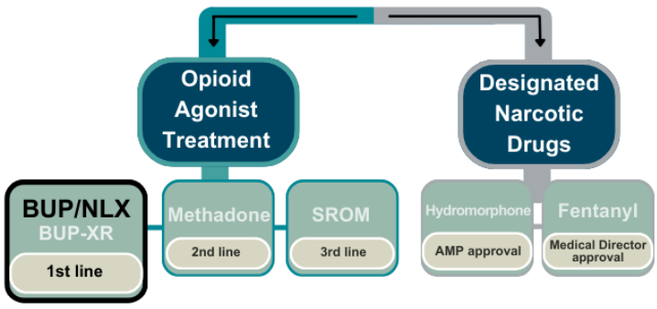
Buprenorphine/Naloxone (BUP/NLX)

For the Treatment of Opioid Use Disorder (OUD)

Opioid Dependency Treatment (ODT) Intensity Continuum

Lower Intensity ← → Higher Intensity

Withdrawal Management | **Opioid Agonist Treatment (OAT)** | **Designated Narcotic Drugs (DND)**

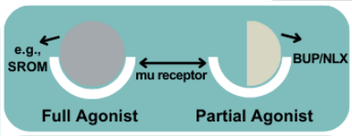


People may use different medications along the treatment continuum at various times depending on their preferences, comorbidities, treatment goals, efficacy of the medications, and life circumstances. Buprenorphine/naloxone (BUP/NLX) is one such treatment that can be used alone or in combination with other ODT medications. Health care providers and individuals need to work together to explore the available treatment options and determine the most suitable intervention based on the individual's unique needs. This personalized approach is essential for successful treatment outcomes, reducing the risk of unregulated opioid use, and mitigating any potential harm.

BUP/NLX, commonly referred to as Suboxone®, is the first line of treatment for individuals with opioid use disorder. BUP/NLX has a superior safety profile due to its ceiling effect for respiratory depression and fewer side effects and medication interactions.

PHARMACODYNAMICS

BUP/NLX is a semi-synthetic opioid that works by partially activating the mu-opioid receptor. It has a strong affinity for the receptor, but its intrinsic activity (or the extent of its activation) is lower compared to other full opioids. BUP/NLX is composed of two medications, buprenorphine, and naloxone, in a 4:1 ratio. When taken sublingually, buprenorphine has good bioavailability, while naloxone has poor bioavailability. The inclusion of naloxone is solely intended to discourage injection and insufflation. The partial agonism of BUP/NLX, combined with a slow dissociation, allows for a long-lasting effect that can relieve pain and/or withdrawal symptoms. This partial agonism also limits other pharmacologic effects, such as euphoria, drowsiness, respiratory depression, gastrointestinal issues, changes in circulation, constriction of the pupils, histamine release, and physical dependence.



Buprenorphine has a rapid onset of **30-60 minutes** and plasma concentration levels peak after approximately **1 to 4 hours.** Duration of action is dose dependent:

- **Dose of 2-4mg/day: ~4 to 12 hours**
- **Dose of 4-8mg/day: ~24 hours**
- **Dose >8mg/day: ~36-72 hours**

CONTRAINDICATIONS

- Hypersensitivity to buprenorphine or naloxone.
- Significant acute intoxication with a central nervous system depressant (an opioid, alcohol, benzodiazepine, etc.)

ADMINISTRATION

Buprenorphine/naloxone should be taken sublingually. The tablets should not be chewed or swallowed. While the medication is dissolving, advise individuals not to eat, drink or swallow. Buprenorphine has poor gastrointestinal absorption and needs to be taken sublingually. If buprenorphine is taken orally, it has a low bioavailability because of a high-first pass metabolism. Once individuals are stabilized on a therapeutic dose, they can take buprenorphine/naloxone in a single dose, once daily.

Suitable for **immediate take-home doses,** including take-home initiation when indicated, which may contribute to increased individual autonomy and cost savings.

Place medication under the tongue. The medication needs to stay under the tongue until fully dissolved (this can take up to 30 min depending on dose) or it will not work.

CAUTIONARY POPULATIONS

Moderate or Severe Hepatic Impairment: use with caution.

Geriatric: use with caution; Monitor for sedation and respiratory depression.

Prior to initiating BUP/NLX a urine drug screen (UDS) should be performed to confirm the presence of opioids.

*A UDS is not to be used punitively but to facilitate open communication. ***Treatment should not be delayed while UDS results are pending.***

TRADITIONAL BUPRENORPHINE/NALOXONE INDUCTION

Day 1: Determine the **TIME** since the **LAST** opioid use

>12 hours since the last short acting opioid (e.g., hydromorphone) | **>24 hours since the last intermediate-acting opioid (e.g., SROM, fentanyl)** | **>72 hours since the last long-acting opioid (e.g., methadone)**

Is the individual in withdrawal?

