Buprenorphine Reference Guide

For the Treatment of Opioid Use Disorder

Contents

Buprenorphine/Naloxone

Mechanism of Action

Specific features combine to create the distinct profile that makes buprenorphine/naloxone both safe and effective in the treatment of opioid use disorder.

1. **High affinity and slow dissociation.** Buprenorphine binds strongly to mu opioid receptors and dissociates slowly, preventing withdrawal symptoms for 24 hours and beyond. The high affinity for opioid receptors means that it is not displaced by other opioids. It blocks the activity of other opioids used concurrently, making the use of other opioids less rewarding and reinforcing.
2. **Partial opioid agonist.** Buprenorphine provides enough opioid agonist activity to prevent withdrawal symptoms and cravings, with less euphoria and sedation than full agonist opioids.
3. **Ceiling effect.** The ceiling effect means that doses beyond 24-32 mg do not have additional opioid effects. As a result, the risk of respiratory depression and overdose is substantially reduced relative to other opioids.

Naloxone is included in order to reduce the risk of diversion through injection. When injected, naloxone acts as an opioid antagonist, or blocker, which would create unpleasant and undesirable symptoms of opioid withdrawal in the user. Naloxone is not absorbed when taken sublingually or orally. Naloxone has no effect (positive or negative) on the activity of buprenorphine.

Drug Interactions

Buprenorphine is metabolized to norbuprenorphine via cytochrome 3A4. Lower doses should be considered for patients who are already taking cytochrome inhibitors such as azole antifungals, macrolide antibiotics, anti-retrovirals and protease inhibitors. Use caution when prescribing buprenorphine for patients taking benzodiazepines or other CNS depressants.

Contraindications

Contraindications for starting buprenorphine/naloxone include:

- patients with acute intoxication/impaired level of consciousness
- patients with severe respiratory compromise
- patients deemed medically or psychiatrically unstable

Precautions

Buprenorphine should be used with caution in the elderly, and patients with severe hepatic, renal or respiratory disease. Lower doses should be considered for concurrent use of CNS depressants such as benzodiazepines, sedatives and alcohol. Using buprenorphine with other sedating medications can increase the degree of sedation. Sudden discontinuation of buprenorphine will lead to opioid withdrawal symptoms.

Buprenorphine/naloxone products are not recommended in patients with severe hepatic impairment.

Elevations of liver enzymes have been observed in patients receiving buprenorphine. Liver enzymes should be measured prior to initiating treatment and periodically during treatment.

All opioids should be stored safely, away from children and others, and should never be shared.

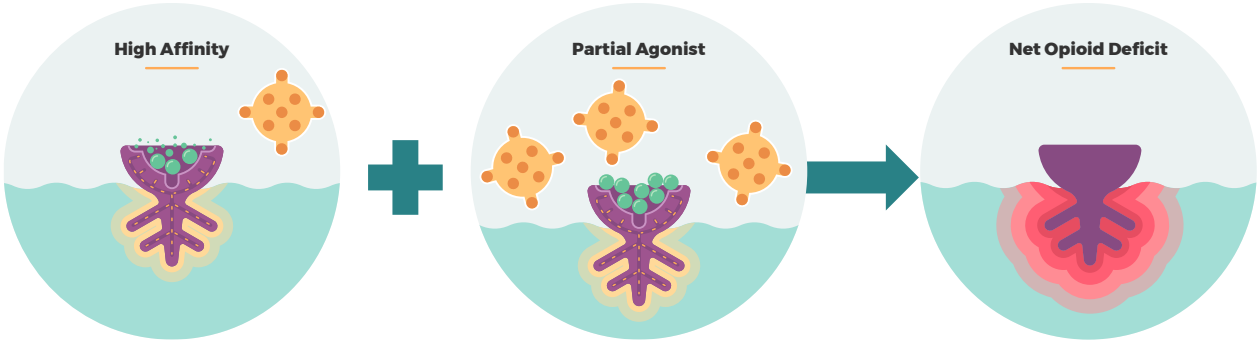
Pregnancy is not a contraindication to buprenorphine; consult with an experienced provider.

Side Effects

Side Effect	Cause	Management
Constipation	Dose-related	Fibre, fluid, stool softeners, polyethylene glycol
Taste perversion	Sensitivity to the taste of the medicine	Have liquids before dosing to increase saliva and speed absorption. Do not crush tablets
Headache	More common in migraine sufferers and early in treatment	Acetaminophen/ibuprofen, but most often no pharmacologic treatment is necessary
Nausea	Often related to taste/empty stomach	Have something to eat prior to dosing Moisten mouth to increase absorption
Sweating	Can be withdrawal symptom (decrease after dose) or side effect (constant)	Decrease or split dose Consider clonidine .1mg TID prn or oxybutynin 2.5-5mg BID if severe (aggravate dry mouth and constipation)
Sedation	Dose too high or using other sedating substances	Assess for polysubstance use and medication changes
Decreased libido	May be related to dopamine effect: increase prolactin, decrease testosterone	Monitor, assess hormone levels, psychosocial issues. Consider testosterone supplementation.

Precipitated Withdrawal

Precipitated Withdrawal – a state of acute and severe withdrawal symptoms brought on by initiating buprenorphine when a patient has other opioids in their system.



Displaces opioids still attached to receptors in the brain

Doesn't produce full opioid effect

Intense withdrawal symptoms

Precipitated withdrawal **only occurs with initiation** of buprenorphine. When a patient already has buprenorphine in their system, using additional opioids will not trigger withdrawal symptoms, and they do not need to abstain from opioids before each dose because the buprenorphine is already active on the receptor sites.

The best way to manage precipitated withdrawal is to prevent it: educate the patient to ensure that they abstain from opioids for long enough that they are in withdrawal, and use a Clinical Opiate Withdrawal Scale (COWS) to ensure a score of at least 12 before offering the first dose of buprenorphine.

Patients should be advised to discontinue opioid use 12-24 hours prior to the scheduled initiation.

Short-acting opioids	**12-16 hours**	**oxycodone, morphine, hydromorphone, heroin**
Intermediate-acting opioids	**18-24 hours**	**controlled-release (e.g. Contin) formulations**
Long-acting opioids	**Minimum 72 hours**	**fentanyl patches, methadone***

Note: *Transitioning patients from fentanyl patches or methadone to buprenorphine without expertise is not recommended because their ultra-long activity creates additional risks of precipitated withdrawal.*

Many patients do not need medication to manage their symptoms, but the following are options:

- Clonidine 0.1mg TID prn for sweats, restlessness and agitation
- Naproxen 225-500mg or ibuprofen 400-600mg q8h prn for myalgias
- Acetaminophen 1000mg q6h prn for arthralgias and myalgias
- Dimenhydrinate (Gravol) 50mg q 4-6h prn for nausea
- Loperamide (Imodium) 2-4mg prn for diarrhea

Avoid prescribing benzodiazepines for the treatment of withdrawal-related anxiety or insomnia.

