SAMHSA
Substance Abuse and Mental Health Services Administration

BUPRENORPHINE
QUICK START GUIDE

Important Points to Review With the Patient

Specifically discuss safety concerns:

- **Understand that discontinuing buprenorphine increases risk of overdose death upon return to illicit opioid use.**
- **Know that use of alcohol or benzodiazepines with buprenorphine increases the risk of overdose and death.**
- **Understand the importance of informing providers if they become pregnant.**
- **Tell providers if they are having a procedure that may require pain medication.**

Facts About Buprenorphine

- FDA approved for Opioid Use Disorder treatment in an office-based setting.
- For those with tolerance to opioids as a result of OUD, buprenorphine is often a safe choice.
- Buprenorphine acts as a partial mixed opioid agonist at the μ-receptor and as an antagonist at the κ-receptor. It has a higher affinity for the μ-receptor than other opioids, and it can precipitate withdrawal symptoms in those actively using other opioids.
- It is dosed daily, has a long half-life, and prevents withdrawal in opioid dependent patients.
- Can be in tablet, sublingual film, or injectable formulations.
- Many formulations contain naloxone to prevent injection diversion. This formulation is the preferred treatment medication. The buprenorphine only version is often used with pregnant women to decrease potential fetal exposure to naloxone.
- There is a "ceiling effect" in which further increases above 24mg in dosage does not increase the effects on respiratory or cardiovascular function.
- Buprenorphine should be part of a comprehensive management program that includes psychosocial support. Treatment should not be withheld in the absence of psychosocial support.
- Overdose with buprenorphine in adults is less common, and most likely occurs in individuals without tolerance, or who are using co-occurring substances like alcohol or benzodiazepines.

Checklist for Prescribing Medication for the Treatment of Opioid Use Disorder

1

Assess the need for treatment

For persons diagnosed with an opioid use disorder,* first determine the severity of patient's substance use disorder. Then identify any underlying or co-occurring diseases or conditions, the effect of opioid use on the patient's physical and psychological functioning, and the outcomes of past treatment episodes.

Your assessment should include:

- A patient history
- Ensure that the assessment includes a medical and psychiatric history, a substance use history, and an evaluation of family and psychosocial supports.
- Access the patient's prescription drug use history through the state's Prescription Drug Monitoring Program (PDMP), where available,

to detect unreported use of other medications, such as sedative-hypnotics or alcohol, that may interact adversely with the treatment medications.
- A physical examination that focuses on physical findings related to addiction and its complications.
- Laboratory testing to assess recent opioid use and to screen for use of other drugs. Useful tests include a urine drug screen or other toxicology screen, urine test for alcohol (ethyl glucuronide), liver enzymes, serum bilirubin, serum creatinine, as well as tests for hepatitis B and C and HIV. Providers should not delay treatment initiation while awaiting lab results.

2

Educate the patient about how the medication works and the associated risks and benefits; obtain informed consent; and educate on overdose prevention.

There is potential for relapse & overdose on discontinuation of the medication. Patients should be educated about the effects of using opioids and other drugs while taking the prescribed medication and the potential for overdose if opioid use is resumed after tolerance is lost.

3

Evaluate the need for medically managed withdrawal from opioids

Those starting buprenorphine must be in a state of withdrawal.

4

Address co-occurring disorders

Have an integrated treatment approach to meet the substance use, medical and mental health, and social needs of a patient.

5

Integrate pharmacologic and nonpharmacologic therapies

All medications for the treatment of the opioid use disorder may be prescribed as part of a comprehensive individualized treatment plan that includes counseling and other psychosocial therapies, as well as social support through participation in mutual-help programs.

6

Refer patients for higher levels of care, if necessary

Refer the patient for more intensive or specialized services if office-based treatment with buprenorphine or naltrexone is not effective, or the clinician does not have the resources to meet a particular patient's needs. Providers can find programs in their areas or throughout the United States by using SAMHSA's Behavioral Health Treatment Services Locator at www.findtreatment.samhsa.gov.

*See The Criteria from American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,. Washington, DC, American Psychiatric Association, page 541.

Induction Considerations

The dose of buprenorphine depends on the severity of withdrawal symptoms, and the history of last opioid use (see flowchart in appendix for dosing advice).

