Part III: Opioids

Introduction

Opioids have long been an important tool in the treatment of acute and chronic pain. Since the 1990s, Canadian physicians have dramatically increased their opioid prescribing. This has benefited many patients with chronic non-cancer pain (CNCP), but it has also been associated with substantial increases in opioid overdose deaths and opioid use disorders (49, 50). Evidence suggests that physicians' prescribing practices, which were influenced by aggressive marketing of opioids by pharmaceutical companies during the 1990s (51, 52), are a major contributor to these harms (53-57). The medical profession has responded to this public health crisis by developing a set of evidence-based guidelines and best practices on opioid prescribing for chronic pain, originally published in 2010 (58) and revised in 2017 (59). However, many family physicians continue to experience discomfort or a lack of confidence about how to prescribe opioids safely, and most do not know how to manage harms related to both licit and illicit opioid use. As well, it is only since 2012 that the *Controlled Drugs and Substances Act* has enabled Canadian nurse practitioners to prescribe opioid medications. This section outlines the role of opioids in acute pain and CNCP management, provides a clear protocol for initiating and monitoring long-term opioid therapy, and advises on how to reduce, mitigate, or prevent the harms associated with chronic opioid use.

We have made every effort to take into account current developments in the opioid field, particularly the 2017 opioid guidelines. We have attempted to interpret the guidelines' broad recommendations to reflect individual patients' clinical

circumstances. These interpretations are highlighted where they occur; practitioners are encouraged to consider the individual needs of patients when making clinical decisions.

Opioids for acute pain (60)

Indications for opioid treatment

- Moderate to severe acute pain that has not responded a trial, of adequate dose and duration, of all evidence-based non-opioid treatments (e.g., acetaminophen, SNRIs, NSAIDs, physiotherapy)

Contraindications to opioid treatment

- Mild acute pain (e.g., low back pain, dental pain, muscle strains)
- Active substance use disorder

Protocol for opioid prescribing

- Use **lowest effective dose** of **immediate-release** formulation, preferably combined with a non-opioid medication (e.g., codeine + acetaminophen).
- Prescribe only enough to last for expected duration of severe pain (usually 3–7 days).

Initiating opioid therapy for CNCP

Indications for opioid trial

- Patient has a well-defined pain condition (nociceptive or neuropathic) that (a) has been shown to respond to opioids, and (b) causes both **pain and disability**.

- Diagnosis is confirmed on physical examination, diagnostic imagining, and/or consultation.
- Non-opioid treatments are contraindicated, have intolerable side effects, or are found to be ineffective after an **adequate trial** (e.g., one month for SNRIs).
- Opioids are usually not effective in conditions where central sensitization has occurred (e.g., fibromyalgia, tension headaches, IBS).
- Systematic review (61) found that opioids provide minimal analgesic benefit for low back pain overall, and this benefit is outweighed by opioid side effects.

Precautions and contraindications to opioid trial

- Use caution when prescribing opioids to patients with a current, active psychiatric disorder (i.e., anxiety disorder, mood disorder, post-traumatic stress disorder).[2]
- Avoid long-term opioid therapy in patients with current, recent, or severe past history of problematic use of alcohol, opioids, cannabis, or other substances.[3]

---

[2] The 2017 opioid guidelines recommend that active psychiatric disorders be stabilized before an opioid trial is considered. However, we suggest that patients with an active psychiatric disorder be considered for a carefully monitored trial of opioid therapy, if they have a severe nociceptive or neuropathic pain condition that impairs daily functioning and has not responded to an adequate trial of all standard non-opioid treatments. The patient should also receive concurrent treatment for their psychiatric disorder. If you decide to initiate a trial of opioids, monitor the patient closely to assess benefits, adverse effects, and signs of misuse.

[3] The 2017 opioid guidelines recommend that opioids not be prescribed to patients with any history of problematic substance use. However, an opioid trial may be indicated for severe pain that has not responded to other treatment modalities if the history of problematic substance use is remote and not severe.

Prior to prescribing opioids

- Ask about current and past use of alcohol and drugs.
- Ask about mood. Depressed patients tend to have a heightened perception of pain and are less responsive to opioid therapy.
- Check renal and respiratory status, especially risk of sleep apnea.
- In elderly patients, assess risk of falls.
- Consider tapering benzodiazepines (see page 102).
- Ask about the impact of pain on activities of daily living, e.g., walking, cooking, visits to family and friends.
- Have the patient rate the severity of their pain on a 0–10 scale, at rest and with activity.
- Reassess their response to non-opioid treatments:
  - Nociceptive pain: acetaminophen, NSAIDs, SNRIs
  - Neuropathic pain: anticonvulsants, SNRIs, TCAs
  - All pain: Mindfulness programs, graded exercise
- Inform patients that opioid therapy will be a **trial**, to be discontinued if side effects outweigh benefits.
- Advise patients not to drink alcohol during titration.
- Warn patients to avoid driving for at least two hours after a dose in the first 1–2 weeks of treatment initiation and the first week of dose increase.
- Warn patients to keep their opioids safely stored, and not to give any opioid medications to relatives or friends.