Dosing Forms

Buprenorphine/naloxone 2/0.5mg SL tablet (ODB covered)

Buprenorphine/naloxone 8/2mg SL tablet (ODB covered)

Buprenorphine/naloxone 12/3mg and 16/4mg SL tablet (Brand name, not ODB covered)

Note: *Buprenorphine Extended-release injection (Sublocade) and extended-release subcutaneous implants (Probuphine) are both approved in Canada but are not currently covered by ODB or many insurance providers. They are intended for patients who have already been stabilized on sublingual buprenorphine and are not the focus of this guide.*

Not currently available in Canada:

Buprenorphine/naloxone Sublingual film: 2, 4, 8, 12 mg

Buprenorphine monoproduct (except through Health Canada)

Initiation and Dosing Guidelines for Buprenorphine/Naloxone

Baseline Assessment

History

DSM-5 confirmed diagnosis of opioid use disorder

Assessment of other substance use issues:

- Alcohol
- Benzodiazepines
- Illicit drugs
- Review concurrent medications

Physical examination

- BP
- Evidence of injection drug use, e.g. injection marks, cellulitis/abscesses
- Cardiovascular exam – signs of endocarditis
- Abdominal exam – signs of liver disease

Laboratory tests

- CBC, creatinine, electrolytes, liver enzymes, pregnancy test, HIV, Hepatitis A,B,C
- Urine drug test positive for opioids

Note: *an opioid positive test is not a prerequisite for opioid agonist therapy, e.g. an individual with a documented history of opioid use disorder who is currently abstinent but at high risk of relapse.*

Laboratory tests are part of a comprehensive assessment; they do not need to be done prior to initiating treatment if they will delay treatment (except a pregnancy test, which should be completed before starting treatment).

**If the patient has other substance use issues, is injecting, or is on long-acting opioids like methadone or fentanyl patches, refer to an addiction expert/clinic.*

Considerations Prior to Starting Buprenorphine-Naloxone

Patients should receive counselling about the goals and expectations of buprenorphine treatment and be able to consent to treatment. A sample treatment agreement can be found in the Resources, R-8. Patients induced on buprenorphine/naloxone in the ED or inpatient settings are not expected to sign a treatment agreement.

- Patients should understand they will need daily dispensing at the beginning of treatment.
- Patients starting treatment in ED/inpatient settings should have a clinic/provider available to provide follow-up care.
- Identify the pharmacy to be used as an outpatient: confirm that they stock buprenorphine/naloxone.
- Patient should have valid identification in order to pick up their prescription.
- Patient should have a valid Health Card in order to be seen at most clinics.
- For planned office starts, remind patients to take their last opioid dose the day before their appointment, so they are in withdrawal with 12+ hours abstinence when they attend the clinic.

Office-Based Buprenorphine Initiation

Day 1

Plan initiation for a weekday morning, allowing for reassessment later the same day.

Consider whether the pharmacy to be used is easily accessible from your office or whether you will prescribe 6 x 2mg buprenorphine/naloxone tablets for the patient to bring with them.

Confirm the patient's intention to start buprenorphine/naloxone, review questions, risks/benefits.

Ask when the patient last used opioids, which, how much and how (what route).

Administer the Clinical Opioid Withdrawal Scale (COWS) (see Resources, R-2)

COWS < 12 – postpone the first dose of buprenorphine until the patient is in sufficient withdrawal

COWS > 12 – (and no methadone or fentanyl patch) -> proceed with first dose

First dose: 4mg (2 x 2mg) SL – if patient is elderly, using benzodiazepines, or low-dose opioids or fentanyl, give buprenorphine 2mg.

Instruct the patient to keep the tablet under the tongue until it fully dissolves and to avoid eating, drinking, or swallowing during this time.

Witnessed ingestion of the first dose is recommended.

Reassess between 1-2 hours

If still feeling withdrawal symptoms give another 2-4mg; patient may be sent home with additional 2 x 2mg tablets to use later as needed.

If no further withdrawal or concern, patient may go home with an additional 2-4 x 2mg tablets to use later as needed.

Usual maximum for Day 1 is 12mg (6 x 2mg tablets).

Write prescription for estimated daily dose (usually 8-12mg) until next visit, typically as daily dispensed.

Follow-up Assessments

Patients should be reassessed within the week of initiation (ideally Day 2-5), then weekly thereafter.

At each visit, the following questions should be reviewed:

☑ How long did the dose last?

☑ What time did it wear off?

☑ What were the specific withdrawal symptoms?

☑ Did they use additional opioids?

☑ Was there any sedation? Any side effects?

If withdrawal symptoms were present, give previous dose + additional 2-4mg.

If opioid use continues, try a dose increase even if the patient does not report withdrawal symptoms.

If no withdrawal symptoms, continue previous day's dose.

If patient reports sedation, decrease by 2mg.

Day 2: Usual maximum dose is 16mg.

Day 3-4: Usual maximum dose is 20mg.

Review same questions.

At each assessment, write Rx until the next visit for the appropriate quantity of tablets.

Doses are typically dispensed daily at the pharmacy.

Home Buprenorphine Initiation

Criteria

☑ No other active substance use issues.

☑ Stable home environment and ability to store medication safely.

☑ Support and monitoring at home.

☑ Able to understand instructions.

☑ Access to MD/NP/RN for questions and support.

May Be Appropriate For:

Patients who have previous experience with buprenorphine treatment.

Barriers to office attendance (e.g. work, childcare).

Patients who are not in sufficient withdrawal for office-based initiation despite planning.

Logistical challenges to office-based initiation.

Patient Preparation

Review SOWS Scoring sheet and "Starting Buprenorphine/Naloxone' patient instruction handout (see Resources R-1 and R 5-6).

Review risks of precipitated withdrawal, and pick up Rx for Day 1: 6 x 2mg buprenorphine/naloxone tablets.

Decide whether you will pre-write prescriptions for Days 2-3 or how to be in touch with the patient.

Patient Instructions

Day 1

Advise the patient to wait until SOWS >17 or more than 5 symptoms on the "Starting Buprenorphine/Naloxone" instruction handout. If in doubt, wait another 1-2 hours before taking first dose.

When withdrawal is at least moderate, take 4mg (2 x 2mg tablets) and let them fully dissolve under the tongue. 2mg (1 tablet) is recommended for illicit opioid users because of the likelihood of fentanyl/carfentanyl exposure.

