ED BRIDGE

Emergency Buprenorphine Treatment

BUPRENORPHINE GUIDE

AUGUST 2018

This guide provides a practical framework for the use of buprenorphine as an effective short-term treatment for pain and opioid withdrawal, and a bridge to long-term treatment of opioid use disorder.

ED-BRIDGE is a partnership with the California Poison Control System and the California Hub and Spoke System to provide 24-7 emergency access to initiation of buprenorphine treatment for opioid use disorder in all California communities.

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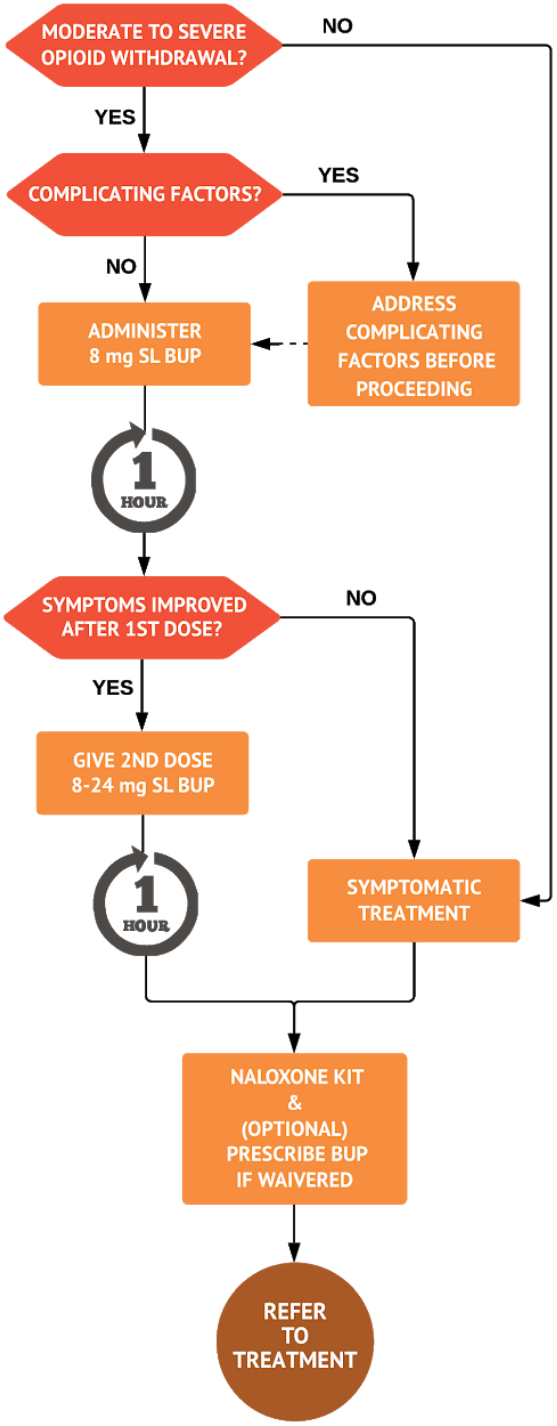
BUPRENORPHINE GUIDE

BUPRENORPHINE (BUP) ALGORITHM

AUGUST 2018



MODERATE TO SEVERE OPIOID WITHDRAWAL

- Use clinical judgement to determine moderate to severe withdrawal.
- If uncertain, use the Clinical Opioid Withdrawal Scale (COWS)
- If using COWS, the score should be ≥ 8 or ≥ 6 with at least one objective sign of withdrawal
- Document: which opioid used, time of last use

COMPLICATING FACTORS

Identify and manage complicating factors prior to proceeding.
The only absolute contraindication is allergy to buprenorphine.

Refer to Buprenorphine Guide before dosing buprenorphine for:

- Clinical suspicion of acute liver failure
- ≥ 20 weeks pregnant
- Intoxicated or altered
- Withdrawal precipitated by naloxone
- Taking methadone or long acting opioid
- Chronic pain patients taking prescribed opioids
- Withdrawal symptoms are inconsistent or borderline (COWS of 6-8), or opioid use within 12 hours; consider beginning with a low dose (2-4 mg SL) and titrating every 1-2 hours

PARENTERAL DOSING

- Use if unable to take sublingual (SL)
- Start with 0.3 mg IV/IM buprenorphine; may repeat as needed; switch to SL when tolerated