Office visits

- See the patient frequently during initiation and titration.
- At each office visit, ask about changes in:
  - Work, school, social activities, daily activities
  - Pain ratings on a 0–10 scale, at rest and with activity
  - Mood
- Ask about side effects:
  - Sedation, dizziness, and other CNS effects
  - Constipation, nausea

Opioid prescribing protocol

Immediate release (IR) vs. controlled release (CR)

- Initiate opioid trial with IR preparations.[4]
- Maintain on IR for brief pain (less than 4 hours) or incident pain (triggered by activity).
- For constant pain throughout the day, switch to CR.
- In long-term therapy for constant pain throughout the day, IR preparations should not exceed 10–30% of total daily opioid dose.

Opioid selection

- Always initiate opioid treatment with weak opioids, i.e., oral codeine, tramadol, or buprenorphine patch. These medications are effective and have much lower risk of overdose, addiction, sedation, and falls than potent opioids.

[4] We concur with the 2017 opioid guidelines regarding the use of CR opioids for constant pain throughout the day; however, as CR formulations are generally very potent, we recommend using IR preparations during initiation and titration in order to minimize the risk of acute toxicity.

- If insufficient analgesia with first-line opioids, prescribe morphine, oxycodone, or hydromorphone.
- Morphine is contraindicated in patients with renal insufficiency.
- Evidence suggests that hydromorphone and oxycodone have fewer cognitive effects than morphine in the elderly.
- Transdermal fentanyl should be avoided if possible in the elderly and in patients with less severe pain. It is very easy to overdose on the patch. Use only if the patient has taken at least 60–100 mg morphine equivalent (MEQ) daily for at least 2 weeks.

Opioid initiation and dose titration

Opioid*	**Max initial dose****	**Max dose increase**	**Min days between increases**	**Min IR dose before CR**
Codeine	200 mg/d	50 mg/d	7 days IR 14 days CR	150 mg
Transdermal buprenorphine	5 µg/7d	5 µg/7d	7 days	-------
Morphine	40 mg/d	10 mg/d	7 days IR 14 days CR	30 mg
Oxycodone	30 mg/d	5 mg/d IR 10 mg/d CR	7 days IR 14 days CR	20 mg
Hydromorphone	8 mg/d	1–2 mg/d IR 2–4 mg/d CR	7 days IR 14 days CR	6 mg
Tapentadol***	150 mg/d	50 mg/d IR 50 mg/d CR	7 days IR 14 days CR	100 mg

* Potent opioids should only be dispensed to patients currently taking weak opioids daily. All dose increases should be based on an individual assessment.
** Starting dose is 40 mg MEQ (less for seniors).
*** Maximum CR dose 250 mg bid. Exert caution when switching from pure mu-opioids.

Morphine equivalency

Opioid	Approximate equivalence value
Morphine (reference)	30 mg
Codeine	200 mg
Oxycodone	20 mg
Hydromorphone	6 mg
Tapentadol	100 mg
Transdermal buprenorphine	No equivalence to morphine established
Transdermal fentanyl	25 μg/hr = 60–134 mg oral morphine/day

Optimal dose

- Effective opioid therapy causes gradual improvement in pain and function as dose increases.
- Optimal dose reached if:
  - Pain relief at least 2 points on 10-point scale, with no benefit from 1–2 additional increases.
  - Improved functioning at work, school, and with family; increased physical activities.
  - No major side effects.
- Most patients respond to a dose of **50 mg MEQ or less**; doses above 90 mg MEQ are rarely needed.
- In some cases, referral for a second opinion regarding the possibility of increasing the dose to more than 90 mg MEQ may be necessary.

Ongoing vigilance

- Opioids have dose-related complications, including overdose, sleep apnea, and falls and fractures.
- Any patient with an ongoing opioid prescription of 40 mg MEQ or more should have **monthly visits** to assess:
  - Pain levels, at rest and with activity
  - Function (mood, activities of daily living)
  - Adverse effects
- At doses of 90+ mg MEQ, the prescriber should reassess the opioid's analgesic effectiveness and side effects, and decide whether to maintain the dose or taper.[5]

Minimizing adverse effects

(a) Falls in the elderly

- Do not prescribe opioids to cognitively impaired patients unless dispensed and overseen by a caregiver.
- Taper benzodiazepines (see page 103).
- Benzodiazepines increase risk and severity of opioid-induced fatigue, sedation, inattention and overdose.
- Avoid use of opioids at night if possible.
- If pain wakes the patient up, prescribe the smallest IR opioid dose and warn patients to take extra precautions when getting out of bed.

