



Daniel Lurie
Mayor

**San Francisco Health Network Behavioral Health Services
Medication Use Improvement Committee**

1380 Howard St. 5th Floor
San Francisco, CA 94103



San Francisco
Health Network

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

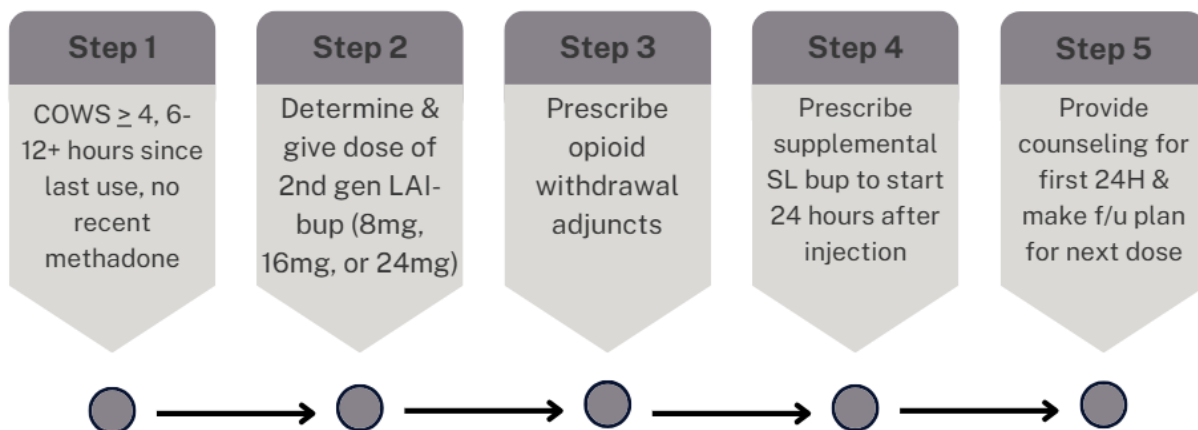
Direct to Inject Buprenorphine Guideline

SCOPE: This Direct to Inject Buprenorphine Guideline is intended to offer prescribing assistance for providers, patients and the interested general public to increase the effectiveness and safety of medication for opioid use disorder (MOUD) in the ambulatory care setting. It is not intended to be comprehensive in scope. These recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient. References can be found in the Opioid Use Disorder References and Further Reading.

BACKGROUND: San Francisco Department of Public Health does not recommend the use of brand names when describing medications, however to reduce the risk of medication errors this protocol will refer to brand names of buprenorphine long-acting injectables as they have the same generic names. Buprenorphine long-acting injection is available as monthly Sublocade, weekly Brixadi and monthly Brixadi.

Direct to inject (DTI) is a term used for initiating buprenorphine long-acting injectable in people who are not currently taking buprenorphine. Given fentanyl's dominance of the drug market and ongoing overdose epidemic, DTI initiation using weekly Brixadi is gaining interest. The evidence for DTI is based on preliminary data coming from Emergency Department settings where patients with moderate-severe opioid use disorder (OUD) were offered DTI Brixadi 24mg for Clinical Opiate Withdrawal Scale (COWS) score ≥ 4 without a sublingual test dose (D'Onofrio, 2023). DTI is feasible because weekly Brixadi serum levels peak at 24 hours post-injection (Braeburn, 2023). This slow increase in buprenorphine serum levels facilitates a gradual build-up of buprenorphine while minimizing the risk of precipitated withdrawal that is seen with the quick serum peak (1-2 hours) of sublingual buprenorphine. A case series of SFDPH patients initiated on buprenorphine via DTI in outpatient settings in 2024 demonstrated that DTI was generally well-tolerated, with most patients experiencing mild to moderate withdrawal and approximately 75% retained on buprenorphine at 30 days (Rosenwohl-Mack, 2025).