Wait for two hours. Take an additional 2mg (1 tablet) every 2 hours until withdrawal symptoms are relieved as long as there is no feeling of sedation to a maximum of 6 tablets.

Maximum dose 12mg.

Day 2

Take the previous day's dose as a single morning dose; wait 2 hours.

If withdrawal symptoms are at least moderate, take an additional 2-4mg.

Maximum dose: 16mg

Dispense Rx in 2mg tablets with instructions in mg and number of tablets; typically dispense 1 day of medication at a time for initiation.

Day 3

Reassess in person.

Microdosing

An alternative approach to buprenorphine initiation uses a protocol called the Bernese Method[1] or "microdosing" to avoid precipitating withdrawal in patients still on opioids. While not currently the standard approach, this method may be helpful in patients transitioning from long-acting opioids, and those who fear or cannot tolerate withdrawal. Speak with an addictions colleague for further information.

1.. Hämmig R, Kemter A, Strasser J, et al. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. Substance Abuse and Rehabilitation. 2016;7:99-105. doi:10.2147/SAR.S109919. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4959756/

Managing Buprenorphine Prescriptions/Maintenance Phase

Assessments

Initially every 1-2 weeks, then every 2-4 weeks with option of decreasing visits as stability increases.

Visits for stable patients are typically monthly.

Very stable patients (i.e. no illicit substance use for one year or more, full carries for one year or more, stable employment and psychosocial situations) can be seen every 6-8 weeks.

At each visit ask about:

- ☑ Withdrawal symptoms, thoughts, urges and cravings
- ☑ Substance use (opioids, illicit drugs, alcohol and cannabis)
- ☑ Sedation and side effects
- ☑ Mood and functioning; review medications, any new symptoms or deterioration in mental health, new psychiatric diagnosis, mental health support
- ☑ Psychosocial update; work, family life, finances
- ☑ Health issues; chronic medical conditions e.g. Hepatitis C, new medical conditions, timing for routine screening
- ☑ Goals
- ☑ Review urine drug screen results

Dose Adjustments

Indications for Dose Increase

- Patient complains of withdrawal symptoms less than 24 hrs post-dose, based on classic symptoms (e.g. sweats, chills, myalgias, restless legs, poor sleep, upset stomach).
- Withdrawal symptoms are triggering opioid use or strong cravings.
- No sedation at current dose.
- No other explanation for symptoms (e.g. new medical conditions/medications).
- Small dose increase of 2-4 mg can be tried with follow-up to re-assess.

Indications for Dose Decrease/Tapering

- Sedation or side effects at current dose.
- Patient wants to taper.
- At least 6 months without illicit substance use.
- Socially stable, with supports, stable mental health and coping strategies.
- Minimal contact with those using drugs on an ongoing basis.

Tapering Protocol

- Decrease by small amounts at a time (e.g. 2mg when the dose is over 4mg, 1mg when the dose is 4mg or less).
- Leave at least 2 weeks between dose decreases.
- Hold the taper if the patient is having withdrawal symptoms triggering thoughts or urges for opioids.
- Increase the dose slightly if the patient begins using opioids again, even in very small amounts.
- Encourage participation in counseling, supportive environments and self-care.
- Some patients do well with alternate day dosing: e.g. take “double dose” every other day, as long as total dose does not exceed 24mg on any one day. Can be helpful for those without carries and those tapering at lower doses.

Missed Doses

Missed doses can contribute to a loss of tolerance to buprenorphine. Dose adjustment and re-stabilization may be necessary if the patient has missed 6 or more consecutive daily doses depending on the patient's dose.

- For missed doses less than 6 days, resume the previous dose.
- For missed doses equal to or more than 6 days, consider:

Dose	Number of Missed Days	Suggested Dose Adjustment
2-6mg	6 or more days	No change
8-12mg	6 or more days	Restart at 6-8mg
> 12mg	6 or more days	Restart at 8mg

Patients who still have buprenorphine in their urine drug screen do not need a new initiation with withdrawal in order to avoid precipitated withdrawal.

Patients who have missed multiple doses, relapsed to full opioid agonist use and no longer have buprenorphine in their systems require a new initiation.

Take-Home Doses

Being able to take buprenorphine at home like a typical medication, as opposed to observed daily dosing at a pharmacy, reduces stigma, cost, and barriers associated with treatment. Take-home dosing may be initiated and increased when a patient is deemed clinically stable and able to safely store medication at home.

Consider observed dosing for patients with:

- Ongoing substance use (including alcohol and benzodiazepines)
- Homelessness or inability to safely store medication
- Evidence of medication diversion
- Erratic appointment attendance
- Severe behavioural issues, unstable mental health or cognitive issues

Patients with these issues may be motivated to stop their substance use in order to get take-home doses. Explain that take-home doses will be given when they are on a stable dose, are not using substances in problematic ways, and can store and manage medication safely.

Suggested approach: no take-home doses for at least 1 month, then increase by 1 take-home dose/week every 2-4 weeks as long as patient is stable, corroborated by urine drug screen.

There is some evidence that more rapid transition to take-home dosing can improve treatment adherence and retention *(A Guideline for the Clinical Management of Opioid Use Disorder, British Columbia Centre on Substance Use and B.C. Ministry of Health, Published June 5, 2017).*

Writing Prescriptions for Buprenorphine/Naloxone

Prescriptions should specify the dose, start and stop dates, pharmacy location, and observed vs. take-home doses. For security, many providers choose to fax prescriptions for opioids directly to the pharmacy rather than having the patient take it themselves.

Dose

The most common tablet strengths are buprenorphine 2mg/naloxone 0.5mg or buprenorphine 8mg/naloxone 2mg

The prescription should specify the buprenorphine dose in mg, e.g. 4mg (2 x 2mg tablets), 6mg (3 x 2mg tablets), 16mg (2 x 8mg tablets), etc.

Start and Stop Dates

Buprenorphine prescriptions should have a clear start and stop date so that prescriptions do not overlap.

The patient should have an appointment booked to coincide with the end of the prescription period.

The total quantity that the prescription refers to should be clearly identified in order to avoid confusion between the number of doses and the number of tablets. In general, it is easier to identify the number of doses, since each dose may be multiple tablets.