PRECIPITATED WITHDRAWAL

- Buprenorphine can cause precipitated withdrawal if too large a dose is given too soon after the last opioid use
- The longer the time since last opioid use (> 24 hours) and the more severe the withdrawal symptoms (COWS ≥ 13) the better the response to initial dosing
- Only patients with objective improvement in withdrawal after the 1st dose should receive subsequent dosing
- Worsening after buprenorphine is likely precipitated withdrawal; no further buprenorphine should be administered in the ED; switch to symptomatic treatment

SYMPTOMATIC TREATMENT

- Supportive medications such as clonidine, gabapentin, metoclopramide, low-dose ketamine, acetaminophen, NSAIDs

LOWER TOTAL DOSE OPTION (16 mg)

- Possible lower risk of sedation or precipitated withdrawal
- Some patients will go back into withdrawal in less than 12 hours increasing risk of early dropout.
- Buprenorphine prescription or next day follow-up should be available

HIGHER TOTAL DOSE OPTION (24-32 mg)

- Increased magnitude and duration of opioid blockade
- More complete treatment of withdrawal in heavy users
- May suppress craving and protect against overdose (opioid blockade) for 2 days or more
- Use with caution in medically complex patients, older patients, and patients using other sedatives such as alcohol or benzodiazepines

RE-EVALUATION TIME INTERVALS

- The time to SL buprenorphine onset is typically 15 minutes and peak clinical effect is typically within 1 hour
- Re-evaluate patient 1 hour after buprenorphine doses
- Observe for 1 hour after the final dose before discharge

DEA 72 HOUR RULE

- Patients may return to the ED for up to 3 days in a row for repeat doses
- At each visit administer 16 mg SL buprenorphine

FOLLOW-UP

- Goal: follow-up treatment available within 3 days

I. Patient Screening

A. **Harm reduction strategy**

Use a harm reduction strategy when communicating with patients, staff and stakeholders.

Harm reduction training resources:

harmreduction.org/

B. **Screen during ED visit**

- Screening can occur at any stage during the ED visit from triage to discharge.
- A sign on the ED registration desk can establish the ED as a safe place to reveal opioid dependence and seek help. Language such as such as “Need help with pain pills or heroin? We want to help you get off opioids and start on Suboxone (buprenorphine). Ask us how.”

Example ED screening resources:

- sbirtoregon.org/sbirt-workflow/
- ed-bridge.org/signage

C. **COWS Score**

Nurse or medical technician initiated screening and evaluation with the clinical opioid withdrawal scale (COWS) can be built into the electronic medical record system to increase efficiency.

- **See page 6 for COWS Scale Template**
- **Online COWS Score Tool:**

mdcalc.com/cows-score-opiate-withdrawal

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

CLINICAL OPIOID WITHDRAWAL SCALE (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. *For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.*

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	*Time:*	*Time:*	*Time:*	*Time:*
Resting Pulse Rate: *Record beats per minute after patient is sitting or lying down for one minute* • 0 - pulse rate 80 or below • 1 - pulse rate 81–100 • 2 - pulse rate 101–120 • 4 - pulse rate greater than 120				
Sweating: *Over past ½ hour not accounted for by room temperature or activity* • 0 - no chills or flushing • 1 - subjective chills or flushing • 2 - flushed or observable moistness on face • 3 - beads of sweat on brow or face • 4 - sweat streaming off face				
Restlessness: *Observation during assessment* • 0 - able to sit still • 1 - reports difficulty sitting still, but is able to do so • 3 - frequent shifting or extraneous movement of legs/arms • 5 - unable to sit still for more than a few seconds				
Pupil size • 0 - pupils pinned or normal size for light • 1 - pupils possibly larger than normal for light • 2 - pupils moderately dilated • 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* • 0 - not present • 1 - mild/diffuse discomfort • 2 - patient reports severe diffuse aching of joints/muscles • 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: *Not accounted for by cold symptoms or allergy* • 0 - none 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 ½ hour* • 0 - no GI symptoms • 1 - stomach cramps • 2 - nausea or loose stool • 3 - vomiting or diarrhea • 5 - multiple episodes of diarrhea or vomiting				
Tremor: *Observation of outstretched hands* • 0 - no tremor • 1 - tremor can be felt, but not observed • 2 - slight tremor observable • 4 - gross tremor or muscle twitching				
Yawning: *Observation 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 of skin can be felt or hairs standing up on arms • 5 - prominent piloerection				
Suggested minimum score to start buprenorphine in the ED ≥ 8 **TOTAL**				
OBSERVER INITIALS				

II. Patient selection

INCLUSION CRITERIA:

1. Daily problem use of non-prescribed opioids. Most emergency department cases are not difficult to diagnose. For example anyone who uses heroin or street purchased pills will meet criteria.
2. If there is uncertainty, check the the Criteria for Diagnosis of Opioid Use Disorder below.

