BRITISH COLUMBIA CENTRE ON SUBSTANCE USE
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# Opioid Agonist Treatment Initiation

*Note: This document provides information on opioid agonist treatment (OAT) options. Regional health authorities may opt to develop relevant pre-printed orders (PPOs), decision support tools (DSTs), workflows, or other tools to support implementation*

## Preamble

### Opioid agonist treatment is the standard of care for opioid use disorder (OUD)

### Patients should receive OAT medications in acute care settings in order to:

- Prevent opioid withdrawal

  Reduce self-management of withdrawal symptoms using unregulated opioids, which increases the risk of overdose
- Support meeting acute medical and surgical needs
- Improve overall health and treatment outcomes
- Enhance comfort and safety
  - Reduce risk of return to use
  - Prevent self-initiated discharge
- Reduce barriers to meeting other treatment, harm reduction, and self-defined recovery and wellness goals

This document provides medication-specific initiation guidance for **buprenorphine**, **methadone**, and **slow-release oral morphine (SROM)**

- Use shared decision-making with the patient to determine the most suitable OAT option, prioritizing patient goals and preferences
- See *Acute Care and Opioid Use Disorder* for information on eligibility and other considerations

## Patient Education Before Initiating OAT

- ☐ Discuss any other medications and medical conditions
- ☐ Discuss common side effects (e.g., constipation, drowsiness)
- ☐ Unless prescribed and carefully monitored, avoid mixing opioids (e.g., OAT medications) and CNS depressants (e.g., other opioids, benzodiazepines, alcohol) as it increases the risk of overdose
- ☐ Advise the patient that it takes time to titrate to a stable dose
  - Patient can be referred to a community OAT clinic for ongoing titration, if interested

## Assessment

### Conduct a baseline assessment for all candidates for OAT.

### Physical and mental health assessment, including:

- Medical history (e.g., prolonged QTc, respiratory disease, co-occurring substance use disorders)
- Mental health history
- A comprehensive review of substance use
- Urine drug test (UDT) to confirm the presence of substances and to identify other relevant substances such as benzodiazepines (UDT is not required)
- Pregnancy test, if applicable
- Review of co-occurring CNS depressant use, including alcohol, benzodiazepines, and sedatives (prescribed or unregulated)
- Review PharmaNet
- Laboratory tests, if indicated

See *Acute Care and Opioid Use Disorder* for more information on conducting a baselines assessment.

Consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports as needed.

# Buprenorphine/naloxone (Suboxone)

Buprenorphine is available in tablets containing 4:1 ratio of buprenorphine and naloxone (8mg and 2mg tablets).

In this document, the dose will refer to the buprenorphine component only.

Tablets are administered sublingually

- Keep the tablet under tongue until it dissolves, which may take 10–15 minutes
- Avoid swallowing, talking, eating, drinking, or smoking during this time to ensure that the full dose is absorbed

**The maximum daily dose of buprenorphine is 32mg.**

### Emergency Department (ED) Buprenorphine Induction (BUP-to-go)

Follow site-specific protocols, if available.

Provide enough medication for the induction and initial continuation to first clinic appointment, as well as non-opioid adjunct medications to alleviate withdrawal symptoms.

Advise the patient to go to an addiction clinic or primary care clinic before medication runs out to get a new prescription.

Provide bup-to-go handout (see Resources).

## Induction Methods

There are 2 induction methods:

### Low-dose induction

Also referred to as "micro-dosing induction" or "micro-induction"

- Slow up-titration while continuing full agonist use (e.g., hydromorphone, fentanyl, methadone, slow-release oral morphine)
- Does not require patients to discontinue using other opioids prior to initiation
- Does not require a period of opioid withdrawal prior to medication initiation
- Time to reach therapeutic dose: 5–10+ days

### Traditional induction

- Requires patient to discontinue opioid use **and** be in moderate withdrawal prior to initiation to avoid precipitated withdrawal
- Therapeutic dose: 1–2 days

## Low-dose Induction

Follow site-specific low-dose induction protocols, if available. An example protocol follows.