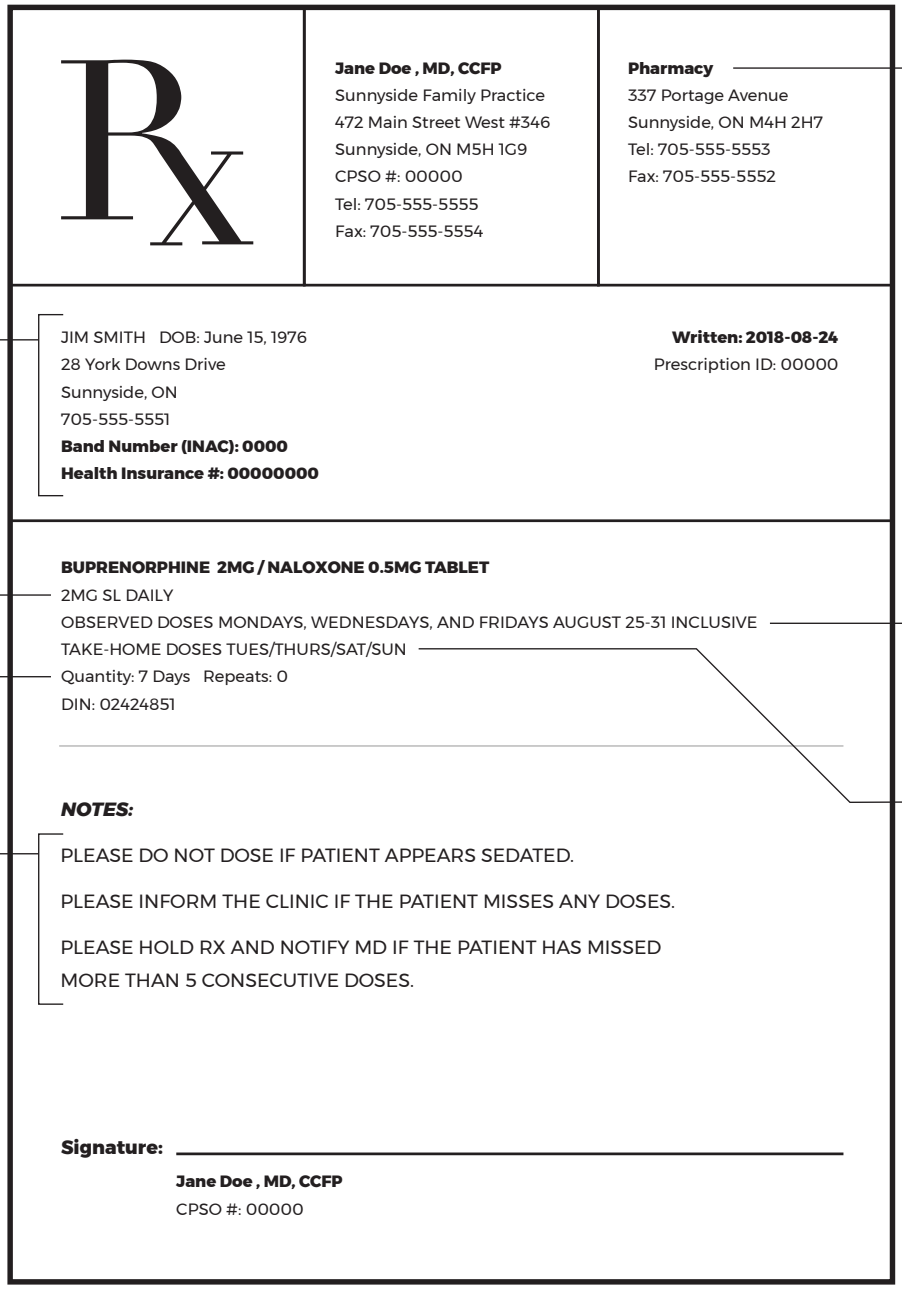
Observed vs. Take-Home Doses

- Each prescription should specify where the patient is dosing.
- For patients early in treatment, all doses may be observed at the pharmacy.
- For patients with take-home doses, specify the days that they dose at the pharmacy and the days for which they have 'carries', e.g.
    - "Observed doses Mondays, Wednesdays and Fridays,
    - Take-home doses Tues/Thurs/Sat/Sun"
- Unless specifically stated otherwise, the pharmacy will expect a patient who picks up medication weekly to take one dose as an observed dose.
- Patients with 6 carries typically pick up medication on a set day of the week. Providers may want to add a note that patients may change the pick-up day to accommodate work/stat days.
- For patients who are extremely stable and pick up medication monthly or less, the prescription should state that they are not required to have a dose observed.
- Many providers add a footnote to the prescription, such as:
    - "Please do not dose if patient appears sedated.
    - Please inform the clinic if the patient misses any doses.
    - Please hold Rx and notify MD if the patient has missed more than 5 consecutive doses."

Buprenorphine and Acute Pain

Buprenorphine should not be stopped for perioperative pain management or the management of other types of acute pain. When opioids are indicated, patients on buprenorphine sometimes need higher doses of opioids for analgesia than opioid-naïve patients because of their baseline opioid receptor saturation. Buprenorphine doses can also be increased temporarily for acute pain. Stopping buprenorphine means that the patient would have to go through at least a brief period of withdrawal again in order to restart the buprenorphine without triggering precipitated withdrawal.

Prescription Pad Example



Patient Information
Including date of birth, health card number and Band number (INAC) if applicable

Buprenorphine Dose

Total Quantity
Specified as doses, tablets or days

Notes
It is recommended that these additional notes be included on all prescriptions

Pharmacy
Information including address and fax number

Dates Valid
Specifies start and end dates (inclusive)

Observed/ Take-Home Doses
Specifies days of the week for observed and take-home doses

Urine Drug Testing

Urine drug testing helps to:

- Assess adherence to medication
- Verify the patient's self-report
- Detect other drugs that may affect safety (e.g. benzodiazepines, alcohol)

Frequency:

- During or just prior to each appointment
- Typically, weekly during initiation/titration
- Monthly once stable (minimum 4 times/year for stable clients)
- Some programs require patients to leave samples between visits

Frequency should be **determined by clinical judgement** and the **purpose** of the information rather than a fixed schedule.