DIRECT TO INJECT (DTI) PROTOCOL:



COUNSELING FOR THE FIRST 24 HOURS:

- Mild to moderate withdrawal may continue to worsen after the injection, as time since last opioid use increases and before buprenorphine has reached adequate serum levels. For most people it is not as severe as precipitated withdrawal and self-resolves.
- It is recommended that patients avoid using any opioids after injection and rely on withdrawal adjunct medicines as much as possible. However, if a patient is going to use, we recommend waiting at least 6 hours after injection. See Appendix 2 for patient-facing handout
- WAIT to take supplemental sublingual buprenorphine for 24 hours after injection to minimize risk of precipitating withdrawal.
- If the patient doesn't start sublingual buprenorphine or receive another injection within 7 days, they will have to start the buprenorphine initiation process over again from the beginning – recommend booking follow up appt for patient within 1-2 days of injection and emphasizing importance of follow up

FOLLOW-UP

- 24 hours after the injection, start taking additional sublingual buprenorphine, 8-32mg/day. Start with smaller doses (e.g., 2mg) at first and increase as tolerated.
- Clinicians should follow up within 24-48 hours to assess patient experience and determine next dose of buprenorphine. Internal data suggests that patients can tolerate a monthly Brixadi or Sublocade as soon as 24 hours after DTI.
- The first dose of weekly Brixadi lasts for 5-9 days. If the patient is planning to continue on buprenorphine, they should receive their next dose of buprenorphine (whether sublingual or long-acting injectable) between 1-8 days after their first injection.

INITIAL VISIT WORKFLOW

Document Initial Visit Assessment:

Time since last use:

Opioid(s) patient uses:

Any other substances used in past week:

COWS score:

Has patient been on buprenorphine before:

Has patient tried DTI before?

Assess Patient Withdrawal and Time Since Last Opioid Use

- Assess patient COWS score and time since last opioid use

Clinical Opiate Withdrawal Scale (COWS)	
Sign / Symptom	Score
Resting Pulse Rate (beats per minute) <i>Measure pulse rate after patient is sitting or lying down for 1 minute</i>	≤80: 0 81-100: +1 101-120: +2 >120: +4
Sweating <i>Not accounted for by room temperature or patient activity over the last 0.5 hours</i>	No report of chills or flushing: 0 Subjective report of chills or flushing: +1 Flushed or observable moistness on face: +2 Beads of sweat on brow or face: +3 Sweat streaming off face: +4
Restlessness observation during assessment	Able to sit still: 0 Reports difficulty sitting still, but is able to do so: +1 Frequent shifting or extraneous movements of legs/arms: +3 Unable to sit still for more than a few seconds: +5
Pupil size	Pupils pinned or normal size for room light: 0 Pupils possibly larger than normal for room light: +1 Pupils moderately dilated: +2 Pupils so dilated that only the rim of the iris is visible: +5
Bone or joint aches <i>If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored</i>	Not present: 0 Mild diffuse discomfort: +1 Patient reports severe diffuse aching of joints/ muscles: +2 Patient is rubbing joints or muscles and is unable to sit still because of discomfort: +4
Runny nose or tearing <i>Not accounted for by cold symptoms or allergies</i>	Not present: 0 Nasal stuffiness or unusually moist eyes: +1 Nose running or tearing: +2

	Nose constantly running or tears streaming down cheeks: +4
GI Upset <i>Over last 0.5 hours</i>	No GI symptoms: 0 Stomach Cramps: +1 Nausea or loose stool: +2 Vomiting or diarrhea: +3 Multiple episodes of vomiting or diarrhea: +5
Tremor <i>Observation of outstretched hands</i>	No tremor: 0 Tremor can be felt, but not observed: +1 Slight tremor observable: +2 Gross tremor or muscle twitching: +4
Yawning <i>Observation during assessment</i>	No yawning: 0 Yawning once or twice during assessment: +1 Yawning three or more times during assessment: +2 Yawning several times/minute: +4
Anxiety or irritability	None: 0 Patient reports increasing irritability or anxiousness: +1 Patient obviously irritable/anxious: +2 Patient so irritable or anxious that participation in the assessment is difficult: +4
Gooseflesh skin	Skin is smooth: 0 Piloerection of skin can be felt or hairs standing up on arms: +3 Prominent piloerection: +5
Total Score: 5-12=mild withdrawal; 13-24 = moderate withdrawal; 25-36=moderately severe withdrawal; more than 36 = severe withdrawal	

- Ideally patient would wait until COWS ≥ 4 **and** at least 6-12 hours since last opioid (eg., fentanyl, heroin) use
- Recent methadone: Methadone has a long half-life, especially when at steady state (e.g., given in regular daily doses). If a patient has taken a single dose of methadone a few days prior to DTI, the risk of withdrawal is much lower than if the patient has been on regularly daily methadone within the past week. To err on the side of caution, it may be advisable to postpone DTI if a patient has taken methadone in the past 72 hours or been on regularly daily methadone dosing within the past week, though this should be a risk/benefit discussion with the patient.
- If patient's COWS < 4 or last use was <6 hours ago, can decide to:
 - *Give injection after conversation and consent from patient* the injection may be reasonable and be given at the clinician's discretion and after a risk/benefit discussion with the patient
 - *Ask patient to return to clinic a few hours later or the next day:* In some cases, it may be possible for the patient to return to clinic a few hours later. Alternatively, if the patient can return the next day, advise them to stop using at least 6-12 hours before visit. Consider offering buprenorphine 0.5mg SL tablets q12 hours until the appointment, as there is some preliminary evidence that small amounts of buprenorphine prior to injection may potentially ease injection experience (Rosenwohl-Mack, 2025).