CRITERIA FOR DIAGNOSIS OF OPIOID USE DISORDER

The Diagnosis of Moderate Opioid Disorder requires at least 4 criteria are met:

- ☐ Opioids are often taken in larger amounts or over a longer period of time than intended.
- ☐ There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
- ☐ A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
- ☐ Craving, or a strong desire to use opioids.
- ☐ Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.
- ☐ Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
- ☐ Important social, occupational or recreational activities are given up or reduced because of opioid use
- ☐ Recurrent opioid use in situations in which it is physically hazardous
- ☐ Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
- ☐ Tolerance, as defined by either of the following:
  - (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect
  - (b) markedly diminished effect with continued use of the same amount of an opioid
- ☐ Withdrawal, as manifested by either of the following:
  - (a) the characteristic opioid withdrawal syndrome
  - (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

III. Complicating Factors

Buprenorphine is easy when you are mindful, but do be aware of these complicating factors: "Mild withdrawal, Methadone, or Mind-altered" patients.

Complicating Factors

a)	**Mild withdrawal** with COWS ≤ 7 Patient who states, *"I feel like the withdrawals are just starting"* is an ideal candidate for counseling and referral and possibly a buprenorphine prescription, but does ***not need ED treatment with buprenorphine.***
b)	**Methadone in last 72 hours** This is not an absolute contraindication but unpredictable precipitated withdrawal can occur; recommend consultation with an addiction specialist.
c)	**Intoxicated ("Mind-altered")** Alcohol, benzodiazepines, stimulants, etc...Do the best to engage and encourage patient to consider the ED an "open door" to return when sober.
d)	**Chronic pain patients** Patients, taking medically prescribed opioids, are great candidates for BUP but use much smaller doses (e.g. 2 mg SL QID) and require care coordination. The transdermal formulation of buprenorphine is FDA approved for chronic pain. ED placement of a 5-20 mcg patch can is a potential option for chronic pain.
e)	**Use caution with patients with decompensated cirrhosis or other severe medical illness** Lab testing is not required prior to starting buprenorphine unless there is clinical suspicion of acute decompensated liver failure. However, do make every attempt to coordinate care for high-risk and complex patients before starting buprenorphine.

IV. Initial Evaluation

A. Quantify daily use: How much of what opioid? For how long?

1. Useful tips to quantify use:
    a) How do they use it? (Snort, smoke, inject, skin pop)
    b) How many times a day are they using?
    c) How much are they spending per day?

B. No lab testing is required, however consider a urine toxicology screen if requested by follow up provider.

C. Offer female patients a pregnancy test. (Upreg is NOT required if patient declines)

D. When was last use? How much of what opioid did they use?

i. In general, patients with larger daily use (e.g. IDU heroin or snorting oxy) do well with larger total daily doses of BUP.

ii. There is a tremendous amount of variability in the onset of withdrawal after last use. A general guide to estimate time till onset of moderate or greater withdrawal is:

1. Heroin: 12-24 hours
2. Long acting opioids (Oxycontin): 24-48 hours
3. Methadone: 48-72+ hours

iii. Withdrawal severity is not well correlated with tolerance. However, the favorable safety profile of buprenorphine limits the risk of respiratory suppression regardless of level of tolerance.

E. Ask patient to describe the severity of their withdrawal.

Do they feel like they are "dope sick" or "kicking." In general, the patient should feel *"very bad"* before starting BUP.

F. Formally evaluate using the Clinical Opioid Withdrawal Scale (COWS):

- **See page 6 for COWS Scale Template**
- **Online COWS Score Tool**

  mdcalc.com/cows-score-opiate-withdrawal

Opioid withdrawal symptoms include:

Tachycardia, sweats, restless, dilated pupils, joint aches, runny nose, nausea/abdominal upset, runny nose, cramps, yawning, anxious/irritable, and tremor.

1. Minimum score to start BUP is **COWS of 8**
2. The more severe the withdrawal (i.e. **COWS ≥ 13**) the more likely rapid titration will be well tolerated.