**Table 1. 8-day Low-dose Induction Protocol**

| Day | Buprenorphine Dose | Other Opioids |
|---|---|---|
| 1 | 0.5mg two times daily | Continue full agonist use |
| 2 | 1mg two times daily | Continue full agonist use |
| 3 | 2mg two times daily | Continue full agonist use |
| 4 | 3mg two times daily | Continue full agonist use |
| 5 | 4mg two times daily | Continue full agonist use |
| 6 | 6mg two times daily | Continue full agonist use |
| 7 | 8mg two times daily | Continue full agonist use |
| 8 | 16mg once daily | Stop other opioid use |

Note that during low-dose induction, buprenorphine doses are not sufficient to address opioid withdrawal. To manage opioid withdrawal:

- Co-prescribe a full agonist (e.g., methadone, slow-release oral morphine, hydromorphone) until induction buprenorphine dose is consolidated into once-daily dose
- Slow down the titration process
- Provide non-opioid adjunct medications (see Non-opioid Adjunct Medications)
- Guidance on additional titration protocols and full agonist dosing can be found in *Managing Acute Opioid Withdrawal*, the BCCSU's *Guideline for the Clinical Management of Opioid Use Disorder (2023)*, and Approach to Microinductions module on the LOUD in the ED Online Lecture Materials page

**The recommended maximum Day 1 dose of buprenorphine is 16mg.**

A Day 1 dose greater than 16mg may be needed to address withdrawal symptoms; 16mg may be exceeded if clinically indicated

**The recommended maximum Day 2 and beyond dose of buprenorphine is 32mg.**

Titration may be safely completed in 1–2 days; however, it may take 5–7 days for the patient to reach complete stability and feel the full effect of treatment.

## Preparation

Ensure that the patient has discontinued opioids prior to induction (see chart below).

Inform patient of the risk of precipitated withdrawal and discuss the actions that can be taken if it occurs.

To avoid precipitated withdrawal, patients should reach moderate withdrawal prior to induction (Clinical Opiate Withdrawal Scale [COWS] >12 for in-hospital traditional inductions) and minimum length of time since last opioid use (see below).

Follow site-specific protocols for buprenorphine home inductions (BUP-to-go).

**Table 4. Recommended Period of Pre-initiation Withdrawal**

| Opioid Formulation | Minimum Length of Time Since Last Dose | Examples |
|---|---|---|
| Short-acting opioids | ≥ 12 hours | *heroin, oxycodone, hydromorphone* |
| Intermediate-acting opioids | ≥ 24 hours | *slow-release oral morphine, fentanyl* (confirmed or suspected)* |
| Long-acting opioids | Minimum of 48–72 hours | *Methadone (may require longer duration off methadone if patient has been taking methadone long enough to reach steady state)* |

*A 48-hour period of abstinence prior to traditional induction may be preferable in order to minimize the risk of precipitated withdrawal, regardless of the COWS score. Alternatively, a low-dose induction method may be preferable for fentanyl-exposed patients or individuals who remain at high risk of precipitated withdrawal beyond 48 hours of withdrawal.

## Dosing

**Starting dose:** 2mg buprenorphine dose

**Titrating dose:** 2–4mg

## Induction

**Day 1:**

- Give 2mg buprenorphine starting dose and wait 1–3 hours
- If withdrawal symptoms or cravings are still present, give patient another 2–4mg buprenorphine dose
- Repeat steps until withdrawal symptoms and cravings are alleviated
- Consider providing additional 2mg buprenorphine doses to manage any withdrawal symptoms or cravings that emerge overnight

**Day 2:**

- Consolidate the total dose given on day 1 and provide as single dose
- If withdrawal symptoms or cravings are present since last dose, provide additional 2–4mg dose and wait 1–3 hours until withdrawal symptoms and cravings are alleviated OR patient reaches maximum day 2 dose (32mg)

Provide Non-opioid Adjunct Medications to help alleviate withdrawal symptoms, as required

## Monitoring

For all doses, hold if intoxicated or sedated.

- Do not administer opioids if POSS score is 3 or greater

Assess COWS 30- and 60-minutes post-dose.