---

[5] The 2017 opioid guidelines recommend that all patients on doses of 90 mg MEQ or higher be tapered. While it is true that the dangers associated with opioid therapy are dose-related, we believe that the decision to taper should be based on the patient's pain, functioning, and adverse effects in addition to the dose. All patients on long-term opioid therapy should be monitored for their response to the treatment, and tapering should be considered for any patient showing adverse effects or insufficient benefit, regardless of the dose. Tapering should be prioritized in patients who have received insufficient analgesia from opioids, who are suffering from opioid-related complications, or patients with an opioid use disorder for whom opioid substitution therapy is contraindicated.

(b) Sedation during initiation or dose increase

- Sedation, slowed speech, or "nodding off" are all early signs of an impending overdose.
- The patient may appear relatively alert in conversation, yet have respiratory arrest at night while asleep.
- Family members should contact the care provider or call emergency services at the first sign of an overdose.

(c) Fatigue

- Opioids can cause fatigue either through a direct sedating effect or by contributing to sleep apnea.
- Patients who report daytime fatigue and/or reduced function should be assessed for sleep apnea. Their opioid dose should be reduced or discontinued, or the opioid should be switched.

(d) Constipation

- Use a stepped approach:
  - Start with dietary fibre, adequate fluid, and activity.
  - Progress to osmotic laxatives (polyethylene glycol, sodium picosulphate, or lactulose).
  - Progress to stimulant laxatives (bisacodyl, senna).
  - Progress to peripheral opioid receptor antagonists (combination oxycodone-naloxone, a-methyl naltrexone, naloxegol).

Opioid switching

Indications for opioid switching

- Inadequate analgesic response to the current opioid (pain relief < 2/10, no improvement in function) despite a reasonable dose (e.g., 60 mg MEQ). Patients who have had minimal analgesic response to a moderate dose are unlikely to benefit from further dose increases.
- Adverse effects with the current opioid, e.g., constipation, sedation, falls.
- Potential tapering strategy.

Opioid switching protocol

- Because the patient will not be fully tolerant to the new opioid, the MEQ should be 50% of the MEQ of original.
- *Example:* When switching a patient from 40 mg/d of oxycodone to hydromorphone:
  - 40 mg/d oxycodone = 60 mg MEQ
  - 60 mg MEQ = 12 mg/d hydromorphone
  - 50% of hydromorphone 12 mg = 6 mg
  - Therefore, start patient on 6 mg/d in divided doses.
- Emphasize that taking extra doses is dangerous.
- Titrate dose as described on page 48.

Opioid tapering

Rationale for opioid tapering

- Tapering is an **active therapeutic decision** made for the patient's benefit when they have failed at opioid therapy.
- Evidence suggests that tapering after a failed opioid trial improves pain, mood, and functioning.
- Tapering is **far safer** than abrupt cessation:[6]
  - Abrupt cessation will trigger severe withdrawal, and patients will lose their opioid tolerance within days, creating a heightened risk of overdose.
  - Abrupt cessation can also lead patients seek illicit sources of opioids, which can result in accidental exposure to fentanyl.

Indications for opioid tapering

- Patient has persistent severe pain and pain-related disability despite an adequate opioid dose (e.g., 60 mg/d MEQ), and the patient has already failed on a trial of at least one opioid previously.
- Patient is on an unusually high dose for pain condition (well above 90 mg MEQ for mechanical low back pain).
- Patient has a complication from opioid therapy, such as sleep apnea, sedation, or dysphoria.
- Patient has suspected opioid use disorder and opioid maintenance therapy is not an option.

---

[6] The 2017 opioid guidelines present very rapid or immediate cessation of opioid therapy as an alternative method of tapering; however, we strongly recommend against this practice. The guidelines advise that this be done in a medically supervised withdrawal centre, but this does not mitigate the risk of subsequent relapse and overdose due to loss of tolerance. If a patient needs to discontinue their opioids more rapidly than a standard taper allows, they should be switched to opioid maintenance therapy.