V. Emergency Treatment with Buprenorphine

Deciding on the first ED dose of buprenorphine:

1. If the patient is **mild withdrawal with COWS ≤7** or you are unsure: Do not administer buprenorphine in the ED**.**

   Provide the patient with an unobserved induction handout and a 3-7 day supply of buprenorphine/naloxone sublingual (SL) tablets (see *Buprenorphine Home Start Guide* on page 15) . If no x-waivered provider is available, provide brief intervention and referral to treatment.

   Note: there is more to discharge than just handing out a script. See: *Discharging a patient* below. Check your PDMP per your local practice as you would for any opioid prescription.

2. For **borderline cases (such as COWS 8-9 without objective signs of withdrawal)** where you would like initiate treatment but are uncertain of withdrawal status consider a **"start low and go slow"** approach.

   Begin with 2 mg SL BUP and repeat with 2-4 mg SL BUP dose every 1-2 hours.

   GOAL: At least 4 mg SL in the ED. If patient responds well with unequivocal improvement after 4 mg SL dose is reached, OK to give another 4-8 mg before discharge.

3. <u>If the patient is in moderate or greater withdrawal</u> (COWS ≥ 8 with at least one objective sign) **<u>AND</u>** this is consistent with expected time since last use, proceed with ***full dose BUP administration***.

   The more severe the withdrawal (COWS 13 and above) the more aggressively BUP can be initiated without risk of precipitating withdrawal.

   a) The first buprenorphine dose: 8 mg SL
   Be sure the patient allows the SL tablets to dissolve completely under the tongue.

   (1) **Observe at least 30-60 minutes to determine response to initial dose.**
   Peak plasma is 60 minutes after dose.

   (a) A responder should feel better with significant improvement by 30 minutes.

   (b) The generic monoproduct tablets taste bad and some patients develop nausea but the overall withdrawal state should improve significantly and unambiguously

   (2) **Re-evaluate after 30-60 min**

   (a) Any worsening in COWS score suggests that initiation has proceeded too rapidly. Halt further dosing and provide supportive care.

(b) Significant and unambiguous improvement in COWS score suggests patient is a responder and an additional dose can be safely administered.

(c) The patient should express feeling "a lot better".

b) Decide on the second dose: 8-24 mg SL

Have a transparent and collaborative discussion with the patient. At this point most patients should be comfortable and able to participate meaningfully in a conversation.

DOSING SUGGESTIONS FOR SPECIFIC SITUATIONS

Dosing suggestions for specific patient situations	TARGET TOTAL DOSE	EXAMPLE ED BUP SL DOSING SCHEDULE		
		Option 1	Option 2	Option 3
Next day outpatient appointment scheduled with no expected delays in access to buprenorphine (insured, no transportation or housing issues)	**16 mg SL**	8 mg, 8 mg	4 mg, 4 mg, 4-8 mg	
Potential barriers to follow up care, such as lack of insurance, transportation, or housing	**24-32 mg SL**	8 mg, 16 mg	8 mg, 24 mg	4 mg, 8 mg, 16 mg
Admitted non-surgical patients (ED)	**16 mg SL**	8 mg, 8 mg	4 mg, 4 mg, 8 mg	
Admitted non-surgical patients (Inpatient regimen to start next day)	**16 mg SL**	BUP SL 8 mg BID	BUP SL 4 mg TID	
Admitted surgical patients	**4 mg SL**	Discuss with inpatient team and suggest 4 mg BUP SL TID as a base regimen in addition to non-opioid multimodal regimen	It's OK to combine BUP with full-agonists (e.g. hydrocodone, oxycodone, fentanyl)	

CONSIDERATIONS FOR A HIGHER OR LOWER TOTAL DOSE

CONSIDERATIONS FOR A HIGHER TOTAL DOSE (24-32 mg SL)

PRO

- Toxicity has not been observed in opioid dependent patients in experimental settings up BUP SL up to 70mg. There have been no reported cases of an adult overdose attributable to oral/SL ingestion of SL BUP alone.
- Increased magnitude and duration of opioid blockade: reduced craving, reduced rewarding effect of additional opioids.
- Increased magnitude and duration of intrinsic rewarding effect from BUP.
- No titration. Patients start **16 mg SL daily** the next day and stay on this until their follow up appointment.
- Increased magnitude and duration of opioid withdrawal suppression of up to 96 hours. (There is significant patient variability in metabolism of buprenorphine: always encourage return to ED if early recurrence of withdrawal occurs).

