MCSTAP
Massachusetts Consultation Service for Treatment of Addiction and Pain

The Nuts and Bolts of Buprenorphine: Basic Buprenorphine/Naloxone Prescribing for Opioid Use Disorder

This guide is meant for providers who are just starting out in prescribing buprenorphine/naloxone (bup/nal). It should be used in conjunction with support from MCSTAP physician consultants, as needed.

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A. Taking a Patient's History/Making the Diagnosis of Opioid Use Disorder (OUD)

OUD is defined by 1) compulsion to use, 2) loss of control, 3) continued use of opioids despite negative consequences, and 4) craving.

Note: If the patient has comorbid chronic pain, OUD is often challenging to tease out, and we recommend a conversation with a MCSTAP physician consultant at **1-833-PAIN-SUD** (1-833-724-6783) to rule out pseudo-addiction (under-treated pain that can present like an addiction).

1. Diagnosing Substance Use Disorder

The following table lists DSM V Diagnostic Criteria for Substance Use Disorder (SUD).

DSM V Diagnostic Criteria		Severity: 2-3 Mild, 4-5 Moderate, 6+ Severe
1	Hazardous use	The patient has used the substance in ways that are dangerous to self and/or others, i.e., overdosed, driven while under the influence, or blacked out.
2	Social or interpersonal problems related to use	Substance use has caused relationship problems or conflicts with others.
3	Neglected major roles to use	The patient has failed to meet their responsibilities at work, school, or home because of substance use.
4	Used larger amounts/longer	The patient has started to use larger amounts or use the substance for longer amounts of time.
5	Repeated attempts to control the use or quit	The patient has tried to cut back or quit entirely but has not been successful.
6	Much time spent using	The patient has spent a lot of time using the substance.
7	Craving	The patient has experienced cravings for the substance.
8	Physical or psychological problems related to use	The patient's substance use has led to physical health problems, such as liver damage or lung cancer, or psychological issues, such as depression or anxiety.
9	Activities given up to use	The patient has skipped activities or stopped doing activities they once enjoyed to use the substance.
10	Withdrawal	When the patient stops using the substance, they experience withdrawal symptoms.
11	Tolerance	The patient has built up a tolerance to the substance so that they have to use more to get the same effect.

2. Is this person a good candidate for bup/nal?

It is important to have a framework for considering whether someone is a good candidate for bup/nal. The table below can help guide your initial decision-making, as well as your conversation with your patient in discussing treatment options in a patient-centered way.

Indications for starting buprenorphine:

Indicated	• Bup/nal is a safer opioid than a full agonist. • The patient has substantial barriers to receiving MOUD methadone, such as they are unable to do early dosing or they have transportation issues. • They do not need a more-structured setting.
Partial Contraindication	• If the patient had an unpleasant experience with buprenorphine products in the past, tease out whether this was due to: ○ precipitated withdrawal ○ difficulty with induction ○ intolerance to a formulation ○ inability to keep the medication safe ○ prior trouble taking as directed ○ concern for diversion They may still benefit from another trial of bup/nal but consider closer monitoring trial vs. long-acting injectable. • The patient is on an extremely high dose of full agonist opioid/fentanyl and will be difficult to transition without an initial taper.
Absolute Contraindication	• The patient had severe side effects or allergic reactions in the past. ○ Note that we would not rule out all buprenorphine products due to side effects. • It is worth discussing the case with a MCSTAP physician consultant, as getting a different formulation approved by insurance can be challenging even with sufficient documentation.

Note: Consider treating OUD with buprenorphine, even with co-morbid alcohol/stimulant/sedative use disorders or prescription.

3. Starting Buprenorphine/Naloxone - is an X-Waiver required to start bup/nal?

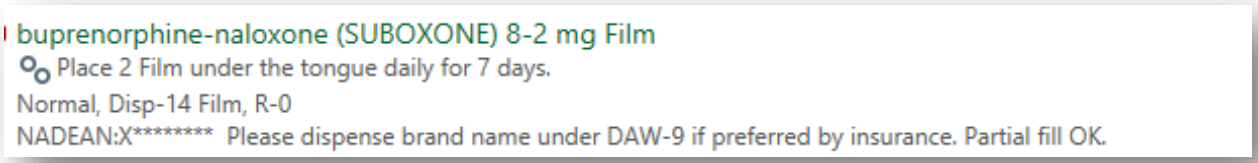
An X-Waiver is no longer required in order to prescribe buprenorphine, as a result of the 2023 Consolidated Appropriations Act (P.L. 117-328), which was signed into law by President Biden on December 29, 2022. Click here for more information.

