#### **Day 1** - Document in office (or at home by patient).

#### 1. 1st dose (note doses are mg/mg buprenorphine/naloxone (bup/nlx) and sublingual)

- Confirm withdrawal using COWS or SOWS.
- If COWS 12-23 (SOWS ≥17): Common starting dose is 4 mg/1 mg bup/nlx.
- Adjust dose if severe withdrawal (COWS≥24) or if abstinent.
- For youth, use an individualized and step-wise approach to dosing, consider call to RACE line.

#### 2. Check-in after 30-60 min

 If patient (office or home) feels terrible/worse, manage symptoms of precipitated withdrawal and encourage continuing with induction – if they choose to continue, give second dose and follow with additional doses every 1–2 hours to max total of 12mg/3 mg bup/nlx.

#### 3. Schedule visit or call to check-in after 1-3 hrs

- If patient feels good, no additional Day 1 doses (consider a take-home dose if concerned may be needed to manage withdrawal symptoms later)
- If withdrawal symptoms persist, provide additional doses of one or two 2 mg/0.5 mg bup/nlx tablets every1–3 hours, if needed, to a max total of 12 mg/3 mg bup/nlx on Day 1.

#### Remainder of first week Day 2 max total: 16 mg/4mg bup/nlx.

Ongoing max total: 24 mg/6mg bup/nlx.

• Aim to reach dose of 12mg/3mg-16mg/4mg bup/nlx.

- Aim to reach dose of 12mg/3mg-16mg/4mg bup/nl: This range is recommended for effective treatment.
- Goal is 24-hour dosing interval with no withdrawal symptoms, medication-related intoxication or sedation.

#### Day 2 onwards (symptoms managed)

Repeat previous total dose + one to two
 2 mg/0.5 mg bup/nlx tablets - taken once daily.

#### Day 2 onwards (feeling withdrawal)

- Repeat previous day total dose + one to two 2 mg/0.5 mg bup/nlx tablets.
- Titrate as needed (by one to two 2 mg/0.5 mg bup/nlx tablets every 1–3 hours to recommended daily max.

#### Day 2 onwards (feeling sedated)

- Decrease dose as needed.

#### Long-term Maintenance

#### Schedule follow-up visits

- Initially every 1–2 weeks or as needed, with longer intervals once stabilized.
- Review effectiveness and side effects.
- Patients are often clinically stable within 7-10 days.
- Consider take-homes once clinically stable and can safely store medications.

#### Urine Drug Testing

- 4 random tests recommended for the first year for patients prescribed take-home doses
- Test for bup/nlx to assess adherence to treatment, test for fentanyl, opioids, and substances that may affect safety.
- Opioid use disorder is a chronic relapsing disease. If patient relapses, reassess treatment plan and continue treatment

# If buprenorphine/naloxone is challenging or not indicated

Methadone opioid agonist treatment or alternative higher intensity treatment options (slow-release oral morphine and injectable opioid agonist treatment)

- Consider taking provincial Provincial Opioid Addiction Treatment Support Program (bccsu.ca) to be able prescribe methadone.
- The *Guideline for the Clinical Management of Opioid Use Disorder* outlines detailed methadone management strategies.
- Alternative, higher intensity treatment options are also available in BC for individuals who do not benefit from first- and second-line opioid agonist treatments, such as slow-release oral morphine and injectable opioid agonist treatment (refer to *Guidance Document for Injectable Opioid Agonist Treatment*), which can be prescribed by experienced addiction medicine practitioners.



## Proceed with caution: Outpatient Withdrawal Management with concurrent long-term addiction treatment

**CAUTION:** "Withdrawal management" (commonly known as detox) alone without long-term opioid agonist treatment or linkage to continuing care is not recommended. Dangers associated with withdrawal management alone include elevated rates of relapse, HIV and HCV infection and overdose death after discharge if there is no linkage to comprehensive and continuing addiction care

The terms "withdrawal management", "withdrawal management alone" and "detox" can have multiple meanings for the general public and experts, which can lead to confusion. In this guideline, the term "withdrawal management" refers to a short-term detox or opioid agonist taper that takes place over days (not months). "Withdrawal management alone" refers to situations where short-term detox or opioid agonist taper is administered without a plan for long-term opioid agonist treatment.