CON

- A new technique without high quality clinical data that is more rapid than traditional office based or unobserved inductions. Requires monitoring after last dose for 60 minutes before discharge.
- Precipitated withdrawal risk increases with rapid escalation and higher doses.
- Some patients will have sedation at higher doses and feel groggy / sleepy for hours to days.
- Higher buprenorphine doses could pose a higher risk for respiratory suppression when combined with benzodiazepines or other sedatives.

CONSIDERATIONS FOR A LOWER TOTAL DOSE (8-16 mg SL)

PRO

- Less time in the ED.
- Lower risk of sedation or precipitated withdrawal.
- Consistent with office based induction practices.

CON

- Some patients will start going back into withdrawal in less than 12 hours. It typically is not as severe withdrawal, but that varies. This may increase risk of early drop out.
- To establish care and actually fill a buprenorphine prescription, there are often practical tasks to accomplish--obtain insurance, establish a pharmacy, make appointments, etc. This can expose your patient to significant stress. Going into withdrawal midway through this process is a likely risk factor for a return to use.
- Arriving in withdrawal--anxious and irritable--at follow up BUP appointment can increase risk of conflict with staff and likely increase risk of early drop out.

VI. Managing potential complications of buprenorphine treatment

Observe for 60 minutes after last dose to evaluate for precipitated withdrawal or sedation. If the patient feels well with neither withdrawal symptoms nor excessive sedation they are eligible for discharge.

A. Managing excessive sedation

Significant respiratory depression is possible when buprenorphine is combined with other sedatives such as alcohol and benzodiazepines. Clinically significant sedation has not been observed during ED buprenorphine initiation. However, you should know what to do if supportive measures fail.

Buprenorphine reversal can be accomplished with high-dose naloxone:

a) Naloxone IV bolus doses of 2-3 mg, followed by a continuous infusion of 4 mg/h

b) If benzodiazepine co-ingestion is suspected, flumazenil reversal with 0.2 mg IV over 30 seconds is an option after careful consideration of contraindications.

B. Managing unexpected precipitated withdrawal

Precipitated withdrawal is often brief and self-resolving with mild to moderate intensity. Most patients require only observation and first line treatments below. However, it can be more severe and you should be prepared to treat it.

UNEXPECTED WITHDRAWAL MANAGEMENT

First line:	Lorazepam 1-2 mg PO or IV/IM or Diphenhydramine 25-50 mg PO ***AND/OR*** 0.2 mg Clonidine PO, Ondansetron 4 mg PO, Loperamide 4 mg PO, Ibuprofen 400 mg PO
Second line:	Fentanyl 25 mcg IV/IM titrated to comfort ***AND*** Prochlorperazine 10 mg IV (or equivalent sedating antiemetic) as needed.
Third line:	Ketamine 15 mg IV over 10-15 minutes or 20 mg IM

C. Resuming treatment with buprenorphine after precipitated withdrawal has occurred

Once the episode of precipitated withdrawal has been treated, every attempt should be made to assist patient to continue with buprenorphine treatment. If a X-waivered provider is available, the patient can be discharged home with a low-dose, slow titration home induction prescription. Otherwise the patient can rest in the ED for 2-4 hours then resume induction with 2mg SL every 2 hours. Patients discharged home can return to the ED the next day to resume treatment.

VII. Discharging a patient treated with buprenorphine

If next day outpatient follow-up is unavailable, attempt to discharge with a prescription for buprenorphine/naloxone SL tablets.

While some patients can be remarkably comfortable for up to several days with maximal dosing, some rapidly metabolize and will need additional buprenorphine within 24 hours.

A. Example prescriptions to build into EMR:

1) ***Buprenorphine/naloxone***
8 mg / 2 mg sublingual (SL) film (OK to substitute sublingual tablets)
2 strips under the tongue once a day.
Quantity #14

2) ***Buprenorphine/naloxone (home titration)*** **[see Buprenorphine Home Start Guide p.15]*)***
8 mg / 2 mg sublingual (SL) film (OK to substitute for tablets)
1/2 strip under the tongue as needed for withdrawal every 2-8 hours up to 16 mg per day
Quantity #56

B. X-waiver training:

X-waiver training resources:

samhsa.gov/medication-assisted-treatment/training-resources/buprenorphine-physician-training

C. Patient unobserved instruction for a home-start:

Example patient unobserved instruction sheet:

- See *Buprenorphine Home Start Guide* on page 15
- ed-bridge.org/home-start

D. All patients should know they can return to the ED for up to 3 days in a row.

1. At each visit administer **16 mg BUP SL;** OK to do this Saturday, Sunday, Monday for example.
2. Ask the patient to arrive early in the day before crowding becomes an issue.

