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Buprenorphine/naloxone Guidance

This document provides a high-level overview on the guidance of buprenorphine/naloxone for the treatment of opioid use disorder (OUD). For full guidance please refer to the BC Centre on Substance Use's A Guideline for the Management of Opioid Use Disorder.

INDUCTION

Table 1: Comparative summary of traditional induction and low-dose induction methods

Induction method	Method features	Candidate characteristics
Low-dose induction (Slow up-titration while continuing full agonist use until therapeutic dose is reached)	• Does not require people to discontinue other opioid use before therapeutic doses of medication has been reached • Gradual titration process is highly variable and may take 5–10 days • Relatively novel method • Can be initiated with take-home doses	• Consider for individuals currently using other opioids • Individuals who are apprehensive about experiencing the period of opioid withdrawal required prior to induction
Traditional induction (1–2–day induction process that starts after a period of abstinence from opioid use)	• Requires people to discontinue other opioids and be in moderate withdrawal prior to initiation, to avoid precipitated withdrawal • Therapeutic dose can often be reached within 1–2 days • Well-established method • Can be initiated with take-home doses	• People currently not using opioids (e.g., after withdrawal management, after administration of naloxone) • People with previous positive experience with traditional induction • People wishing to complete induction in a shorter time frame

LOW-DOSE INDUCTION

The general starting doses provided here should be combined with individualized assessment.

Table 2. Sample 7-day low-dose induction protocol

Day	Buprenorphine /naloxone Dose	Number of times a day	Other opioids
1	0.5mg/0.125mg	2	Continue full agonist use
2	0.5mg/0.125mg	3	Continue full agonist use
3	1mg/0.25mg	2	Continue full agonist use
4	2mg/0.5mg	2	Continue full agonist use
5	2mg/0.5mg	3	Continue full agonist use
6	4mg/1mg	3	Continue full agonist use
7	12mg/3mg	1	Stop other use

An 8-day BID induction protocol may be preferable for some individuals due to consistent dosing during induction.

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TRADITIONAL INDUCTION

Step 1

Instruct individual to discontinue opioid use prior to the first day of scheduled induction. The person should reach moderate withdrawal (COWS score>12) prior to induction (see table 3)

Table 3: Recommended period of pre-initiation withdrawal, based on the type of opioids currently used

Short-acting opioids	≥12 hours since last dose	***Examples:*** *heroin, oxycodone, hydromorphone*
Intermediate-acting opioids	≥ 24 hours since last dose	***Examples****: slow-release oral morphine, fentanyl* (confirmed or suspected)*
Long-acting opioids	48–72 hours or more since last dose	***Example****: methadone*

***Note on fentanyl**: In general, **a minimum of 24 hours of withdrawal from fentanyl is recommended**. Individuals should be supported to sustain this withdrawal period for as long as tolerable beyond the 24-hour point in order to minimize their risk of precipitated withdrawal. **Alternatively, a low-dose induction method may be preferable for people exposed to fentanyl.**

Step 2

Select starting dose and titrate by 2mg–4mg every 1–3 hours based on withdrawal symptoms (see table 4)

Table 4: Starting buprenorphine/naloxone doses based on risk of precipitated withdrawal

Indication	Starting dose	Total Starting Dose
Concern about precipitated withdrawal	One 2mg/0.5mg buprenorphine/naloxone tablet	2mg/0.5mg buprenorphine/naloxone
Low risk of precipitated withdrawal	Two 2mg/0.5mg buprenorphine/naloxone tablet	4mg/1mg buprenorphine/naloxone

- Individuals who use fentanyl are at higher risk of precipitated withdrawal; start these individuals at 2mg/0.5mg buprenorphine/naloxone
- For people at lower risk of precipitated withdrawal (e.g., recently completed withdrawal management, known time of last opioid use, fentanyl-negative UDT), consider a higher starting dose of 4mg/0.5mg buprenorphine/naloxone

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TRADITIONAL INDUCTION (CONTINUED FROM PREVIOUS PAGE)

Step 3

Day 1 is complete once withdrawal symptoms are adequately relieved
- The day 1 max dose is 16mg/4mg, but higher doses may be reasonable to address persisting withdrawal symptoms

Step 4

Prescribe the total day 1 dose for day 2

Step 5

If needed, continue the same titration process and stop at a dose that adequately relieves withdrawal symptoms and cravings

Step 6

Daily doses of **up to 32mg/8mg buprenorphine/naloxone** may be reasonable and can be provided safely to address high opioid tolerance