Individuals need to have a Clinical Opiate Withdrawal Scale (COWS) > 12 before starting Suboxone® (buprenorphine/naloxone)

YES → **If the is sufficient time since LAST opioid use and COWS is > 12, give:**

BUP/NLX 2 mg/0.5 mg SL (1 tab) sublingually

How does your client feel?

- If symptoms worsen, the individual may be experiencing **precipitated withdrawal.**
- If all withdrawal symptoms are relieved. **Continue to Day 2**
- If withdrawal symptoms persist, continue to take BUP/NLX **2 mg/0.5 mg SL (1 tab) sublingually each hour,** until a maximum dose of **16mg/4mg (8 tabs)** is reached, or sedation occurs.

Reassess COWS after 1 hour, if there are no signs of precipitated withdrawal, give:

BUP/NLX 2 mg/0.5 mg SL (1 tab) sublingually

NO → **If COWS is <12, do not proceed with traditional BUP/NLX induction, this could force an individual into precipitated withdrawal. Reassess in 1 hour.**

Day 2:

The total therapeutic dose administered on Day 1 is the starting dose on Day 2

- If all withdrawal symptoms are relieved. **This is your dose.**
- If withdrawal symptoms persist, continue to take buprenorphine/ naloxone **2 mg/0.5 mg SL (1 tab) sublingually each hour,** until withdrawal symptoms are relieved to a maximum dose of **32mg/8mg (16 tabs)** is reached, or sedation occurs.

The total therapeutic dose of BUP/NLX administered on day 2 is the maintained dose starting on day 3.

Day 3 with Traditional Induction: Benzodiazepine (BZD) Withdrawal Management

Assess for BZD contamination:

- Hx of hallucinations, seizures, disorientation when decreasing opioid use
- Nausea, vomiting, sweating, restlessness, not relieved with buprenorphine/naloxone.
- Non-prescribed benzodiazepine on UDS
- Use of at least 2pts of fentanyl per day

NO → Continue to monitor for withdrawal symptoms. Will likely not require BZD withdrawal management.

YES → People who use BZD > 4 weeks are more likely to develop significant dependence. Consider **Diazepam** for daily dispense:
5mg TID x 2 days; 5mg BID x 2days; 5mg OD x 2 days; then stop.

A negative UDS result alone does not exclude the risk of benzodiazepine withdrawal

Each individual should be provided with harm reduction resources and education, including a community based naloxone kit and information on where to access Supervised Consumption Services.

PRECIPITATED WITHDRAWAL

- Can occur due to the replacement of a full opioid receptor agonist (e.g., fentanyl) with a partial agonist that binds with a higher affinity.
- Occurs 30-60 min after the medication has been given.

Symptoms

- Similar to opioid withdrawal (e.g., increased heart rate, sweating, agitation, diarrhea, tremor, unease, restlessness, tearing, runny nose, vomiting, and goose flesh)

WITHDRAWAL SYMPTOM MANAGEMENT

Gabapentin helps manage withdrawal related aches and pains.
Dose: 300mg PO TID

Loperamide helps manage withdrawal related diarrhea.
Dose: 4 mg (2 tabs) PO initially, then 2 mg (1 tab) PO after each loose bowel movement (max daily dose: 16 mg)

Clonidine helps relieve sweating, diarrhea, vomiting, abdominal cramps, anxiety, and irritability.
⚠ **HR** <60bpm and/or **BP** <90/60mmHg
Dose: 0.1-0.2 mg PO Q4-8H PRN

Clonazepam helps reduce seizure activity.
Dose: 0.5 mg PO Q6-8H PRN

References

British Columbia Centre on Substance Use. (2022, January). *Opioid Use Disorder, Practice Update.* Retrieved from https://www.bccsu.ca/wp-content/uploads/2022/02/Opioid-Use-Disorder-Practice-Update-February-2022.pdf

British Columbia Centre on Substance Use. (2023, November). *A Guideline for the Clinical Management of Opioid Use Disorder.* Retrieved from https://www.bccsu.ca/wp-content/uploads/2023/11/BC-OUD-Treatment-Guideline_2023-Update.pdf

Vancouver Coastal Health. (2021). *Benzodiazepine Withdrawal Risk Due to Contaminated Illicit Opioid Supply Screening Tool.*

Alberta Health Services

Buprenorphine/Naloxone (BUP/NLX) Micro & Macro Inductions

For the Treatment of Opioid Use Disorder (OUD)

* BUPRENORPHINE/NALOXONE MICRO-INDUCTION DOSING SCHEDULE

- Educate the individual to keep the medication under the tongue until fully dissolved (this can take up to 15 min).
- Advise the individual not to eat, drink, or swallow while BUP/NLX is dissolving.
- Clinicians may ask for the below titration schedule to be prepared in a bubble pack for ease of use.
- Clinicians may consider co-prescribing a full agonist (e.g., SROM) during the micro-dosing induction if clinically indicated.