Point-of-Care Tests	***Lab-Based Testing***
Real-time information that can be reviewed with the patient at the same visit	Results available after the visit
Not always accurate: false positives (especially for benzodiazepines) and false negatives (poor sensitivity for certain synthetic opioids such as hydromorphone)	More specific regarding opioids and opioid metabolites
Do not assess alcohol	Can also see substances that do not show up on point-of-care testing, e.g. alcohol (depending on the timing of ingestion), THC, and other psychotropic medications
Different panels are available: typical components include methadone, buprenorphine, morphine, oxycodone, fentanyl, methamphetamines, cocaine, and benzodiazepines	Results depend on request: Target Drug Testing: Assesses and reports only the specific drug or group of drugs requested Drugs of Abuse Screen: Typically includes opioids, benzodiazepines, methadone metabolite, cocaine metabolite, oxycodone and amphetamines Broad Spectrum Toxicology: The lab will provide a list of the drugs they test for, which includes antihistamines, opioids, sedative/hypnotics, opioid agonists, anti- depressants, anticonvulsants, stimulants

'Expected' results:

For a patient on buprenorphine/naloxone, expected UDS results could be:

- Buprenorphine + norbuprenorphine (a metabolite) + naloxone OR
- Buprenorphine + norbuprenorphine (no naloxone) OR
- norbuprenorphine only

'Unexpected' results:

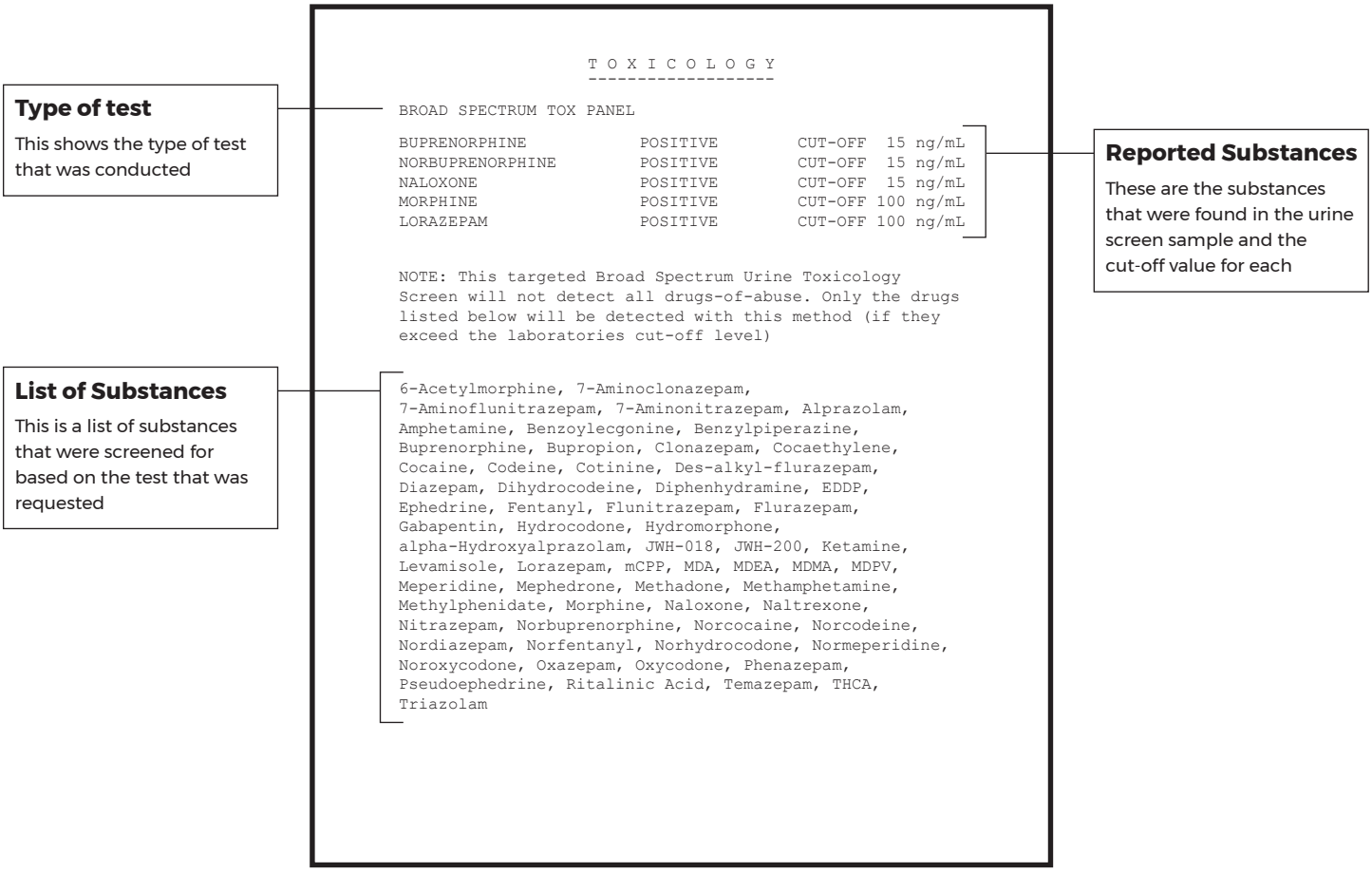
UDS results can include unexpected prescription medications and/or illicit substances. This should prompt questions about what they have been taking and why. For example:

- Are they supplementing their dose because it is wearing off early? Is this a slip or a relapse?
- Did they receive a prescription for an opioid?
- Are they taking non-prescription acetaminophen with codeine without considering it an opiate?
- Is illicit substance use a one-time occurrence, or part of a larger issue?

Urine drug screens are one tool in assessing stability to plan take-home doses. The number of take-home doses can be kept the same for an isolated slip or decreased by one for each abnormal urine drug screen. Patients then rebuild carries as their urine drug screen results demonstrate restabilization.

One more important point: avoid the language of 'clean' and 'dirty' with respect to urine samples.

Urine Drug Screen Example



The Buprenorphine Reference Guide (Guide) was developed as part of the Opioids Clinical Primer Program led by the University of Toronto in collaboration with McMaster University. Clinical leadership for the development of the reference guide was provided by Dr. Jennifer Wyman, Dr. Meldon Kahan and Dr. Anthony Levinson and was subject to external review by health care providers and other relevant stakeholders. McMaster University's Division of e-Learning Innovation (DeLI) led the instructional design and development. The Guide was funded by the Government of Ontario as part of a suite of programs collectively described as Ontario Pain Management Resources: a partnership to help clinicians support their patients.

Subjective Opiate Withdrawal Scale (SOWS)

Patient Instructions: Circle the number that best fits how you feel right now, for each of the items below. Then add your scores to calculate your total score.

Item	Symptom	Not at all	A litlle	Moderately	Quite a bit	Extremely
1	I feel anxious.	0	1	2	3	4
2	I feel like yawning.	0	1	2	3	4
3	I am perspiring.	0	1	2	3	4
4	My eyes are teary.	0	1	2	3	4
5	My nose is running.	0	1	2	3	4
6	I have goosebumps.	0	1	2	3	4
7	I am shaking.	0	1	2	3	4
8	I have hot flashes.	0	1	2	3	4
9	I have cold flashes.	0	1	2	3	4
10	My bones and muscles ache.	0	1	2	3	4
11	I feel restless.	0	1	2	3	4
12	I feel nauseous.	0	1	2	3	4
13	I feel like vomiting.	0	1	2	3	4
14	My muscles twitch.	0	1	2	3	4
15	I have stomach cramps.	0	1	2	3	4
16	I feel like using now.	0	1	2	3	4

Total Score: _____

Referecnce:

Adapted from Handelsman L, Cochrane KJ, Aronson MJ, Ness R, Rubinstein KJ, Kanof PD. Two New Rating Scales for Opiate Withdrawal. 1987. American Journal of Alcohol Abuse 13, 293-308.