Reluctance to taper

If patient expresses reluctance to taper their opioid dose:

- Explain **why** you are tapering the opioid dose: to prevent future harms (e.g., falls) and to improve the patient's mood and well-being (e.g., energy and sleep).
- Explain that tapering does not usually increase pain, and may actually improve it:
  - Opioids often stop working after many months or years.
  - Opioids can even make pain worse by lowering the pain threshold.
- Explain that you are not necessarily going to stop the opioids altogether, but lower it to a safer dose that improves mood and function while still keeping the pain manageable.
- Explain that you will be lowering the dose **gradually**, and that you will adjust the rate of the taper according to how the patient is doing.

Failed taper

A *failed taper* occurs when the patient persistently refuses to taper the dose further due to severe pain. A failed taper may occur for several reasons:

- Patient has an underlying opioid use disorder and cannot tolerate even small reductions in the opioid dose.
- The taper was done too quickly and/or the patient is suffering from end-dose withdrawal symptoms.
- The patient's pain condition responds to a higher dose.

In response to a failed taper, the prescriber has the following options:

- Switch to buprenorphine/naloxone. While this is particularly important for patients with an underlying opioid use disorder, it can also be helpful in other patients, as the long duration of action of buprenorphine often makes the taper more tolerable.
- Hold the taper and refer patient to a multidisciplinary pain program (if available).

Tapering protocol

Formulation	CR preferred (until low dose reached).
Dosing interval	Scheduled doses rather than PRN Keep dosing interval the same for as long as possible (bid or tid). Advise patients not to skip doses.
Rate of taper	Taper slowly, typically 10% of the total daily dose at each office visit, no more than 10% of total daily dose **every 1–2 weeks**. Adjust rate of taper according to patient's pain and withdrawal symptoms. If patient experiences mild withdrawal symptoms, reassure them they will resolve after 1–2 weeks. Let patient choose which dose is decreased (AM, PM, or HS). Taper even more slowly when 1/3 of total dose is reached.
Dispensing interval	If patient runs out early, increase frequency to weekly, alternate day, or daily.
Endpoint of taper	Dose well below 90 mg MEQ. Controls pain with minimal side effects. Similar or improved mood and function.
Frequency of visits	If possible, see patient prior to each dose decrease.
Approach at each visit	Ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood, improved pain, etc. If pain persists, consider referral to a multidisciplinary program (if available) if the patient does not show signs of opioid misuse or use disorder.[7]

[7] The 2017 opioid guidelines recommend that patients showing behaviours indicating opioid misuse or use disorder be referred to a multidisciplinary program. However, patients displaying these behaviours should first be assessed for an opioid use disorder; in these patients, opioid maintenance therapy with methadone or buprenorphine/naloxone is likely to improve pain and functioning.

Opioid misuse

Limiting diversion

- Warn patients to store their medication in a locked box or other secure location, not to show them to younger relatives, and not to share them with anyone.
- Avoid using fentanyl patches in elderly patients with younger adults at home (patches can be easily lifted off the skin of a sleeping patient).
- Consider a fentanyl patch exchange program (http://www.patch4patch.ca).
- Without anyone else in the office, ask parents and grandparents on opioids if younger relatives could be using their medication, especially if the patient requires high doses, runs out early, or is accompanied by a younger adult to the office visits.
- Use part fill prescriptions. The 2017 opioid guidelines suggest a maximum of 28 days, but in patients with personal or environmental risk factors, weekly or two-week prescriptions may be appropriate.

Monitoring for misuse

- Any patient with an ongoing opioid prescription of 40 mg MEQ or more should be monitored for signs of misuse.
- At each visit, the clinician should assess the patient for:
  - Changes in their mood, relationships, or functioning
  - Concerns expressed by family or close friends
  - Unauthorized changes to dose, schedule (i.e., binge use), or route of delivery (e.g., biting oral tablets)
  - Euphoric effects (e.g., relaxation, confidence, energy) immediately after taking a dose
  - Withdrawal symptoms

- Drug-seeking behaviours: running out of medication early, frequent requests for dose increases, etc.
- These features may indicate that the patient is at risk for an **opioid use disorder** (see below).

Opioid use disorder (OUD)

The DSM-V defines an OUD as a "problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period" (17):[8]

(a) Opioids taken in larger amounts or over a longer period of time than intended.
(b) Repeated unsuccessful efforts to reduce use.
(c) Significant amount of time spent obtaining or using opioids, or recovering from their effects.
(d) Strong cravings or urges to use opioids.
(e) Recurrent opioid use resulting in a failure to fulfill responsibilities.
(f) Continued use despite opioid-related social or interpersonal problems.
(g) Reduction of major activities because of opioids (e.g., missing work, spending less time with children or spouse).
(h) Repeatedly using opioids in situations or activities where intoxication is dangerous.
(i) Continued use despite knowledge of opioid-related physical or psychological problems.
(j) Tolerance (need to use more to achieve the same effect, or diminished effects with continued use of the same amount).
(k) Withdrawal (e.g., myalgias, chills, sweating, nausea/vomiting, cramps, diarrhea, insomnia, anxiety, dysphoria).