- A significant increase in COWS or patient self-report of worsening withdrawal symptoms may indicate precipitated withdrawal (see Managing Precipitated Withdrawal)

# Managing Precipitated Withdrawal

**Precipitated withdrawal**: a sudden worsening of withdrawal symptoms after taking buprenorphine (<1-hour post-dose)

Primarily a concern during traditional inductions, though still possible during a low-dose induction

- Can occur when the first dose of buprenorphine is administered to a patient who has been using full agonist opioids before they are in a moderate stage of opioid withdrawal
- Risk is typically lower after a total of 8mg buprenorphine have been taken

**Actions to take in all cases of precipitated withdrawal:**

- Explain what has occurred
- Discuss the options available and engage in shared decision-making in developing a plan for management

  Discuss with the patient that they may feel unwell for up to a week after precipitated withdrawal occurs
- Offer non-opioid adjuncts to treat withdrawal symptoms (see Non-opioid Adjunct Medications)
- Precipitated withdrawal can cause harm to patients, including fear of continuing or restarting OAT, withdrawing from care, and returning to unregulated opioid use

  If adequately managing a patient's precipitated withdrawal is challenging, consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports to guide management

## Option 1: Continue induction

1. Administer additional doses of 2–4mg of buprenorphine every 1–2 hours until withdrawal symptoms are resolved
2. Inform the patient that additional doses of buprenorphine can initially result in worsening of withdrawal symptoms before improvement

   Offer non-opioid adjuncts for symptom management

## Option 2: Delay induction

1. If the patient chooses to continue, consider waiting a few hours so the patient is in moderate withdrawal before administering the next buprenorphine dose
2. Offer non-opioid adjuncts for symptom management
3. Continue up to the Day 1 maximum or until withdrawal symptoms are resolved

## Option 3: Stop induction

1. Provide reassurance that symptoms will resolve
2. Offer non-opioid adjuncts and/or short-acting full opioid agonists to treat withdrawal symptoms as needed
3. Offer to discuss a plan for a future induction attempt or an alternate form of OAT

## Option 4: High-dose buprenorphine

1. Treat with additional doses of buprenorphine in close succession, typically ranging from 8mg–24mg in total. Doses above 24mg may be beneficial; consult with addiction medicine.
2. It is strongly suggested to consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine consultation resources to get support on the high-dose buprenorphine approach

# Non-opioid Adjunct Medications

Non-opioid adjunct medications to support addressing withdrawal symptoms include:

| Medication | Symptoms | Dosage |
|---|---|---|
| **Clonidine** | Sweating, tremors, chills, and anxiety | 0.1–0.2mg po q4h PRN for <12 hours |
| **Acetaminophen** | Pain | 650–975mg po q6h PRN; maximum 4000mg/day or 2000mg/day for older adults or those with liver impairment |
| **Ibuprofen** | Pain | 400mg po q6h PRN |
| **Loperamide** | Diarrhea | 2–4mg po q6h PRN; maximum 16mg/day |
| **Dimenhydrinate** | Nausea and vomiting | 25–50mg po q4h PRN or 25–50mg IV q4h PRN |
| **Ondansetron** | Nausea and vomiting | 4–8mg po q8h PRN |

Other non-opioid adjunct medications may be used to manage withdrawal symptoms based on clinician discretion and patient needs and preferences.

# Methadone

Methadone is a full opioid agonist most commonly administered as a liquid for oral consumption.

## Initiation

The starting methadone dose will depend on factors that affect the risk of toxicity (e.g., sepsis, delirium).

Consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports as needed (e.g., if higher starting dose is required).

**Table 5. Methadone starting doses**

| Tolerance level | Dose |
|---|---|
| **No/low tolerance** (recent withdrawal management completion, no current opioid use, heavy use of other sedating agents, severe comorbidities that affect toxicity) | 5–10mg/day |
| **Unknown/moderate tolerance** (co-occurring sedative use or alcohol use disorder) | 10–20mg/day |
| **Known high tolerance** (active opioid use) | 20–30mg/day |
| **Known very high tolerance** (current fentanyl use **AND** previous methadone experience) | 30–40mg/day |

## Titration

After a dose increase, it takes approximately 5 days of continuous use for methadone to reach a steady concentration and maximum therapeutic effect.

Can cause a delayed emergence of serious adverse effects such as respiratory depression or sedation

A stabilized dose can range from 60–150mg or more per day.