4. How to write a prescription for buprenorphine/naloxone

Buprenorphine is a DEA Schedule III controlled substance. Massachusetts requires that all controlled substances are sent via E-script (EPCS – Electronic Prescribing for Controlled Substances), effective January 2020.

In an urgent situation, providers can fax or call the prescription into the pharmacy over the phone. For phone prescriptions, the prescriber is required to send a paper script to the pharmacy within seven business days. Massachusetts pharmacists are required by law to accept an emergency prescription, so do not take no for an answer.

Sample prescription:



5. Use the PDMP (MassPAT)

You, or a delegate, are required to check the Massachusetts Prescription Drug Monitoring Program for every bup/nal prescription.

6. OK, I'm ready to prescribe…my patient is currently:

a. Actively using a non-prescribed opioid agonist

What is the patient taking? In Massachusetts, it is prudent to assume that all pressed opioid pills and street "heroin" is either all fentanyl or have fentanyl in them. Due to illicitly manufactured fentanyl's variable potency and tail, we are seeing that even though individuals are needing to use the substance several times per day to avoid withdrawal, fentanyl which appears often to remain on the mu-opioid receptor longer and can create a situation in which a precipitate

withdrawal can occur from the introduction of bup/nal even when a person abstains from use for >24h.

b. Switching from prescribed full agonist

What is the patient taking? If the patient is taking their own prescribed opioid agonist, the transition to buprenorphine is more controlled. If they are taking from a friend or supplementing with non-prescribed, assume there may be illicitly manufactured fentanyl in it.

c. Taking Methadone

For the specifics of transitioning from methadone to buprenorphine, which is a special case due to the long half-life of methadone and variable metabolic clearance, call MCSTAP at **1-833-PAIN-SUD** (833-724-6783) and see the OBAT TTA Massachusetts Nurse Care Manager Model of Office Based Addiction Treatment: Clinical Guidelines, page 33.

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B. Initiating Buprenorphine

It is important to set expectations for the patient by reviewing the day-to-day process.

1. Should I perform the bup/nal induction in the office or have the patient do it at home?

The following chart, developed by IT MATTTRS, University of Colorado School of Medicine lists the pros and cons of induction at home versus in the office.

Induction at the Doctor's Office		Induction at Home	
Pros	**Cons**	**Pros**	**Cons**
• Your care team is there to check on you and answer questions. • You can build a connection and relationships with your care team. • In some practices, a peer counselor or a behavioral health provider might be there to talk with you.	• You might not be as comfortable as home. • Someone should drive you there and home, ideally.	• You might be more comfortable at home. • You do not need to drive anywhere.	• Waiting to be in withdrawal before taking your first dose of buprenorphine can be difficult. If you take your first dose too soon, you increase the chance of an intense withdrawal that comes on very quickly (precipitated withdrawal). • Your health care team is not there to check on you and talk with you.

2. What to expect: How long should the patient wait after a full agonist has been administered?

Note: see "precipitated withdrawal" (see question 10 below) for the risk of taking buprenorphine too soon.

	Opioid Agonist			
Duration of Action	*Short*	*Long*	*Long*	*Mixed*
Medication/Substance	• Heroin • Oxycodone • Hydrocodone • Morphine	• Oxycodone ER • Morphine ER	• Methadone	• Fentanyl (Illicit manufacture & distribution)
Recommended minimum time until starting induction: ***A longer wait is better***	8-18 hrs	24 hrs	36 hrs. 24 - 72 hrs	Variable, ~18 - 24 hrs

3. Medications to Manage Withdrawal Symptoms (aka "Comfort Meds")

Tips: Limit prescribing < 10-12 tabs of each type of comfort med. Carefully monitor what medication the patient eventually uses. Given close follow-up, additional prescriptions can always be provided based on the patient's needs.