[8] Please refer to the DSM-V p.541.

Patients who meet two or three of these criteria have a **mild** OUD, four to five criteria indicate a **moderate** OUD, and six or more indicate a **severe** OUD.

Symptoms, signs, and behaviours

OUDs are difficult to diagnose; patients are often reluctant to disclose key symptoms and behaviours for fear that the practitioner will discontinue the opioid. A diagnosis often requires collateral information from family members and observation of a pattern of behaviour over time. The following patterns tend to emerge in patients with an OUD:

- Patient's opioid dose high for underlying pain condition
- Aberrant behaviours: Running out early, crushing or biting oral tabs, or accessing opioids from other sources
- Strong resistance to tapering or switching current opioid
- Importance patient attaches to the drug far outweighs its analgesic benefit (e.g., "pain is 10/10, hydromorphone only takes edge off, but I would die if you stopped it")
- Binge rather than scheduled opioid use
- May be currently addicted to other drugs, e.g., alcohol
- Depressed and anxious
- Deteriorating mood and functioning
- Concerns expressed by family members
- Reports recurrent, frightening withdrawal symptoms
- May acknowledge that they experience immediate improvement in mood after taking the opioid

Harm reduction advice

All patients with a suspected OUD should be given advice on harm reduction and reducing the chance of a fatal overdose:

- Never use opioids alone; always use with a friend and make sure you are both aware of the signs of overdose (pinpoint pupils, falling asleep, slowed or stopped breathing, bluish skin around lips or under nails).
- If a friend has overdosed:
  - Shake them and call their name.
  - Call 911.
  - Administer naloxone and start chest compressions.
  - If they are drowsy and nodding off but not unconscious, do not let them fall asleep; keep talking to them until they are awake and alert for at least an hour without slurred speech/nodding off. If they cannot remain alert, take them to the ED.
- If you are taking opioids after a period of abstinence of any length, take a much smaller dose than you used to.
- Be aware that drug dealers often add fentanyl to their product without informing their customers. Only medications obtained from a prescription and purchased at a pharmacy are guaranteed to be free of fentanyl.
  - Fentanyl is many times more potent than heroin.
  - Even a tiny amount and kill a heavy and experienced opioid user.
- Do not inject opioids.
- Do not mix opioids with other substances, especially alcohol or benzodiazepines.
- Always carry naloxone (see page 61).
- The only sure way to prevent overdose is to stop using. The most effective way to do this is through opioid maintenance therapy (see page 65).

Take-home naloxone

Naloxone is a competitive opioid antagonist with a duration of action of 15–30 minutes. Take-home naloxone is available in two bioequivalent formulations: parenteral naloxone 0.4 mg and intranasal naloxone 4 mg. The latter is much more expensive but is more acceptable to oral opioid users. In most provinces, public health departments offer naloxone kits and training through their needle exchange programs, and some provinces have made parenteral and/or intranasal naloxone available at community pharmacies at no charge and without a prescription.

Indications for naloxone

- On a high dose of prescription opioids (200+ mg MED)
- On prescription opioids and also taking benzodiazepines or drinking heavily.
- Previous overdose
- Suspected OUD
- Intermittent recreational use or illicit opioids
- Has regular contact with friends or relatives who have OUD
- Heavy users of cocaine or other non-opioid drugs (drug dealers sometimes add fentanyl to non-opioid drugs)

When giving or recommending naloxone, the clinician should spend a few minutes advising the patient on overdose prevention (see page 60). This advice will reinforce the education they will receive from the public department or pharmacy.

Options for management of OUDs

(a) Abstinence-based psychosocial treatment

Abstinence-based treatment is the cessation of all alcohol and drugs, including methadone and buprenorphine/naloxone; it is usually accompanied by psychosocial interventions, such as counselling or self-help groups (e.g., Narcotics Anonymous). This form of treatment is **less effective than opioid maintenance therapy** but often preferred by patients. Patients are at increased risk for opioid overdose after leaving abstinence-based programs, so it is crucial that they are given harm reduction advice and overdose prevention strategies (see pages 60–61).

(b) Structured opioid therapy

Structured opioid therapy is continued opioid prescribing under conditions that limit misuse. Preliminary evidence suggests it is effective, convenient for patients, and easier to organize than opioid substitution therapy. Refer patients for opioid substitution therapy if structured therapy fails.