Clinical Opioid Withdrawal Scale (COWS)

Interval	0	30 min	2 hrs	4 hrs
Date: DD/MM/YYYY **Time**				
	Score	**Score**	**Score**	**Score**
Resting Heart Rate (measure after lying or sitting for 1 minute): **0** HR 80 or below **1** HR 81-100 **2** HR 101-120 **4** HR greater than 120				
Sweating (preceding 30 minutes 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 possibly larger than normal for room light **2** pupils moderately dilated **5** pupils so dilated that only the rim of the iris is visible				
Bone or joint aches (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 three or more 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**	**Total**	**Total**	**Total**
	Initials	**Initials**	**Initials**	**Initials**

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs, 35(2), 253-9.

Buprenorphine/Naloxone Treatment:

What to Know and Expect

The Day Before

You will need to stop all opioids at least 12-24 hours before starting buprenorphine.

Opioids include oxycodone (Percocet, Oxys), morphine, hydromorphone (Dilaudid) and codeine (including Tylenol #1 or cough syrup with codeine/hydrocodone).

We need you to be in withdrawal before you start buprenorphine in order to avoid what is called "Precipitated Withdrawal" (which is like the worst flu of your life).

To help with withdrawal symptoms, you may take:

- **Clonidine** 0.1mg every 8 hours (by prescription) – many people do not need this
- **Ibuprofen (Advil)** up to 600 mg every 8 hours
- **Acetaminophen (Tylenol)** up to 1000mg (2 Extra Strength) every 6 hours
- **Dimenhydrinate (Gravol)** 50mg every 6 hours
- Walking, resting, hot baths or showers (but not right after taking clonidine) can all help.

Day 1

You should not drive the day of the initiation. Please make other arrangements for getting to and from the clinic. When you come to the clinic you will be assessed to make sure you are in enough withdrawal to start buprenorphine. You will then go to the pharmacy to pick up your medication. The dose of buprenorphine will be observed by either the pharmacist or the doctor.

Expect that you will be in the clinic for 2-3 hours. Bring something to do: a book, music, knitting, etc. After the first dose you may wait in the waiting room or you may leave the clinic. You will be seen again by the doctor one hour after your first dose to see how you are feeling and whether you need more medication. After 1 hour, if the medication is effective and all is well, you are free to go home. You will have an extra dose of medication with you in case your withdrawal symptoms come back later in the day.

Reminders

You should not have any alcohol or take any other sedating medications while starting buprenorphine. This includes sleeping pills, dimenhydrinate (Gravol), and diphenhydramine (Benadryl). If you regularly take sleeping pills by prescription, discuss this with your doctor.

You should not take any other opioids while starting buprenorphine.

Day 2-3

Your doctor will tell you when you need to come back to the clinic. You will need one more appointment to assess your dose during the first week.

Your prescription will be sent to your community pharmacy.

You can expect to feel well and close to the right dose by the end of one week of treatment. The right dose is the dose at which you feel 'normal'; no withdrawal symptoms for 24 hours, not sleepy or dozy, and not high or buzzed.

When your withdrawal symptoms are managed, your cravings will improve and it will be easier to stick to your plan of not using extra opioids or other substances.

Maintenance and Beyond

For the first month or so you can expect to see the doctor every week.

After that, your visits will drop to every two weeks and eventually to once a month.

A urine drug test will be required at every visit.

While you are stabilizing, you will take your buprenorphine at the pharmacy every day.

Once you are stable (not using other opioids or other drugs of abuse), you may start to pick up your medication to take at home. Take-home doses (also called 'carries') will be discussed with your doctor and increased gradually.

Remember that buprenorphine is just one part of your recovery from substance use.

Seeing a counselor, attending meetings, and finding other supports are all helpful to understand how you developed an addiction and how to establish healthier patterns going forward. Your doctor can help to look at important issues like pain, depression and anxiety, and link you to appropriate resources.

Buprenorphine can be taken for months or years - as long as it is needed to prevent relapse. If you are stable in recovery and want to stop taking buprenorphine, it should be tapered gradually, with planning with your care team.

Warnings

While taking buprenorphine you should not take other medications without consulting your doctor first.

While taking this medication you should not use illegal drugs, drink alcohol, or take sedatives, tranquilizers, or other drugs that slow breathing. Taking any of these substances in large amounts along with buprenorphine can lead to overdose.

Buprenorphine kept at home must be locked in a safe place to prevent accidental use by others, especially children.

Starting Buprenorphine/Naloxone

When am I ready to start buprenorphine/naloxone?

1. You have NOT taken an opioid in the last 12 hours. Starting earlier could make you sick. If you have taken methadone or fentanyl, do NOT start buprenorphine/naloxone following these instructions, discuss with your nurse/MD.
2. You are experiencing at least 5 symptoms of withdrawal (use the list of symptoms below).

Withdrawal Symptoms:

- ☐ Sweating
- ☐ Bone or joint aches
- ☐ Vomiting/diarrhea
- ☐ Stomach cramps
- ☐ Restlessness
- ☐ Runny nose or tearing
- ☐ Yawning more often
- ☐ Goose bumps
- ☐ Muscle twitching
- ☐ Irritable

How do I take buprenorphine/naloxone?

1. Before taking buprenorphine/naloxone, drink some water.
2. Put buprenorphine/naloxone under your tongue.
3. Don't eat or drink anything until the buprenorphine/naloxone has dissolved completely, this can take 7-10 minutes.
4. DO NOT SWALLOW the buprenorphine/naloxone as it will not work very well if swallowed. It gets into your body by dissolving under your tongue.

Do not use buprenorphine/naloxone with benzodiazepines, alcohol, methadone or other opioids.

Reminder

It is important that you see your health care provider or visit a Rapid Access Addiction Medicine (RAAM) Clinic within a few days of starting buprenorphine/naloxone to report how you are feeling and have your dose assessed.

If you develop worsening symptoms after taking buprenorphine/naloxone

or before seeing your health care provider, go to the emergency department.

What is my buprenorphine/naloxone treatment plan?