HOME INDUCTION

- Where safe and appropriate, consider offering unobserved traditional induction or "home" induction to reduce barriers and avoid unnecessary disruptions to individuals' daily lives
- Provide regular follow-up and support via telephone or video within clinic hours
- Provide contact information, in-person education, and written instructions for dosing and timing

NON-OPIOID ADJUNCTS TO TREAT WITHDRAWAL SYMPTOMS

Dosing regimens for non-opioid adjuncts to treat withdrawal symptoms:

- Clonidine: 0.1–0.2mg PO PRN every 4 hours for <12 hours
- Acetaminophen: 325–1000mg PO PRN every 4 to 6 hours (maximum 4000mg/day; 2000mg for older adults or those with liver impairment)
- Dimenhydrinate: 50–100mg PO PRN every 6 hours
- Ibuprofen: 400mg PO PRN every 4 hours
- Loperamide: 2–4mg PO PRN every 6 hours (maximum 16mg/day)

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OPTIONS FOR MANAGING PRECIPITATED WITHDRAWAL

In all cases explain what has occurred and offer non-opioid adjuncts for symptom management.

Option 1: Continue induction

1. Give additional doses of 2mg/0.5mg buprenorphine/naloxone every 1–2 hours until withdrawal symptoms are resolved.
2. Inform the person that additional doses of buprenorphine/naloxone can initially worsen withdrawal symptoms before improvement.

Option 2: Delay induction

1. Wait a few hours to allow the full agonist to clear opioid receptors before administering the next buprenorphine/naloxone dose.
2. Continue giving doses until withdrawal symptoms are resolved or Day 1 maximum dose is reached.

Option 3: Stop induction

1. Provide reassurance that symptoms will resolve as the full agonist can resume its activity.
2. Offer full opioid receptor 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 of buprenorphine/naloxone (novel approach based on clinical experience)

1. Provide additional doses of buprenorphine/naloxone, typically from 8mg/2mg to 24mg/6mg. Several high doses of buprenorphine/naloxone may be necessary.
2. Inform the person that they can expect to feel better within a few hours of receiving a high dose of buprenorphine/naloxone.

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MISSED DOSES

- Separate protocols based on if the person has returned to full opioid agonist use
- The dispensing pharmacy is required to cancel the prescription and notify the prescribing clinician if the individual misses:
  - 6 consecutive days, without return to full opioid agonist use
  - 4 consecutive days, with return to full opioid agonist use

Table 5: Suggested protocol for managing missed doses without return to full opioid agonist use:

Consecutive missed once-daily doses	Suggested protocols
≤5 days without return to full agonist use	Resume without dose reduction
≥6 days without return to full agonist use	Re-titration is required. The re-titration process should be individually tailored with the goal to re-titrate to previous stable doses within a few days.

Table 6: Suggested protocol for managing missed doses with return to full opioid agonist use

Consecutive missed once-daily doses	Suggested protocols
≤3 days with return to full opioid agonist use	Safe to continue buprenorphine/naloxone without re-induction
4 days with return to full opioid agonist use	Discuss the risk of precipitated withdrawal and weigh them against the benefits of continuing buprenorphine/ naloxone
≥5 days with return to full opioid agonist use	New induction may be required

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TAKE-HOME DOSING

For people who meet the following criteria, take-home dosing should be considered immediately, including during induction:

- Clinical and psychosocial stability:
  - Ability to attend appointments
  - Absence of unstable psychiatric comorbidities (e.g., psychosis, suicidality)
  - Absence of severe behavioural issues at the clinic
  - Absence of severe sedation
  - Absence of uncontrolled substance use patterns that cause frequent overdoses or blackouts
- Ability to safely store medication (access to a secure lockbox or cabinet)

Monitoring of take-home buprenorphine/naloxone dosing

People receiving take-home buprenorphine/naloxone dosing should be seen at least monthly to assess progress and stability. The following are considerations for follow-up and reassessment:

- Self-reported or other indication of increase in unregulated opioid use
- Missed appointments or doses, or repeated reports of lost, stolen, or vomited doses
- Requests to increase a previously effective dose
- Other evidence of diversion (e.g., tampering with blister packs, UDT negative for buprenorphine, repeated inability to provide urine tests)

URINE DRUG TESTING

Table 7: Suggested urine drug testing frequency

Treatment stage	UDT schedule
Initial confirmatory testing	Performed to confirm unregulated opioid use prior to initiating OAT
Buprenorphine/naloxone	
Induction and stabilization	**Monthly** or more or less frequently as required and when clinically indicated
Maintenance	When clinically indicated
Take-home doses	**2–4 tests per year** or when there are any safety concerns Frequency of UDT is as required when clinically indicated