Indications

- Has or is at high risk for opioid use disorder (younger, personal or strong family history of addiction, anxiety or mood disorder).
- Has pain condition requiring opioid therapy.
- Only uses opioids supplied by one prescriber.
- Does not alter route of delivery (inject or crush oral tabs).
- Is not currently addicted to alcohol or other drugs.

Protocol

- Perform taper (see page 53).
- Dispense small amounts frequently (e.g., 1–2 times per week).

- Do not refill if patient runs out early.
- Monitor closely with urine drug screens, pill counts, office visits.
- Switch to buprenorphine/naloxone or methadone treatment if structured opioid therapy fails (e.g., patient continues to access opioids from other sources).

(c) Involuntary taper

Opioid tapering is often difficult for people with moderate to severe OUDs; they usually experience intense and frightening withdrawal symptoms along with powerful cravings, leading them to access illicit opioids. Although opioid maintenance therapy with methadone or buprenorphine/naloxone (see page 65) is indicated in these cases, patients may be resistant to this treatment. In this situation, the patient should be slowly tapered off their opioid.

Tapering gives the patient several weeks or months to consider and make an informed decision about the need for opioid substitution treatment. As well, tapering is safer to the patient and the public than ongoing prescribing of high doses or abrupt cessation. The former allows the patient to put off treatment indefinitely, maintaining the risk of diversion and overdose; the latter will cause the patient to lose tolerance, increasing their risk of overdose.

Note that you should not discharge patients with OUDs from your practice unless they have been abusive towards you, your staff, or other patients, or if you have concrete evidence that they have been selling your medications.

Indications

- Has an opioid use disorder (if you are unsure about the diagnosis, consult with an addiction physician or pain physician who is knowledgeable about OUDs).
- Does not have a pain condition requiring long-term opioid therapy.
- Suspected of injecting, crushing, or snorting oral tabs.
- Suspected of accessing opioids from more than one source (either double-doctoring or purchasing from the street) or of selling their medication.

Patient reluctance

If the patient expresses resistance to an involuntary taper, deliver the following message:

> You have an opioid use disorder. The opioid I am prescribing may be making it harder for you to function and may be worsening your mood. It is also putting you at risk of serious harm, including death from overdose.
>
> The most effective treatment for opioid use disorder is opioid maintenance treatment. This treatment will result in improved mood, function, and pain. It will eliminate your cravings and withdrawal symptoms. However, since this is not an option at this time, your opioid dose needs to be lowered for safety reasons. As you will lose tolerance as the dose is lowered, it is important that you take steps to prevent opioid overdose (see pages 60–61).
>
> If you change your mind about opioid maintenance therapy at any point, I will arrange treatment for you, either with me or at an addiction clinic. If you disagree with this decision, please feel free to find another care provider. Until then, we will proceed with the taper.

Protocol

- Provide patient with naloxone and advice on harm reduction.
- Dispense frequently (as often as daily).
- Taper by 10% of total baseline dose per week (e.g., if patient is on 600 mg MED, taper by 60 mg per week).
- Slow taper to 10% every 2 weeks once dose of 200 mg MEQ is reached.
- See the patient frequently, every 1–2 weeks.
    - During each visit, emphasize that opioid maintenance therapy with methadone or buprenorphine/naloxone will relieve their withdrawal symptoms while improving their mood and function.
    - If patient agrees to opioid maintenance therapy, refer to addiction physician or initiate buprenorphine/naloxone treatment (see below).
- Taper completely off opioid.
    - If patient has a severe biomedical pain condition that warrants opioid therapy, prescribe once-daily long-acting morphine, daily dispensed, at a maximum dose of 50 mg.

(d) Opioid maintenance therapy

Opioid maintenance therapy is substituting an illegal and/or euphoria-inducing opioid with a longer-acting, less euphoric opioid (i.e., methadone or buprenorphine/naloxone). While all methadone prescribers in Canada are required to have an exemption under section 56 of the *Controlled Drugs and Substances Act*, each province and territory has its own requirements about prescribing buprenorphine/naloxone:

AB	Approved training course required
BC	Indivior[9] training course recommended
MB	Methadone exemption required Indivior training course required
NB	Formal approval not required Evidence of training may be requested
NL	Training course strongly recommended
NS	Centre for Addiction and Mental Health training course required
NT	No known requirements
NU	Prescribers must provide proof of competence
ON	Training course recommended One-day clinical observership recommended Ongoing continuing medical education recommended
PE	Indivior training course required Course on fundamentals of addiction medicine required within first two years Minimum of 20 hours of formal continuing medical education in addiction medicine required every five years
QC	Indivior training course required Additional day-long training course required
SK	Methadone exemption required Approved training course required Six hours of formal continuing medical education in addiction medicine required every two years
YT	No requirements

Indications

- Has an OUD.
- Failed at opioid tapering.
- Currently misusing alcohol or other drugs.