- Dangers associated with "withdrawal management alone" include elevated rates of relapse, HIV and HCV infection and overdose death after discharge if there is no linkage to comprehensive, continuing care.
- Risk of overdose and death increases after a reduction or the cessation of opioids because of lower tolerance to opioids.
- The safest and most effective treatment option is long-term opioid agonist treatment.
- If patient request withdrawal management, slow (months, not days), outpatient withdrawal management with supporting long-term addiction and recovery-oriented treatment is recommended after discussion of risks. This can be done in the primary care setting as an outpatient. The primary care setting offers less risk of loss to follow-up, continuity of care, and a supportive patient-practitioner relationship. Refer to the provincial *Guideline for the Clinical Management of Opioid Use Disorder*, *Associated Document: Withdrawal Management Safety Bulletin*, and consult RACE line as needed.



# **Appendix B: Literature Review**

#### Continuum of opioid use disorder care

Adapted from Table 1 of the Guideline for Clinical Management of Opioid Use Disorder available at bccsu.ca

# **WITHDRAWAL** MANAGEMENT 1-3

Tapered methadone, buprenorphine, or alpha<sub>2</sub>-adrenergic agonists +/- psychosocial treatment<sup>4</sup> +/- residential treatment +/- oral naltrexone<sup>5</sup>

#### **AGONIST THERAPIES**

Buprenorphine/ naloxone<sup>6</sup>

Methadone 7,8

# SPECIALIST-LED ALTERNATIVE **APPROACHES**

Slow-release oral morphine 9,10 Diacetylmorphine Hydromorphone

#### LOW

If opioid use continues, consider treatment intensification. TREATMENT INTENSITY

HIGH

Where possible, simplify treatment.



# HARM REDUCTION 11-13

Across the treatment intensity spectrum, evidence-based harm reduction should be offered to all, including:

- Education re: safer user of sterile syringes/needles and other applicable substance use equipment
- Access to Supervised Injection Sites (SIS)
- Take-Home-Naloxone (THN) kits

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# **Appendix C: Opioid Agonist Treatment Medication Table**

DRUGS FOR OPIOID AGONIST TREATMENT									
Generic Name	Trade Name	Available Dosage Forms	Recommended Adult Dose	Adverse Effects	Drug Interactions <sup>A</sup>	PharmaCare Coverage <sup>B</sup>	Approx. Cost <sup>c</sup>		
buprenorphine/ naloxone	Suboxone <sup>®</sup> , G	SL tabs: 2 mg / 0.5 mg, 8 mg / 2 mg	Day 1 Induction: Two 2 mg/0.5 mg SL tabs when COWS > 12 and no long-activing opioid used for at least 30 hours May be increased to three 2 mg/0.5 mg SL tabs when COWS > 24 and patient experienced severe withdrawal symptoms [max total: 12 mg/3 mg] Day 2 Onward: Continue once-daily dose equal to the total amount administered on the previous day titrating up as needed in subsequent days to a target dose of 16 mg/4 mg per day or greater. [max total: 24 mg/6 mg per day]	Hyperhidrosis, abdominal pain, constipation, nausea, vomiting, headache, insomnia.	alcohol benzodiazepines and other CNS depressants naltrexone CYP3A4 inhibitors <sup>D</sup> CYP3A4 reducers <sup>E</sup> monoamine oxidase inhibitors	Yes, LCA	\$153 (G) \$215 Per 30 days		
clonidine	G	<b>Tab:</b> 0.1, 0.2 mg	0.1 to 0.2 mg every 4 hours as needed for up to 12 hours. (max total: 0.6 mg)  Check blood pressure prior to each dose and hold the dose if hypotension is present.	Sedation, dry mouth, orthostatic hypotension, dizziness.	alcohol diuretics beta-blockers ACE-inhibitors angiotensin receptor blockers calcium channel blockers digoxin atypical antipsychotics SSRIs methylphenidate	Yes	\$1.00 per day		

Abbreviations: G generics; LCA low cost alternative program; max maximum dose; SL sublingual

 $<sup>^{\</sup>text{A}} \, \text{Not an exhaustive list. Check the product monographic or an interaction checker (e.g., Lexicomp^{(c)} \, before \, prescribing)} \, \text{ and } \, \text{ or an exhaustive list.} \, \text{ or a$ 

<sup>&</sup>lt;sup>8</sup> PharmaCare coverage as of December 2017 (subject to revision). Obtain current coverage, eligibility, and coverage information from the PharmaCare Formulary Search website at https://pharmacareformularysearch.gov.bc.ca/

<sup>&</sup>lt;sup>c</sup> Cost as of December 2017 and does not include retail markups or pharmacy fees. Generic and brand name cost separated as indicated by (G).

<sup>&</sup>lt;sup>D</sup> May increase buprenorphine plasma concentrations (e.g., protease inhibitors, macrolide antibiotics, and azole antifungals)

<sup>&</sup>lt;sup>E</sup> May decrease buprenorphine plasma concentrations (e.g., phenobarbital, carbamazepine, phenytoin, and rifampicin)