# Buprenorphine FAQs

## ABOUT BUPRENORPHINE

### What is the difference between buprenorphine and Suboxone®?

Buprenorphine is the active opioid found in buprenorphine/naloxone combination tablets (trade name Suboxone®), which have been marketed in Canada since 2007. Buprenorphine is a treatment for opioid use disorder (OUD), although it is increasingly being used to treat chronic pain. In Canada, buprenorphine is also available as a film for buccal use and as a monthly injectable (Sublocade®) for the treatment of OUD, and as a transdermal patch for the treatment of chronic pain.

### What is the role of naloxone in buprenorphine/naloxone tablets?

Naloxone is an opioid receptor blocker that causes withdrawal symptoms when injected or snorted. It is added to buprenorphine tablets to deter people from injecting the tablets. Naloxone is not absorbed when taken sublingually or orally; it has no effect on the activity of buprenorphine and does not cause withdrawal or any other symptoms if other opioids are used concurrently.

### What are the contraindications for buprenorphine/naloxone?

The main contraindications for buprenorphine/naloxone are allergy or hypersensitivity to buprenorphine or naloxone and severe liver dysfunction. Patients should not be started on buprenorphine if they are acutely intoxicated, in acute severe respiratory distress, have decreased level of consciousness, or are unable to provide informed consent.

### What is precipitated withdrawal? How often does it occur? Is it dangerous? How can it be treated?

Precipitated withdrawal is a state of severe and acute withdrawal that can occur if the initial dose of buprenorphine is given when the patient still has other opioids active on the receptor. Because buprenorphine is a partial opioid agonist with high affinity, it displaces other opioids but doesn't fully replace their effect, leaving the patient with a net opioid deficit.

The risk of precipitated withdrawal is very low. A retrospective chart review of 158 patients treated with buprenorphine for opioid withdrawal symptoms in an emergency department setting found no cases of precipitated withdrawal (1).

Precipitated withdrawal can be dangerous for patients with unstable cardiac conditions or those who are pregnant. It is also extremely distressing and may cause patients to be reluctant to try buprenorphine again. Avoiding precipitated withdrawal by delaying initiation of buprenorphine until enough time has passed from last opioid use or using a microdosing strategy is the best option.

For mild cases of precipitated withdrawal, treatment includes non-opioid therapies, such as clonidine, dimenhydrinate, ondansetron, and loperamide. For moderate or severe cases, therapy with additional buprenorphine should be considered (8–16 mg at once and up to 32 mg total); additional buprenorphine provides additive opioid effects, even as a partial agonist, and mitigates withdrawal symptoms (see **High-Dose Buprenorphine Initiation ("Macrodosing") for ED Providers**).

### Is buprenorphine safe in pregnancy?

Buprenorphine/naloxone is safe in pregnancy. All pregnant patients should be started on opioid agonist therapy (OAT) urgently and connected to prenatal care and supports. Pregnant patients can be started on buprenorphine either using a traditional approach if they are in withdrawal or with microdosing (see below).

### Can someone overdose on buprenorphine?

Because of its partial activity on the opioid receptor and ceiling effect on respiratory depression, the risk of overdose with buprenorphine is very low, and lower than that of any other opioids. Buprenorphine is actually protective against overdose with unregulated opioids because the high affinity of buprenorphine on the opioid receptor blocks other opioids from attaching to the receptor. Starting buprenorphine in the ED is much less likely to be associated with an opioid overdose than discharging someone with OUD without any treatment. For the elderly or people on high doses of benzodiazepines, start with lower doses of buprenorphine (e.g., 2 mg starting dose and maximum Day 1 dose of 8 mg) to lower the risk of respiratory depression.

## STARTING BUPRENORPHINE

### What is the right timing to start buprenorphine?

Previously, patients were required to be in withdrawal before starting buprenorphine to avoid precipitated withdrawal. There are now accepted protocols to address different scenarios related to timing of opioid use and ability to tolerate withdrawal.

**Traditional induction patients must be in withdrawal:** (**COWS** ≥ 13). Timing from last opioid use depends on the opioid that was used:

- 12–16 hours for short-acting prescription opioids (e.g., IR oxycodone, hydromorphone, morphine)
- 18–24 hours for intermediate-acting prescription opioids (e.g., CR oxycodone, hydromorphone)
- 48+ hours for fentanyl or any opioids from the unregulated supply*
- 72+ hours for methadone

Patients can either be started on buprenorphine in the ED or sent home with a **prescription** and **instructions** to take their first dose when they are in withdrawal and sufficient time has passed from last use.

*Heroin itself is a short-acting opioid, but since 2019 most of Canada's heroin supply has been replaced by unregulated fentanyl and fentanyl analogues, which are long-acting opioids for the purposes of buprenorphine initiation.

**Microdosing (low-dose induction):** Patients do not have to be in withdrawal and can be actively using other opioids during induction. Low doses of buprenorphine are started and increased very gradually over the course of seven days. This approach can be used with a **prescription** from the ED and **instructions** on how to start buprenorphine at home.