Sample medication doses* **Note: Adjust dosing using clinical judgment and individual patient's biopsychosocial situation & comorbidities*	**Symptoms Treated**
Clonidine 0.1mg BID x2d	Restless leg, anxiety, agitation
Lorazepam 1mg TID x2 days	Anxiety, insomnia
Ondansetron 4mg TID x 2 days	Nausea
Dicyclomine 10mg TID x 2 days	Abdominal cramps
Ibuprofen 600mg QID x 2 days	Sweats, chills

4. Initial bup/nal prescription and counseling

Provide the patient with a prescription for buprenorphine/naloxone films 4/1 mg*

Rx:
Sig: 1 film up to 4 times daily as needed for withdrawal
Disp: #28 (~ 7-day supply)

Suggested Workflow

Schedule the patient for a face-to-face visit within 1 week of starting the process (in-person office visit or via telehealth)

**Note: if your pharmacy does not carry 4-1mg bup/nal, order 8-2mg films #14 and have the patient cut films in half*

5. Patient directions

Note: There are several handouts freely available for patients to take home. It is helpful to print and review the handout with the patient during the visit.

Suggested Workflow

Day 1:

- Wait until the person is experiencing mild/moderate withdrawal (COWS score 8+) extending time with comfort medications
- Give buprenorphine 4mg x1 SL
- Wait 30-60 minutes
- If symptoms are not relieved, give an additional 4-8mg
- Continue 4-8mg q4-6 hours until comfortable
- Advance to 16-24mg

Day 2:

- Consolidate into one (1) daily dose (note some patients prefer QD, others prefer split dose)

6. Resources

- SAMHSA quick start guide helps with the basics of induction
- COWS scale for Assessing Severity of Opioid Withdrawal
  - SAMHSA quick start guide helps with the basics of the COWS scale
- Sample patient handout (each has slightly different dosing recommendations) are available in several languages.
  - CA Bridge Buprenorphine Self-Start

7. Induction Pearls

- Review prior toxicology test(s) to confirm whether fentanyl is present, which could complicate induction.
- **Note:** A toxicology result is **NOT required** before starting the bup/nal (but you are required to make the clinical diagnosis of OUD).
- Review the PDMP and pertinent labs, if available. You do NOT need to wait for labs to initiate buprenorphine for the patient with OUD. You do not need to perform an exhaustive exam.
- Avoid scheduling the withdrawal /induction process over a weekend. Instead, if possible, initial the withdrawal process on a Monday and, depending on symptoms, aim to initiate the bup/nal on a Thursday.
- It is recommended that a nurse or physician is responsible for calling the patient daily or every other day throughout the entire withdrawal/induction process.

8. Information for the patient for first-time use of bup/nal

- Bup/nal comes as a dissolvable film or pill that you place under your tongue or in your cheek.
- The medication contains buprenorphine (an opioid) and naloxone (an opioid blocker).
- When absorbed under the tongue, the buprenorphine works in the body, but the naloxone is poorly absorbed via the stomach and therefore has no effect noted.
- Buprenorphine is a partial opioid agonist, so only halfway activates the opioid mu receptors.
- This makes buprenorphine a safer medication than full opioids because it is less likely to cause a decrease in the body's drive to breathe.
- The goals of buprenorphine are to stop withdrawal, block the effects of other opioids, reduce cravings, and restore the normal reward pathway.

9. The patient has OUD and is not on opioids currently but is at risk of return to use after a period of abstinence and wants to start bup/nal.

- Given this patient does not have current opioid tolerance, a lower initial dose of buprenorphine is appropriate to avoid the patient feeling overmedicated.
- For example, it is reasonable to start with ~2mg of buprenorphine/naloxone SL up to twice daily and have them return for office visit in one week to adjust the dose for ongoing cravings.

10. Precipitated withdrawal: what it is and how to manage it if it occurs

- Precipitated withdrawal occurs when bup/nal is administered too soon after a full opioid agonist.
- This leads to abrupt dissociation of the opioid from the mu receptors and causes severe, acute opioid withdrawal symptoms.
- This phenomenon occurs because buprenorphine (a partial mu-opioid agonist), which has a much higher mu-opioid receptor binding affinity than any of the full opioid agonists, effectively displaces the most if not all of the existing full agonist opioids (e.g., morphine, oxycodone, and etc.) off of the mu-opioid receptors in the body. (This is NOT caused by the naloxone component of the bup/nal.)
- Counsel patients that illicitly manufactured fentanyl can be found in most pressed street pills and heroin around Massachusetts.
- Clinically, people with exposure to fentanyl have a fast onset of opioid agonist symptoms followed by a rapid opioid withdrawal which requires people to use it multiple times per day to avoid being sick from withdrawal.