Determine Injection Dose

- Clinicians can choose between 8, 16, and 24mg doses of weekly Brixadi
- Most patients receive 16mg or 24mg, with 8mg more often for those with suspected low opioid tolerance or significant worry of worsening withdrawal
- Higher doses are likely associated with increased withdrawal with DTI but may be needed for patients using fentanyl with higher opioid tolerance (see Table 1 for dosing equivalents).
- It is recommended to weigh the risks and benefits of worsening withdrawal vs subtherapeutic dosing in determining which dose to give.
- See Appendix 1 for administration instructions

TABLE 1: CONVERSION FROM SUBLINGUAL BUPRENORPHINE TO WEEKLY BRIXADI

Daily Dose of Sublingual Buprenorphine	Brixadi Weekly Dose Equivalent	Brixadi Monthly Dose Equivalent
<6mg	8mg	--
8-10mg	16mg	64mg
12-16mg	24mg	96mg
18-24mg	32mg	128mg

Prescribe Opioid Withdrawal Adjuncts

We recommend the following opioid adjunct orders (if using SFDPH Epic, can use 'Opioid Withdrawal Adjunctive' orderset):

- Clonidine 0.1mg q6h prn withdrawal and restlessness, #12
- Ondansetron 4mg q8h prn nausea or vomiting, #9
- Hydroxyzine 50mg q6h prn anxiety, #12
- Loperamide 2mg q6h prn diarrhea; #12
- Trazodone 100mg qhs prn insomnia, #3 (if appropriate)
- Ibuprofen or acetaminophen (if no contraindications)

Prescribe Supplemental Sublingual Buprenorphine

Patients should not start supplemental sublingual buprenorphine until 24 hours after their injection (though they should ideally pick up the prescription on the day of the injection, along with the opioid withdrawal adjuncts). As a general rule, most patients need a maximum of 32mg sublingual

buprenorphine equivalent per day, and the following suggested PRN total daily doses are based on providing patients a total of 32mg sublingual buprenorphine equivalence per day x 1 week. At the time of the injection, we recommend booking a follow up appointment in 1-2 days, as well as informing patient that if they miss this appointment they can return any time in the next 7 days, so we recommend sending a 1 week supply of sublingual buprenorphine.

TABLE 2. SUBLINGUAL BUPRENORPHINE OVERLAP AFTER DTI

DTI Brixadi Weekly Dose	Goal Total Daily Dose of Sublingual Buprenorphine	Example SIG
8mg	28mg/day	8mg q6h prn withdrawal or cravings #28, do not take first dose until 24h since injection
16mg	22-24mg/day	8mg q8h prn withdrawal or cravings #21, do not take first dose until 24h since injection
24mg	16-20mg/day	4mg q6h prn withdrawal or cravings #28, do not take first dose until 24h since injection

Counseling and Follow-up for Ongoing Buprenorphine

- The patient should abstain from using any opioids for as long as possible after injection (and for at least 6 hours); rely on withdrawal adjunct meds as much as possible. See Appendix 2 for patient-facing handout.
- WAIT to take supplemental sublingual buprenorphine for 24 hours after injection to minimize risk of precipitating withdrawal.
- Clinician should follow-up with in 24-48 hours after injection. Clinicians should counsel patients at the follow up visit they will give additional sublingual or injectable buprenorphine, depending on the patient's preference
- Patient can safely receive monthly Brixadi or Sublocade starting 24 hours after DTI (see 'Follow Up Visits')

FOLLOW-UP VISITS

Deciding on Subsequent Buprenorphine at Follow-up Visits:

At 24 hours after weekly Brixadi injection, the dose is at its peak, and it is safe to give more buprenorphine without concern about precipitating withdrawal. At that time, sublingual buprenorphine, a second weekly injectable, or a monthly injectable buprenorphine can be given. Factors to consider in determining dose and timing of subsequent buprenorphine:

- Patient preference for sublingual vs. weekly vs. monthly injection

- If there is uncertainty about the dose of buprenorphine a patient is likely to need, starting with a few days of sublingual dosing gives patients the ability to titrate to the dose they need
- If concern for low tolerance, waiting 2+ days between injections can minimize concern for dose stacking

Documentation for Follow-up Visits:

24-48-hour f/u documentation:

Any withdrawal in 24 hours after injection (yes/no):

- If yes, how many hours after injection?
- If yes, mild/moderate/severe?