**Macrodosing (high-dose induction):** This approach is appropriate for patients who use fentanyl who have had an overdose reversed with naloxone or are in withdrawal (**COWS** ≥ 13) and at least 18 hours from last fentanyl use. Patients should be observed throughout the **induction**.

## Fentanyl is a short-acting drug. Why the concern about fentanyl and starting buprenorphine?

Although fentanyl is thought of as a rapid-acting opioid with a short duration of action, it is highly lipid soluble. With multiple doses, fentanyl accumulates in fat tissues and effectively has a long half-life, with activity in the brain long after its analgesic and euphoric effects have passed. Anecdotally, precipitated withdrawal has been observed in people reporting significant withdrawal symptoms and abstinence from fentanyl for three or more days before starting buprenorphine (3). Microdosing is a good alternative for people using fentanyl or opioids from the unregulated supply who wish to start buprenorphine.

## My patient had an overdose reversed by naloxone by EMS three hours ago. Their COWS is 20. Can I start them on buprenorphine?

Yes (as long as they are not on methadone). High-dose buprenorphine initiation can be used in this situation. The person is in withdrawal because naloxone has displaced opioids from the opioid receptors; high doses of buprenorphine can attach to the receptors, effectively treating withdrawal and starting OAT. In this situation, treating earlier is better than waiting for more time to elapse between opioid use and the first dose of buprenorphine. Traditional starts with doses of 2–4 mg would be likely to cause precipitated withdrawal within hours of last opioid use. Options would be to offer a prescription (or tablets from the ED) for a **home start** or **microdosing**.

## What if a patient says their last opioid use was more than four days ago but COWS is < 12? Can they be started on buprenorphine?

Yes. Someone whose last use was more than four days ago could already be past the peak of withdrawal. In this case, the person is no longer at risk of precipitated withdrawal but still at risk of resuming opioid use, and their risk of overdose is higher due to loss of tolerance. Buprenorphine can be started without worrying about precipitated withdrawal. A starting dose of 2–4 mg should be used, depending on opioid tolerance and any other risk factors.

## Is it safe to give take-home doses of buprenorphine for a home start or microdosing to someone who has opioid use disorder?

The risk of a negative outcome from a take-home dose of buprenorphine is low relative to the risk of ongoing opioid use. With a home start, it's possible that the patient could take the medication too soon, get sick due to precipitated withdrawal, and be less inclined to try it again. The same is true with microdosing if the patient doesn't follow instructions and takes too many tablets at a time. However, these risks are outweighed by the potential benefit of getting someone on to treatment.

With respect to other risks, misuse of buprenorphine by injecting is uncommon in most settings. While diversion of buprenorphine does occur, some studies have shown that the majority of diverted buprenorphine was used to treat withdrawal in people without a prescription (4).

## How long should patients be observed in the ED? Do they need special monitoring?

Patients should be observed for at least 60 minutes after their first dose of buprenorphine to ensure that they do not experience buprenorphine-precipitated withdrawal or over-sedation. Serious adverse events are rare. The most common adverse effect is nausea, which can be difficult to distinguish from withdrawal-associated nausea, and can be treated with ondansetron if necessary. Longer periods of observation are prudent for patients with serious co-occurring medical disease, older age, or intoxication with other substances.

### The product monograph says maximum Day 1 dose of buprenorphine is 12 mg. Why do these guidelines say 16 mg?

Higher initial doses are associated with more effective control of withdrawal symptoms and may be more protective against overdose. Studies suggest that higher doses and longer prescriptions are associated with better treatment follow-up (5-8). Given the lower risk of buprenorphine relative to other opioids, especially unregulated opioids, a Day 1 dose of 16 mg is reasonable and supported by consensus.* Caution should be used with patients with heavy alcohol or benzodiazepine use and medically complex or older patients.

*Note that this Day 1 maximum is for traditional induction; high-dose induction (*macrodosing*) uses Day 1 doses of 24–32 mg.

## CLINICAL SCENARIOS

### What if a patient who recently started buprenorphine missed their follow-up appointment and missed three doses in a row? Do they need to restart with a new induction?

A patient who has been on 4 mg or more can resume their previous dose without a formal restart, as long as they have not missed more than six days of buprenorphine. Patients who are microdosing because of continuing opioid use should typically restart their microdosing schedule from the beginning if they miss three days in a row.

### If someone has missed three doses of methadone, why shouldn't we switch them to buprenorphine?

Because of methadone's very long half-life, there is a significant risk of triggering precipitated withdrawal, even in patients who missed three consecutive doses, if their dose of methadone was more than 30 mg. For people who have been stable on methadone, switching them can be very destabilizing. This is not a decision to be made hastily. Resuming methadone with the guidance of a methadone prescriber is a safer choice.

### How should acute pain be handled when a patient is on buprenorphine?

Acute pain can be treated with short-acting opioids if the patient's pain presentation would typically warrant opioids for patient management in any other patient. The dose of opioids required to achieve pain control may be higher for a patient on buprenorphine because of the activity of buprenorphine on the opioid receptor. Administering additional opioids to a patient on buprenorphine will not cause precipitated withdrawal. **Buprenorphine should not be stopped while the patient is receiving additional opioids.**

## REFERENCES


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