Initiation of Buprenorphine Extended-Release (BUP-XR) Injection

BUP-XR QUICK REVIEW

- An extended-release subcutaneous injection of buprenorphine for moderate to severe opioid use disorder (trade name Sublocade).
- Approved in Canada for clients stabilized on 8–24mg of sublingual buprenorphine (BUP-SL) for at least seven days.
- Health Canada Certification required for prescribing only.
- Covered under ODB (LU code 577), NIHB, Veterans Affairs, most private plans.
- Available in 300mg/1.5mL and 100mg/0.5mL.
- Dosing schedule:
  - 300mg x1 month, then 100mg monthly ongoing for those previously on 8–18mg BUP-SL, or
  - 300mg x2 months, then 100mg monthly ongoing for those previously on >18mg BUP-SL, or
  - 300mg monthly ongoing for those demonstrating instability
- Doses can be provided 26–42 days apart.
- Steady state occurs after four to six months.
- Average buprenorphine plasma concentration in steady state compared to BUP-SL:
  - 300mg BUP-XR: 6.54ng/mL
  - 100mg BUP-XR: 3.21ng/mL
  - 24mg BUP-SL: 2.91ng/mL

BUP-XR RAPID INITIATION (OFF-LABEL USE)

Given the potency and toxicity of the unregulated drug supply, clients may require high doses of buprenorphine for stabilization. BUP-SL often requires daily pharmacy attendance, which increases the risk of missed doses, making stabilization even more difficult. These combined risks make the high concentration of buprenorphine delivered with BUP-XR and the subcutaneous extended-release delivery system an effective and valuable option for many.

The product monograph recommends clients to have stabilized on BUP-SL 8mg or greater for a minimum of seven days before BUP-XR initiation. While this recommendation is appropriate for stable clients who are interested in BUP-XR as an alternative, it poses a significant barrier and health risk to clients who have difficulty reaching stabilization and/or present to short-term care facilities that are more transient by nature. For example, the average length of stay at a withdrawal unit is five to seven days, largely precluding on-label initiation of BUP-XR before discharge. This misses a critical opportunity for treatment, both because cessation of opioids results in a rapid loss of tolerance and because client motivation is typically high in live-in settings. BUP-XR ensures medication continuation beyond this period and provides overdose protection in case of relapse post-discharge.

There is growing evidence that BUP-XR is safe to be initiated with fewer than seven days of BUP-SL initiation. In these studies, BUP-XR has been provided within seven days, and as early as one hour after a single dose of BUP-SL. The few cases of PW that were reported received symptomatic treatments and were resolved within twelve hours. No elevation in sedation was noted. Please see the **Guide to the Use of Depot Buprenorphine** for more details.

Initiation of BUP-XR

BUP-XR CONTRAINDICATIONS & PRECAUTIONS (see product monograph for full details)

Contraindications

- Known hypersensitivity to buprenorphine or to any component of the Atrigel delivery system.
- Unable to provide informed consent.
- Altered mental status, depressed level of consciousness or delirium.
- Acute intoxication.
- Severe medical illness such as sepsis, respiratory distress, severe liver dysfunction.
- Currently pregnant or desiring pregnancy (there is limited evidence to guide treatment recommendations for pregnancy and breastfeeding; consider alternate treatment).

Precautions

- Reported methadone use in the last 72h.
- Concurrent withdrawal from alcohol or benzodiazepines.
- Moderate hepatic impairment.
- Elderly.
- Combination with other CNS depressants.

NO CONCERN IDENTIFIED

CONCERN IDENTIFIED → **Do not proceed with BUP-XR**; continue with current treatment and consult with an addiction medicine team if available.

On-label recommendations are to proceed with BUP-XR after induction and stabilization on BUP-SL ≥ 8mg for seven days.

To be considered for early administration of BUP-XR, ensure the following conditions are met:

1) **The client can tolerate buprenorphine.**
   The client has been exposed to buprenorphine without adverse events such as hypersensitivity.
2) **The client tolerates ≥ 8mg buprenorphine.**
   The client has tolerated at least 8mg of BUP-SL without respiratory depression or sedation. I**f not tolerant of ≥ 8mg BUP-SL DO NOT proceed with BUP-XR**.
3) **The client is not at risk for precipitated withdrawal.**
   Monitor the client for severely worsening withdrawal, typically occurring within 1h of BUP-SL administration (limited research showed that when worsening withdrawal occurred after BUP-XR, it was mild to moderate and resolved with symptomatic support within 12h).

***NOTE:** If the above conditions are met, BUP-XR can be provided. Same or next day BUP-XR initiation should be considered for those at highest risk of treatment discontinuation and opioid harms. Initiation before discharge is appropriate for those in live-in settings (e.g., withdrawal management). Longer periods of stabilization should be considered for those with a precaution as listed above, e.g., elderly**.**

Has the client been on BUP-SL ≥ 8mg for at least seven days OR does the client meet the three criteria for early administration as listed above?

YES

Provide BUP-XR

- Arrange outpatient follow-up. Ensure the outpatient clinic provides BUP-XR, and have the client present to the clinic at least one week before their next scheduled injection for treatment planning, earlier for management of adverse events or ongoing withdrawal.
- Provide naloxone kit.
- Review harm reduction resources.

NO

Do not proceed with BUP-XR; continue with current treatment and consult with an addiction medicine team if available.

Considerations for unmanaged withdrawal, cravings, or urges after initial BUP-XR:

1) Insufficient buprenorphine plasma concentration. More common in those with high opioid tolerance. Consider the following options:

- Provide "top-up" BUP-SL titrated until the client is stabilized, until their next injection.
- Provide the second BUP-XR injection early (based on expert recommendation).

2) Non-opioid withdrawal. Consider co-occurring withdrawal (e.g., benzodiazepines) if symptoms do not improve despite increasing buprenorphine. Investigate and treat appropriately.

3) Untreated health condition, e.g., infection, hypo- or hyperglycemia. Investigate and treat appropriately.

If insufficient relief of opioid withdrawal, cravings, or urges with ongoing 300mg injections, consider transition to methadone and/or slow-release oral morphine.