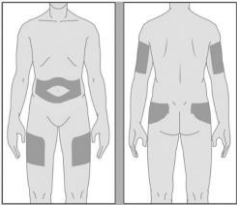
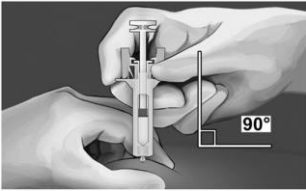
Opioid use since injection (fentanyl/heroin/other), if so how long after & did they feel effects:

Any sublingual buprenorphine since last injection, if so how long after & did it help withdrawal:

How does this compare to prior buprenorphine experiences:

Plan for next steps (note and confirm w patient plan for next buprenorphine injection):

APPENDIX 1: ADMINISTRATION INSTRUCTIONS

Steps for injection	
1	Provide patient education and anticipatory guidance: - Pain usually lasts 1-3 min after injection; ice packs are typically sufficient for analgesia - Advise the patient that they will NOT have a lump, in contrast to Sublocade
2	Prepare the syringe: Take the plunger and while holding the syringe, twist clockwise until the plunger is in place.
3	Select the injection site: for first 4 injections, do NOT offer the upper arms (plasma levels are 10% lower after injection here). Options include the buttock, thighs, and abdomen. 
4	Clean the injection site with 1-4 alcohol swabs in circular motion moving outward from site.
5	Grasp the syringe and remove the needle cap. There may be a small amount of liquid at the tip of the needle.
6	Pinch skin between your thumb and index finger.
7	Insert needle fully into the subcutaneous tissue at a 90-degree angle. Insert fully (hub the needle). 
8	After the needle is inserted, release the skin you are grasping. Slowly push down the plunger until it latches in the safety device 'wings.' This will ensure all of the medicine has been injected.
9	Keep the plunger pressed fully down while you hold the safety syringe in place for an additional 2 seconds. 

10	Gently pull the needle out. Once removed, you can take your thumb off of the plunger (this will retract the needle tip). 
11	Dispose of the needle in a sharps container.

APPENDIX 2: PATIENT HANDOUT

Direct-to-Inject Buprenorphine: Is it for me?

What is it?

- Buprenorphine is a medication for people who use opioids (for example, fentanyl or heroin)
- Being on buprenorphine can help you stay well and avoid cravings and withdrawal. It can help you cut down or stop using opioids, if that is your goal. It can also protect you from overdose.
- There is a new long-acting buprenorphine injection that you can start directly (without taking buprenorphine pills or strips first)

How does it work?

- When you are in mild opioid withdrawal, ideally at least 6 hours after the last time you used fentanyl or heroin, you can get an injection
- The injection reaches its full dose 24 hours after you get it
- You may feel a little rough for the first 24 hours until the medicine takes full effect, but precipitated withdrawal is very unlikely
- After 24 hours from the injection, the buprenorphine is at a good level in your body and most people feel much better

How should I expect to feel?

- Some people feel better as soon as they get the injection
- Some people don't notice anything at all
- Some people feel a little rough for 24 hours

What should I do if I feel worse after the injection?

- Tell someone! There are many options to help.
- You can get medications for anxiety, nausea, diarrhea, difficulty sleeping, or pain
- You should try to avoid using heroin or fentanyl, but if you do decide to use, it is best to wait at least 6 hours after the injection (to decrease your risk of worsening withdrawal)

What next?

- Once it's been 24 hours since the injection, the buprenorphine is at a stable level in your body and you should feel pretty good
- If your first dose wasn't high enough, you can take additional buprenorphine (pills or films) or get another injection
- The first injection only lasts 1 week, so it's important to return to see your provider within a week for more bup, so you don't have to start the process over again

What do people who get it say?

- "I felt a little under the weather overnight, but I feel fine now"
- "I thought I might have to go out and use, but I tried to just sleep through it and I felt good in the morning"
- "I never thought this could work for me! Everyone should try this."