Titration protocol differs based on tolerance.

Consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports if the patient's tolerance is uncertain or dose exceeds 150mg per day.

**Table 6. Suggested methadone titration protocols**

| Opioid tolerance | Dose increase |
|---|---|
| **High tolerance** (documented history of fentanyl use **AND** experience with methadone) | Increase by maximum of 15mg every 3 days<br><br>Once daily dose reaches 85mg or more: titrate to a maximum of 10mg every 3–5 days |
| **Lower or unknown tolerance** (no active fentanyl use, no experience with methadone, or patients with severe comorbidities that affect toxicity risks) | Increase by maximum 5–10mg every 3–5 days |
| Concerns of methadone toxicity: monitor the patient at 3-hours post-dose after each dose for 5 days | |

# Slow-release Oral Morphine (Kadian)

Slow-release oral morphine is a full opioid agonist administered as an oral capsule.

## Initiation

The starting SROM dose will depend on factors that affect the risk of toxicity.

Consult the local inpatient consult team, 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports as needed (e.g., if higher starting dose is required).

**Table 7. SROM starting doses**

| Tolerance level | Dose |
|---|---|
| **No/low tolerance** (recent withdrawal management completion, no current opioid use, heavy use of other sedating agents, severe comorbidities that affect toxicity) | 50mg/day |
| **Unknown/moderate tolerance** (co-occurring sedative use or alcohol use disorder) | 100–150mg/day |
| **Known high tolerance** (active opioid use) | 200mg/day |
| **Known very high tolerance** (current fentanyl use **AND** previous SROM experience) | 300mg/day |

## Titration

A stabilized dose may exceed 1200mg per day.

Consult the local inpatient consult team 24/7 Addiction Medicine Clinician Support Line, RACEapp, or other regional addiction medicine supports if dose increase is uncertain or dose higher than 1200mg per day is required.

**Table 8. Suggested SROM titration protocol**

| Titration Dose | Frequency | Maximum Dose |
|---|---|---|
| Up to 100mg | Every 24–48 hours until cravings and withdrawal symptoms are resolved | Doses greater than 1200mg per day may be required to achieve therapeutic dose |

# Discharge Planning Considerations for OAT Initiation

Provide discharge prescriptions or medications

- **Buprenorphine** can be given or prescribed as take-home doses
- **Methadone** and **SROM** prescriptions to be filled by a community pharmacy must be written by a prescriber who has completed POATSP and a preceptorship
  - Liaise with local inpatient consult team, virtual addiction clinic, or community OAT clinic to ensure a discharge prescription is faxed to a community pharmacy
  - Follow organizational protocols on how to discharge a patient when a prescriber is not immediately available

If initiating BUP-to-go in an ED, provide and review BUP-to-go home induction handouts with the patient

Offer the patient resources to support continuity of care.

Contact the community pharmacist and/or prescriber directly, when possible, before patient is discharged

- If patient does not have a community pharmacy, help locate an accessible pharmacy
- If the patient requires a community-based OAT prescriber, refer to a local Rapid Access to Addiction Care Clinic (if available in your region) or community addiction clinic
  - OAT Clinics Accepting New Patients
  - **Note:** Some community OAT providers charge additional clinic fees. Contact clinics before referral to determine if clinic fees are required and discuss with the patient
  - In collaboration with the patient, book an appointment before discharge

Further discharge planning considerations can be found in Acute Care and Opioid Use Disorder.

# Consultation

Consult with an addiction specialist, such as the local inpatient addiction medicine consult team (available at some acute care sites), for any questions or concerns.

24/7 Addiction Medicine Clinician Support Line

- Consult with an addictions medicine specialist 24 hours a day, 7 days a week
- Available to physicians, nurse practitioners, nurses, midwives, and pharmacists who are involved in addiction and substance use care and treatment in BC
- 778-945-7619

Rapid Access to Consultative Expertise (RACE)

- Online application where primary care providers (physicians and nurse practitioners) can receive specialist advice

# Resources

**BCCSU:** *A Guideline for the Clinical Management of Opioid Use Disorder (2023)*

**BCCSU:** *The Provincial Opioid Addiction Treatment Support Program*