[9] Indivior is the manufacturer of brand-name buprenorphine/naloxone.

Prescribing buprenorphine/naloxone

Buprenorphine

- Partial opioid agonist with a ceiling effect.
  - Unlike full agonists such as morphine, even very high doses rarely cause respiratory depression unless combined with alcohol or sedating drugs.
- When taken in the appropriate dose, relieves withdrawal symptoms and cravings for 24 hours without causing euphoria.
- Binds very tightly to the opioid receptors, displacing other opioids that occupy the receptor site; this minimizes the psychoactive effect of other opioids taken concurrently.
- Has a slow onset and long duration of action because it dissociates very slowly from the receptors.
- Side effects similar to those of other opioids: nausea, constipation, and sedation.
- Buprenorphine is often combined 4:1 with naloxone, an opioid antagonist, in order to prevent misuse: the naloxone in the preparation has no effect when taken sublingually, but will trigger severe withdrawal if injected.

Initiation protocol

- Ensure that patient has no opioid in their serum before taking the first dose.
  - Buprenorphine/naloxone is very safe, even in patients who have never taken it before, but it does displace opioids currently attached to the receptor.
  - This precipitates opioid withdrawal in patients who are physically dependent on those opioids.
  - Precipitated withdrawal is rarely severe or dangerous, but patients who experience it are reluctant to try buprenorphine/naloxone again.
  - Use the Clinical Opioid Withdrawal Scale (COWS) to gauge the patient's withdrawal:

Clinical Opioid Withdrawal Scale (COWS) (62)

Interval	0	30m	2h	4h
Date **Time**				
	Score	**Score**	**Score**	**Score**
Resting heart rate (measure after lying or sitting for one minute): **0** HR ≤ 80 **2** HR 101–120 **1** HR 81–100 **4** HR > 120				
Sweating (preceding 30m and not related to room temp/activity): **0** no report of chills or flushing **1** subjective report of chills or flushing **2** flushed or observable moistness on face **3** beads of sweat on brow or face **4** sweat streaming off face				
Restlessness (observe during assessment): **0** able to sit still **1** reports difficulty sitting still, but is able to do so **3** frequent shifting or extraneous movements of legs/arms **5** unable to sit still for more than a few seconds				
Pupil size: **0** pupils pinned or normal size for room light **1** pupils larger than normal for room light **2** pupils moderately dilated **5** pupils so dilated that only the rim of the iris is visible				

Interval	0	30m	2h	4h
Date **Time**				
	Score	**Score**	**Score**	**Score**
Bone or joint pain (not including existing joint pains): **0** not present **1** mild diffuse discomfort **2** patient reports severe diffuse aching of joints/ muscles **4** patient is rubbing joints / muscles plus unable to sit still due to discomfort				
Runny nose or tearing (not related to URTI or allergies): **0** not present **1** nasal stuffiness or unusually moist eyes **2** nose running or tearing **4** nose constantly running or tears streaming down cheeks				
GI upset (over last 30 minutes): **0** no GI symptoms **1** stomach cramps **2** nausea or loose stool **3** vomiting or diarrhoea **5** multiple episodes of vomiting or diarrhoea				
Tremor (observe outstretched hands): **0** no tremor **1** tremor can be felt, but not observed **2** slight tremor observable **4** gross tremor or muscle twitching				
Yawning (observe during assessment): **0** no yawning **1** yawning once or twice during assessment **2** yawning 3+ times during assessment **4** yawning several times/minute				
Anxiety or irritability **0** none **1** patient reports increasing irritability or anxiousness **2** patient obviously irritable or anxious **4** patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin **0** skin is smooth **3** piloerection (goosebumps) of skin can be felt or hairs standing up on arms **5** prominent piloerection				
SCORE INTERPRETATION 5–12 MILD 13–24 MODERATE 25–36 MODERATELY SEVERE > 36 SEVERE	Total Initials	Total	Total	Total Initials