Day one	Dose: 0.5mg twice daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**0.5mg/0.125mg is 1/4 of a 2 mg tablet.** Doses given a minimum of 4 hours apart.	**1st dose:** 0.5 mg = 1/4 of a 2 mg tablet	**2nd dose:** 0.5 mg = 1/4 of a 2 mg tablet	✕	
Day two	Dose: 0.5mg three times daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**0.5mg/0.125mg is 1/4 of a 2 mg tablet.** Doses given a minimum of 4 hours apart.	**1st dose:** 0.5 mg = 1/4 of a 2 mg tablet	**2nd dose:** 0.5 mg = 1/4 of a 2 mg tablet	**3rd dose:** 0.5 mg = 1/4 of a 2 mg tablet	
Day three	Dose: 1 mg twice daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**1mg/0.250 is half of a 2 mg tablet.** Doses given a minimum of 4 hours apart.	**1st dose:** 1.0 mg = 1/2 of a 2 mg tablet	**2nd dose:** 1.0 mg = 1/2 of a 2 mg tablet	✕	
Day four	Dose: 2 mg twice daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**Give 1 whole 2 mg/0.5mg tablet** Doses given a minimum of 4 hours apart.	**1st dose:** 2.0 mg = 1 tablet	**2nd dose:** 2.0 mg = 1 tablet	✕	
Day five	Dose: 2 mg three times daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**Give 1 whole 2 mg/0.5mg tablet** Doses given a minimum of 4 hours apart.	**1st dose:** 2.0 mg = 1 tablet	**2nd dose:** 2.0 mg = 1 tablet	**3rd dose:** 2.0 mg = 1 tablet	
Day six	Dose: 4 mg three times daily	Individual can continue to use prescribed and/or non prescribed opioids.			
	**Give 2 whole 2 mg/0.5mg tablets** Doses given a minimum of 4 hours apart.	**1st dose:** 4.0 mg = 2 tablets	**2nd dose:** 4.0 mg = 2 tablets	**3rd dose:** 4.0 mg = 2 tablets	
Day seven	Dose: 12 mg once daily	Cessation of prescribed and/or non prescribed opioids is encouraged to prevent precipitated withdrawal.			
	**Give 6 whole 2 mg/0.5mg tablets**	**1st dose:** 12.0 mg = 6 tablet	✕	✕	

* BUPRENORPHINE/NALOXONE MACRO-INDUCTION DOSING SCHEDULE

- **Benefits:** faster resolution of withdrawal symptoms, fewer tablets to dissolve, fewer nursing assessments, and a faster titration to a therapeutic dose
- **Risks** (as per clinical studies): precipitated withdrawal, nausea, and hypotension (unlikely with doses <32mg).
- Consider administering an **anti-emetic 30 mins prior** to Suboxone® if the individual is complaining of nausea.

Day 1: Determine the **TIME** since the **LAST** opioid use:

>12 hours since the last short acting opioid (e.g., hydromorphone)	>24 hours since the last intermediate-acting opioid (e.g., SROM, fentanyl)	>72 hours since the last long-acting opioid (e.g., methadone)

2 8mg/2mg tablets

Is the individual in withdrawal?

Individuals need to have a Clinical Opiate Withdrawal Scale (COWS) > 10 before starting Suboxone® (BUP/NLX) macro-induction

YES → Give **16mg/4mg BUP/NLX** sublingually.

NO → **If COWS is <10, do not proceed with BUP/NLX, this could force an individual into precipitated withdrawal. Reassess in 1 hour.**

Reassess in 60 mins

In the event of precipitated withdrawal, it is recommended to provide the individual with the remaining dose of BUP/NLX, **totaling 24mg**, promptly. Should any withdrawal symptoms persist after **30-60 minutes, an additional 4-8mg can be administered, up to a maximum of 32mg on Day 1.**

COWS >8

Repeat BUP/NLX **8mg/2mg–16mg/4mg** every 1–2hrs until withdrawal is resolved or sedation occurs. **(recommended Day 1 maximum dose is 32mg)**

→ **Provide the individual with a prescription for the total dose administered on day 1 until the planned follow-up (max 7 days)**

** Both micro and macro inductions of BUP/NLX are considered off-label and should be discussed with the individual and documented in their chart*

References

1. META PHI. (n.d.). *Buprenorphine Macro dosing Initiation*. Retrieved from MacrodosingOnePager.pdf (metaphi.ca).
2. Alberta Health Services. (2022). *Calgary ODP micro dosing Buprenorphine/Naloxone.*

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amh.practicesupports@ahs.ca

Alberta Health Services