DAY 1

1. If it has been at least 12 hours since you took your last opioid AND you are experiencing 5 withdrawal symptoms, then you are ready to start.
2. Your first dose of buprenorphine/naloxone will be _____ **mg (**_____ **tablets).** Place this dose under your tongue.
3. You should start feeling better within 30-45 minutes. If you are still experiencing withdrawal symptoms after two hours, take another _____ **mg (**_____ **tablets).**
4. If you are still not feeling well and experiencing withdrawal symptoms, you can take _____ **mg (**_____ **tablets)** every 2 hours until you feel more comfortable.
5. On Day 1 do NOT take more than: **8mg** **12mg** **16mg**
6. Record your dose and time of dose in the table provided below.

DO NOT DRIVE ON DAY 1

DAYS 2 and 3

1. Take the same total dose you took the first day all at once.
2. If you feel that you are still in withdrawal, you can adjust your daily dose upwards by 2mg or 4mg (1 or 2 tablets).
3. If you feel overly sleepy, reduce your dose by 2mg or 4mg (1 or 2 tablets).

Treatment Record Log

Day	Time of Dose	Dose
	am/pm	mg
	am/pm	mg
	am/pm	mg
	am/pm	mg
	am/pm	mg
	am/pm	mg
	am/pm	mg

FOLLOW UP:

Date: _____ **Time:** _____

Clinic Address: _____ **Phone:** _____

Buprenorphine Initiation

Quick Reference Guide

machealth

Office-Based

Preparation — **Patient education; withdrawal management; prescription**

- ☐ **Review the need to stop opioids 12+ hours prior** to planned initiation to ensure moderate withdrawal.
- ☐ Consider medication to assist with **withdrawal** symptoms:
  - Rx: Clonidine 0.1mg TID for sweats, restlessness, agitation
  - OTC: Ibuprofen or naproxen, acetaminophen, dimenhydrinate, loperamide
- ☐ **Write Rx** for 6x2mg buprenorphine/naloxone tablets; specify date and pharmacy.

Day 1 — **COWS; initiation; reassessments; and titration**

- ☐ **COWS score <12: postpone the first dose** until the patient is in sufficient withdrawal. May continue as office initiation or move to home initiation if appropriate (see beside ➞).
- ☐ **COWS >12 AND more than 12 hours from last opioid use -> initiate** first dose.
  - Buprenorphine/naloxone 4mg SL (2x2mg tablets)
  - Consider 2mg for elderly or those on BZDs
- ☐ **Reassess 1-2 hours:**
  - COWS >12 or ongoing discomfort give an additional 2-4mg SL.
- ☐ After reassessment, patient may take remainder of Day 1 dose home to **maximum 12mg.**
- ☐ **Provide Rx for daily dispensed dose** until next assessment (Day 2-4) with patient instructions:
  - If withdrawal symptoms were present, take previous day's dose + additional 2-4mg.
  - If no withdrawal symptoms, continue previous day's dose.

Day 2 — Usual maximum dose is 16mg.

Day 3-4 — Usual maximum dose is 20mg. Reassess in person by Day 5.

Home-Based

Criteria

- ☐ No other active substance use issues.
- ☐ Stable home environment; able to store medication safely, support and monitoring at home.
- ☐ Able to understand instructions.
- ☐ Access to medical/nursing support.
- ☐ May be appropriate for:
  - Patients who have previous experience with buprenorphine treatment/restarting.
  - Barriers to office attendance/Insufficient

Preparation — **Patient education; prescriptions**

- ☐ **Review** SOWS and Starting Buprenorphine/Naloxone patient instruction sheet
- ☐ **Write Rx** for Day 1 (6x2mg tablets) and Day 2 (8x2mg tablets), daily dispensed.

Day 1 — **COWS; initiation; and titration**

- ☐ **When SOWS > 17 and more than 5 symptoms on the patient instruction sheet** (moderate withdrawal) take 4mg (2x2mg) tablets SL; if in doubt, wait another 1-2 hours.
- ☐ Take another **2mg every 2-4 hours** until withdrawal symptoms controlled.
- ☐ Hold dose if any **sedation.**
- ☐ **Maximum dose 12mg.**

Day 2

- ☐ Take the **previous day's dose** as a single morning dose; wait 2 hours.
- ☐ If withdrawal symptoms are at least moderate, take an additional 2-4mg.
- ☐ **Maximum dose 16mg.**

Day 3

- ☐ Reassess in person.

Patient Agreement for Buprenorphine/Naloxone Treatment

Acknowledgements

I acknowledge that:

1. Buprenorphine is an opioid and its use will result in the development of physical dependence to this medication. A sudden decrease in dose or abrupt discontinuation of this medication will likely lead to symptoms of opioid withdrawal.
2. Taking mood-altering substances with buprenorphine can be potentially dangerous. There have been adverse events including reported deaths associated with the combination of buprenorphine with alcohol, opioids, cocaine, and sedatives.
3. It is important that I inform any prescribing physician (including surgeons and anaesthetists), nurse practitioner, or dentist that I am receiving buprenorphine, so my treatment can be tailored to prevent potentially dangerous interactions with buprenorphine.
4. It may be unsafe for me to drive a car, other vehicle, or operate machinery during the stabilization period (initial start of taking buprenorphine) and/or dose adjustments.
5. The common side effects of buprenorphine are sweating, constipation, decreased sexual function, drowsiness, weight gain, and water retention. These symptoms are usually mild and can be lessened with the assistance of my doctor. There are no known serious long-term effects from taking buprenorphine. Many of these side effects will subside in time.
6. Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of opioids during pregnancy. I will advise my physician if I become pregnant so that my care can be optimized. It is my responsibility to make and keep all appointments at the clinic and make sure that my buprenorphine prescription does not run out.
7. Buprenorphine treatment will be stopped if my doctor determines that it has become medically unsuitable (for example, if treatment is not effective or if I develop a medical condition that could be made worse by taking buprenorphine).
8. I agree to provide a urine sample when requested.
9. I understand that the pharmacy may not give me a dose of medication if I appear to be intoxicated or under the influence of some other substance. If this occurs, I may be asked to seek medical attention.

Prescriptions for "Carries" (take-home doses) medication:

1. I understand that I will take my buprenorphine dose daily at the pharmacy until my prescriber determines that I am ready for take-home doses. I understand that the number of take-home doses I receive will be increased gradually based on my stability, in discussion with my prescriber.
2. **Buprenorphine is a potent medication. A single dose taken by a patient who is not tolerant to opioids can be fatal, especially if taken by a child.** I agree to store my medication safely out of sight and out of reach of children and others.
3. I agree not to share my buprenorphine with anyone else under any circumstances.

My signature below indicates that I agree to follow the obligations and responsibilities outlined in this agreement. Should I fail to meet my responsibilities as a participant in this agreement, I understand that I may be asked to leave the buprenorphine/naloxone treatment program.

I have had the opportunity to discuss and review this agreement with my doctor and/or IHP and my questions have been answered to my satisfaction.