- Office induction is preferred, as it will ensure patient does not go into precipitated withdrawal.
- Home induction may be necessary in certain situations:
  - Patient is unable to abstain from opioids long enough to attend the office in withdrawal.
  - Patient is at high risk for treatment drop-out (e.g., younger, injection opioid user, unstable housing).
  - Patient is in an acute care setting (e.g., ED, withdrawal management), is not yet in withdrawal, and is unlikely to keep a clinic appointment.
- **Office induction protocol:**
  - At least 12 hours since last oral IR dose, 24 hours since last oral CR dose.
  - Patient reports typical withdrawal symptoms.
  - COWS score of 12+
  - First dose: 4 mg SL. Dose may take several minutes to dissolve.
  - Reassess in 2 hours. If patient improved but still in withdrawal, give another 4 mg to take in office or at home. **Maximum dose first day** is **12 mg**.
- **Home induction protocol:**
  - Prescribe 2 mg SL q4H PRN, up to 6 tabs over 24 hours, x 1–3 days (e.g., 18 tabs all as take-home or 6 tabs daily dispensed for 3 days).
  - Warn patient to wait at least 12 hours after last opioid use and be in at least moderate withdrawal before taking first dose.
  - Take 2 mg x 2 tabs SL.
  - If still in withdrawal after 2 hours, take another 2 mg x 2 tabs SL. **Maximum dose** is **12 mg** in 24 hours.

Titration

- Reassess in 1–3 days. Increase dose by 2–4 mg at each visit if patient reports withdrawal symptoms or cravings towards the end of a dosing interval. Each dose increase should increase duration of relief from withdrawal and cravings.
- **Optimal maintenance dose** is usually **8–16 mg SL OD**; **maximum dose** is **24 mg SL OD**. The optimal dose should relieve withdrawal symptoms and cravings for 24 hours without causing significant sedation or other side effects.
- If feasible, at the beginning of therapy, buprenorphine/naloxone should be dispensed daily under observation by the pharmacist.
    - This is particularly important if the patient has been accessing opioids from other sources.
    - If the patient is unable to attend daily because of limited mobility, lack of transportation, or work or family commitments, arrange supervised dispensing at home by a nurse or reliable relative.
    - Take-home doses may be prescribed once patient is at optimal dose and has stopped unauthorized use.
- Arrange frequent office visits for counseling and urine drug screen monitoring.

Buprenorphine/naloxone prescriptions

Prescription should include:

- Patient's name, date of birth, and health card number
- The pharmacy address and fax number
- The dose
- Start and end dates
- Day(s) of the week the patient takes a dose at the pharmacy under the observation of the pharmacist, and days of the week the patient takes the dose at home. Stable patients usually attend the pharmacy once a week to take a single dose under the observation of a pharmacist and receive 6 tablets to take home.

The cost of generic buprenorphine/naloxone is covered on the provincial formularies of Alberta, British Columbia, Manitoba, Newfoundland and Labrador, Ontario, and Québec. In the other provinces and territories, as well as on the Non-Insured Health Benefit (NIHB) plan, special authorization is required for coverage.

Follow-up visits for stable patients on buprenorphine/naloxone

- Ask about withdrawal symptoms or cravings; sometimes patients require minor dose adjustments of 2–4 mg/day.
- Ask about alcohol and cannabis use.
- Ask about overall mood and functioning.
- Manage chronic medical conditions (e.g., hepatitis C) or psychiatric conditions (e.g., anxiety, depression).
- Perform regular screening and health maintenance (e.g., pap tests, mammograms, immunizations, etc.).
- Identify any new medical or psychiatric conditions.

- Review urine drug screen results.
  - Stable patients should leave at least one urine sample per month.
  - Review unexpected results with patient and, if necessary, with addiction physician.

Interpretation of unexpected urine drug screen results

Result	Interpretation	Action
Absence of norbuprenorphine	Noncompliance or diversion	If diversion suspected, resume daily supervised dispensing. Consider consult with addiction physician.
Presence of opioids or benzodiazepines	Innocent slip Early relapse	If inadvertent, warn patients not to take meds from family or friends. Increase testing frequency. If relapse: • Assess adequacy of buprenorphine/naloxone dose. • Counsel about avoiding triggers. • Assess mood. • Increase testing frequency. • If persists, reduce number of take-home doses.
Presence of cocaine or crystal methamphetamine	Possible stimulant use disorder	Consider consult with addiction physician

Indications for buprenorphine/naloxone tapering

- Patient wants to taper.
- Patient has at least six months without any substance use.
- Patient is socially stable and has a supportive family or social network.
- Patient has a stable mood and good coping strategies.
- Patient has minimal contact with drug users.

Buprenorphine/naloxone tapering protocol

- Decrease by small amounts, e.g., 2 mg or even 1 mg (half of a 2 mg tablet) at a time.
- Leave at least two weeks, preferably longer, between dose decreases.
- Put the taper on hold at the patient's request, or if the patient experiences withdrawal symptoms or cravings.
- Return to the original dose if the patient begins using opioids again, even in small amounts or intermittently.
- Provide regular support and encouragement.
- Emphasize that it is not a "failure" if the taper has to be held or reversed, and it is safe and acceptable to remain on buprenorphine/naloxone for long periods when necessary.