- **Long acting opioids, such as methadone, require at least 48-72 hours since last use before initiating buprenorphine.**
- **Short acting opioids (for example, heroin) require approximately 12 hours since last use for sufficient withdrawal to occur in order to safely initiate treatment. Some opioid such as fentanyl may require greater than 12 hours.**
- **Clinical presentation should guide this decision as individual presentations will vary.**

Determine Withdrawal

Objective withdrawal signs help establish physical dependence

The risk with initiating buprenorphine too soon is that buprenorphine has a very high affinity for the mu receptor and will displace any other opioid on the receptor, thereby causing precipitated opioid withdrawal.

COWS Clinical Opiate Withdrawal Scale

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying 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	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea *5* Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient 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	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
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting 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	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
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	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates 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	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms *5* Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms 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	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Information on Precipitated Withdrawal

- Precipitated withdrawal can occur due to replacement of full opioid receptor agonist (heroin, fentanyl, or morphine) with a partial agonist that binds with a higher affinity (Buprenorphine).
- Symptoms are similar to opiate withdrawal.
- Avoid by ensuring adequate withdrawal before induction (COWS > 12; Fentanyl may require higher COWS score and lower initial dosing), starting Buprenorphine at a lower dose (2.0mg/0.5 mg), and reassessing more frequently.
- Should precipitated withdrawal occur, treatment includes:
  - Providing support and information to the patient
  - Management of acute symptoms
  - Avoid the use of benzodiazepines
  - Encourage the patient to try induction again soon

Buprenorphine Side Effects

- **Buprenorphine's side effects may be less intense than those of full agonists. Otherwise, they resemble those of other mu-opioid agonists.**
- **Possible side effects include: Oral numbness, constipation, tongue pain, oral mucosal erythema, vomiting, intoxication, disturbance in attention, palpitations, insomnia, opioid withdrawal syndrome, sweating, and blurred vision**
- **Buprenorphine FDA labels list all potential side effects**

Co-prescribing of overdose reversal agents such as Naloxone is also recommended

Maintenance Therapy

Goal = once-daily dosing, no withdrawal between doses. Ideally, average dosing does not exceed 16 mg/4 mg (See flowchart in appendix)

- **Check PDMP regularly to ensure prescriptions are filled, and to check other prescriptions.**
- **Order urine drug testing (UDT) and consider confirmatory testing for unexpected results. UDT can facilitate open communication to change behavior.**
- **Assess for readiness for extended take-home dosing**

Psychosocial Therapies

- **Although people often focus on the role of medications in MAT, counseling and behavioral therapies that address psychological and social needs may also be included in treatment. To find treatment, please consult www.findtreatment.gov.**

Diversion

Diversion is defined as the unauthorized rerouting or misappropriation of prescription medication to someone other than for whom it was intended (including sharing or selling a prescribed medication); misuse includes taking medication in a manner, by route or by dose, other than prescribed.

How can providers minimize diversion risk?

1. Early in treatment patients should be seen often, and less frequently only when the provider determines they are doing well.
2. Providers should inquire about safe and locked storage of medications to avoid theft or inadvertent use, especially by children. Patients must agree to safe storage of their medication. Counsel patients about acquiring locked devices and avoiding storage in parts of the home frequented by visitors.
3. Limit medication supply. Prescribe an appropriate amount of medications until the next visit. Do not routinely provide an additional supply "just in case."
4. Use buprenorphine/naloxone combination products when medically indicated. Reserve daily buprenorphine monoproducts for pregnant patients and/or patients who could not afford treatment if the combination product were required.
5. Counsel patients on taking their medication as instructed and not sharing medication.
6. Ensure that the patient understands the practice's treatment agreement and prescription policies. Providers can utilize the sample treatment agreement in SAMHSA's TIP 63, Page 3-78. A treatment agreement and other documentation are clear about policies regarding number of doses in each prescription, refills, and rules on "lost" prescriptions.
7. Directly observe ingestion randomly when diversion is suspected.
8. Providers should order random urine drug testing to check for other drugs and for metabolites of buprenorphine. Providers should also consider periodic point of care testing.
9. Doctors should schedule unannounced pill/film counts. Periodically ask patients to bring in their medication containers for a pill/film count.
10. Providers should make inquiries with the Prescription Drug Monitoring program in their state to ensure that prescriptions are filled appropriately and to detect prescriptions from other providers.
11. Early in treatment, providers can ask the patient to sign a release of information for a trusted community support individual, such as a family member or spouse, for the purpose of communicating treatment concerns including diversion.

What should I do if a patient diverts or misuses the medication?