Dated (dd/mm/yyyy)

Patient (Print Name) | **Witness (Print Name)**

Patient (Signature) | **Witness (Signature)**

Emergency Department Buprenorphine/Naloxone Order Set Template

For patients not ready for an Emergency Department start because of recent opioid use (e.g. post-overdose) consider discharging with instructions and a prescription for a "home start".

Time of last opioid: _____ **Opioid used:** _____ **Route:** _____

Vitals/Monitoring:

- ☐ Clinical Opioid Withdrawal Scale (COWS) score q1h while awake (document on COWS flowsheet)
- ☐ If COWS ≤5 on two consecutive occasions discontinue COWS monitoring
- ☐ T, HR, RR, BP, SpO_2, Level of Consciousness as per Vital Signs Patient Care Standard

Lab Investigations

- ☐ Urine Toxicology
- ☐ Point of Care Urine Drug Screen (if available)
- ☐ Urine hCG
- ☐ Additional Labs: (e.g. CBC, ALT, ALP, BILI, Hep B, Hep C, HIV)
- ☐ EKG- 12 lead

Medications

- ☐ Buprenorphine/naloxone 4 mg SL for COWS score > 12 **AND** 12 hours since last opioid
- ☐ Buprenorphine/naloxone 2 mg SL **if elderly, on benzodiazepines, fentanyl use, or unsure of last opioid**
- ☐ Directly observe patient until each buprenorphine/naloxone tablet is dissolved; up to 10 minutes
- ☐ Repeat same dose of buprenorphine/naloxone SL q1h PRN if the patient's COWS score is > 8 **AND** NOT drowsy, to maximum of 12 mg buprenorphine in first 24 hours
- ☐ Notify MRP if COWS score **increases** by 2 or more after first dose
- ☐ Notify MRP if COWS still > 8 after 12 mg of buprenorphine/naloxone
- ☐ Dimenhydrinate 25 -50 mg PO/IM/IV q4h PRN
- ☐ Ondansetron 4-8 mg PO/IM/IV q6h PRN for nausea
- ☐ Ibuprofen 400 mg PO q6h PRN for pain
- ☐ Acetaminophen 500 mg 1-2 tablets q4h PRN for pain
- ☐ Loperamide 2mg 2 tablets at once, then 1 tablet q2h prn

Discharge Planning

- ☐ Advise patient that withdrawal symptoms may return and dose adjustments may be required
- ☐ Provide take-home naloxone kit and provide education
- ☐ Confirm follow-up plans/provide appropriate contact numbers
- ☐ Fax prescription for buprenorphine/naloxone to community pharmacy **(daily observed dosing with specified dates until anticipated appointment date)**

Adapted with permission from Lakeridge Health.

Inpatient Buprenorphine/Naloxone Order Set Template

These orders apply to patients on short-acting opioids during their admission.

For patients on intermediate-acting opioids (i.e. SR,CR formulations), convert to short-acting opioids at least 24 hours prior to initiating buprenorphine.

For patients who may have been using street fentanyl, maintain short-acting opioids for at least 48 hours and start buprenorphine at lower doses to avoid precipitated withdrawal.

For patients on long-acting opioids (e.g. methadone, fentanyl patches) consult a colleague with expertise in the management of buprenorphine.

Opioid Withdrawal Management

- ☐ Discontinue short-acting opioids at midnight if administered SC, oral doses at 18:00
- ☐ Start clonidine 0.1mg po q8h (as long as SBP>100)
- ☐ Dimenhydrinate 25-50mg PO/IM/IV q4h PRN
- ☐ Ondansetron 4-8mg PO/IM/IV q6h PRN
- ☐ Ibuprofen 400mg PO q6-8h PRN for pain
- ☐ Acetaminophen 500mg 1-2 tablets q4h PRN for pain
- ☐ Loperamide 2mg 2 tablets at once, then 1 tablet q2h prn

Initiating Buprenorphine/Naloxone

- ☐ Start Clinical Opioid Withdrawal Scale (COWS) scores at 08:00 and repeat q1h while awake until COWS score >12 [document on COWS flowsheet]
- ☐ Buprenorphine/naloxone 4mg SL for COWS score > 12 (consider 1-2mg test dose for patients who have been using fentanyl)
- ☐ Directly observe patient until each buprenorphine/naloxone tablet is dissolved (up to 10 minutes)
- ☐ Reassess with COWS score in 1 hour after initial dose; give additional 4mg buprenorphine/naloxone SL if COWS > 8. Thereafter reassess with COWS score q 2 hours.
- ☐ Give additional 2-4mg buprenorphine/naloxone SL q2h if COWS > 8 and patient not drowsy to maximum 16mg in first 24 hours
- ☐ If COWS score **increases** by 2 or more after first dose notify MRP, do not give additional buprenorphine until further assessment for precipitated withdrawal
- ☐ If COWS score still > 8 after 16mg of buprenorphine/naloxone notify MRP
- ☐ If COWS is not 12 by noon consider whether the patient has been using additional opioids; reassess readiness for buprenorphine start, consider retrying next day

Discharge Planning

- ☐ Provide take-home naloxone kit and provide education
- ☐ Confirm follow-up plans/provide appropriate contact numbers
- ☐ Fax prescription for buprenorphine/naloxone to community pharmacy **(daily observed dosing with specified dates until anticipated appointment date)**

Adapted with permission from Lakeridge Health.

Letter of Understanding for Peripherally Inserted Central Catheter (PICC)

Letter of Understanding

_____ is committed to partnering with patients to deliver high quality patient-centred care that is safe and is in the best interest of the patient. There are significant risks associated with a peripherally inserted central catheter (PICC) when used for purposes other than to deliver medications prescribed by your physician.

I understand that I have the following responsibilities:

- I will not tamper with my PICC or use my PICC for any purpose other than to deliver medications prescribed by my physician. Doing so could result in serious illness and possibly death.
- I will disclose any drug use to my health care team so they can assess the safest treatment plan for me.
- I will come to an agreement with staff as to when/for how long I can leave the unit and/or hospital property and I will let them know when I leave/return. I understand that I may be discharged and my PICC removed if I leave without notifying staff and/or do not return at the agreed upon time.

I understand that my health care team has the following responsibilities:

- My health care team will continuously monitor my treatment and assess any risks to my safety.
- If it is felt that continuing this treatment poses significant risks to my health, my health care team may remove my PICC and explore a different treatment.

I've discussed the risks associated with misuse of my PICC with my physician and understand that the hospital cannot be held responsible for any adverse outcomes experienced as a result of tampering with/using my PICC to inject substances.

Patient signature: _____ **Date:** _____

Physician signature: _____ **Date:** _____

Source: Adapted with permission from London Health Sciences Centre