More information on the 3-day-rule (72 hour rule):

naabt.org/documents/Three-day-rule.pdf

E. Always attempt to discharge with a referral to an outpatient provider who can prescribe buprenorphine.

1. Local resources vary. Attempt to locate at least one addiction treatment location that a patient can contact upon discharge. Not necessary for a warm handoff.
2. If you have a bridge program that links ED care to outpatient follow up, follow the warm handoff procedures developed with your outpatient partner.
3. At minimum attempt to document and confirm a contact telephone number.

F. ED staff should have clear direction on how to refer patients.

1. During regular weekday hours
2. After hours
3. Weekends

G. Establishing patient in long-term term care is always the goal, but do not let lack of follow up be a barrier to administering or prescribing a short course of buprenorphine.

Patients typically go on and off buprenorphine several times before stabilizing. Three days on buprenorphine is potentially a powerful harm reduction intervention. Given your local resources, provide information on the best possible options available to your patient.

H. All patients should be given overdose education and a naloxone overdose kit.

Information on overdose education and naloxone:

harmreduction.org/issues/overdose-prevention/tools-best-practices/manuals-best-practice/od-manual/

BUPRENORPHINE HOME START GUIDE

Day 1 (Today)

- Wait until you start feeling really bad from withdrawals (about 24 hours since you last took an opioid).
- Put **one-fourth (¼) (2 mg)** of an 8 mg buprenorphine/naloxone strip under the tongue. DO NOT SWALLOW. (If you accidently swallow it, it will not hurt you, but you will get no effect.) Let it dissolve under your tongue for at least 10 minutes.
- Take another **one-fourth (¼) (2 mg)** of an 8 mg strip **every 1-2 hours as needed** if you are still feeling sick from withdrawal (up to 16 mg total per day

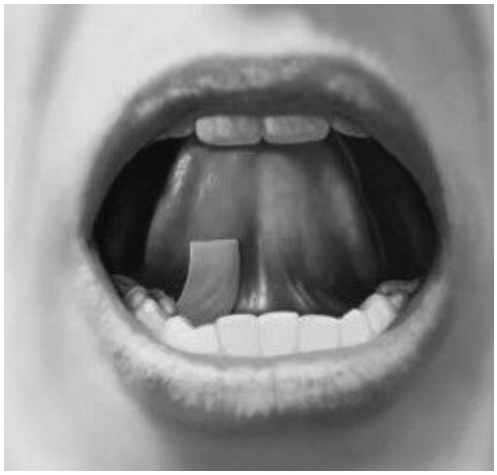
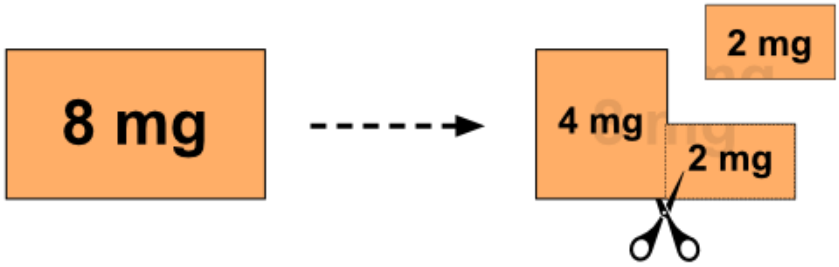


Image courtesy of Rx Resource



Day 2 (Tomorrow Morning)

- Remove the buprenorphine patch if that was placed for pain control in the ED.
- In the morning, put **one-half (½) (4 mg) OR an entire (8 mg) strip** (total 4 - 8 mg) under your tongue and let it dissolve.
- In the evening, put **one-half (½) (4 mg) OR an entire (8 mg) strip** (total 4 - 8 mg) under your tongue and let it dissolve - **every 6 hours while awake**.

Day 3 (The Following Morning)

- Put **two (2) entire 8 mg strips** (total 16 mg) under your tongue and let them dissolve.