- Misuse or diversion doesn't mean automatic discharge from the practice.
- Document and describe the misuse and diversion incident. Also document the clinical thinking that supports the clinical response, which should be aimed at minimizing future risk of diversion while still supporting the use of MAT.
- Strongly consider smaller supplies of medication and supervised dosing.
- Treatment structure may need to be altered, including more frequent appointments, supervised administration, and increased psychosocial support.
- When directly observed doses in the office are not practical, short prescription time spans can be considered.
- In situations where diversion is detected, open communication with the patient is critical. Providers may consider injectable and implantable buprenorphine to reduce diversion, once verified.

DSM-5 Criteria for Diagnosis of Opioid Use Disorder

Diagnostic Criteria*
These criteria not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Check all that apply

	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

Total Number Boxes Checked: _____

Severity: **Mild**: 2-3 symptoms. **Moderate**: 4-5 symptoms. **Severe**: 6 or more symptoms

*Criteria from American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,. Washington, DC, American Psychiatric Association page 541. For use outside of IT MATTTRs Colorado, please contact ITMATTTRsColorado@ucdenver.edu

Important Considerations: Buprenorphine/Naloxone Dosing

- Tablets/film may be split if necessary
- May take up to 10 min to dissolve completely (no talking, smoking, or swallowing at this time)
- Absorption better with moistened mouth

SUBOXONE sublingual tablets, including generic equivalents	Corresponding dosage strength of ZUBSOLV sublingual tablets
One 2 mg/0.5 mg buprenorphine/naloxone sublingual tablet	One 1.4 mg/0.36 mg ZUBSOLV sublingual tablet
One 8 mg/2 mg buprenorphine/naloxone sublingual tablet	One 5.7 mg/1.4 mg ZUBSOLV sublingual tablet
12 mg/3 mg buprenorphine/naloxone taken as: • One 8 mg/2 mg sublingual buprenorphine/naloxone tablet AND • Two 2 mg/0.5 mg sublingual buprenorphine/naloxone tablets	One 8.6 mg/2.1 mg ZUBSOLV sublingual tablet
16 mg/4 mg buprenorphine/naloxone taken as: • Two 8 mg/2 mg sublingual buprenorphine/naloxone tablets	One 11.4 mg/2.9 mg ZUBSOLV sublingual tablet

Algorithm for In-Office Induction (for home induction prescriptions may be given)

Initial Assessment

History and Physical
Concurrent medical issues and substance use
Medication history (with review of the PDMP)
Allergies
Mental health status and social history
Social history

Lab Workup
CBC, CMP, HIV, hepatitis A, B & C
Urine drug testing, and
consider pregnancy & STD screen

Referral
Refer to specialists as indicated
Refer to counseling
Refer to case management

Provide Patient Education
Treatment goals and medication education
Side-effects
How to store medication at home
Patient should update provider with new medications or other changes
Establish open communication

Discuss Safety Concerns
Altered tolerance to opioids on buprenorphine/suboxone
No co-administration of alcohol or benzodiazepines
Alert provider if planning pregnancy or pregnant
Planned procedures that may require opiate analgesia

Day One (Induction)

Last opioid use >6-12 hours ago → Moderate Withdrawal (COWS >12) → **Give First Dose of Buprenorphine/Naloxone (2 – 4mg)** → After 1 Hour: Monitor for precipitated withdrawal; If present, treat symptoms; Attempt induction 24 hours later

2 – 4 Hours Later: Withdrawal Symptoms Relieved?
- No → Give further 2 – 4mg dose
- Yes → Prescribe one dose; Return to clinic on day two for observation and review

2 – 4 Hours Later: Withdrawal Symptoms Relieved?
- No → Give further 2 – 4mg dose, up to 8mg total
- Yes → Prescribe one dose; Return to clinic on day two for observation and review

Day Two

Adequate symptom relief achieved After induction?
- No → Give day 1 dose and additional 2 – 4mg up to 16mg total
- Yes → Induction Complete - Give induction dose as ongoing dose, and review in 1 day

2 – 4 Hours Later: Withdrawal Symptoms Relieved?
- No → Give further 2 – 4mg dose, up to 16mg
- Yes → Induction Complete - Give induction dose as ongoing dose, and review in 1 day

Maintenance

Patient Stable On Current Dose?
- No → Consider further 2 – 4mg dose, up to 16mg
- Yes → Continue once daily dosing with regular review

Perform monthly urinary drug screens, and check PDMP regularly. Ensure on-going attendance at counseling and support groups. When patient stable on medication, assess readiness for take-home dosing