- The half-life of illicitly manufactured fentanyl is quite variable because of storage in fat stores and other unique pharmacokinetics, making it harder for many people to transition onto buprenorphine during a traditional induction.
- Despite waiting extended times for typical withdrawal symptoms to start, individuals still sometimes develop a precipitated withdrawal after their initial dose of sublingual buprenorphine.
- **NOTE:** Review this risk with patients; discuss options for comfort medications so they can delay the first dose of bup/nal as long as possible.

11. Low dose buprenorphine induction, a.k.a. "micro-dosing"

- Some patients are afraid of going through withdrawal to get on buprenorphine despite comfort medications. This may be due to co-morbid pain or having previously experienced precipitated withdrawal.
- In this case, off-label, low-dose buprenorphine induction may be an option.
- The concept of low-dose buprenorphine induction is administering very low doses of bup/nal while continuing to take the full agonist, in order to sneak the bup/nal onto the opioid receptors in a slow enough manner to not displace all the full agonist.
- This allows the patient to avoid going into significant withdrawal while transitioning to the bup/nal and needing to completely stop the agonist during this process.
- **NOTE:** Discuss the case with a MCSTAP physician consultant if you have not prescribed low-dose buprenorphine before.

C. Maintaining and Monitoring Buprenorphine Treatment

1. What frequency for follow-up should occur after successful completion of the buprenorphine induction?

There is no evidence supporting an optimal frequency; however, a reasonable approach could look like this:

- **Month 1: Weekly follow-up with the nurse and/or the prescribing clinician**
  - Obtain a weekly toxicology test. Make sure to include a test for fentanyl since it is often not part of standard drug toxicology screening panels.
  - Continue weekly testing until the patient has at least 2-4 weeks of 100% appropriate test results, (+) Buprenorphine, (-) for all non-prescribed substances (use clinical judgment in cases where cannabis use is noted).
  - If there is ongoing, non-prescribed use of opioids, it is important to consider whether the dose of bup/nal is sufficient to meet the treatment goals and whether there are other factors impacting ongoing use that would warrant escalation of supports (e.g., behavioral health team, coaching, community supports).

- Ongoing use of non-opioid substances is not an indication for discharge from bup/nal treatment.
- NOTE: These are great cases to discuss with MCSTAP consultants.

- **Months 2-3 (or until at least 2-4 weeks of appropriate drug testing results): Bi-weekly follow-up and testing**
  - If spreading out toxicology testing to q1-3 months it is important that your patient is in remission from active opioid use, as the less-frequent touch would imply stability.

- **At 3 months:** If the patient is on a stable dose, has remained fully engaged in treatment and follow-up, and has had few or no inappropriate drug tox results, urine drug testing can be decreased to every other month or even quarterly. Toxicology testing should be coordinated to occur with in-person visits as often as possible. Further decreases in frequency are not advised in the first years, depending on the patient's stability and ongoing progress in recovery. It is important to remember that although bup/nal is a Schedule III substance and can legally be prescribed for 30 days with up to 5 refills, MCSTAP only advises a maximum of 28 pills with a max of 3 refills for patients who have greater than a year of continuous abstinence.

2. Can Buprenorphine be prescribed via telemedicine, or does my patient need to come into the clinic for every prescription refill?

Since the onset of COVID-19 in 2020, practitioners can prescribe buprenorphine to patients using telemedicine without conducting an in-person evaluation according to DEA guidelines.

3. What should I look for during a follow-up visit?

Ask patients about withdrawal, sleep, cravings, or any ongoing opioid use at follow- up visits and adjust the dose as needed.

D. Harm Reduction and Overdose Prevention

1. How do I prescribe Narcan? What are some teaching points around it for patients?

The following are useful resources related to prescribing Narcan and talking to patients about it:

- Webpage for patients, from Prevent & Protect
- AHOPE video: Identifying an overdose and using Narcan, produced November 5, 2021
- Massachusetts Medical Society: Preventing Opioid Overdose Deaths with Naloxone