Opioid Use Disorder

In 2019, Sesame Street's Karli revealed her mother was struggling with opioid use disorder

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Introduction

Buprenorphine saves the lives of people with opioid use disorder (OUD). Not only does it reduce fatal drug overdoses, but its use is associated with a lower risk of death from suicide, cancer, heart disease, and alcohol.

With a rate of death that exceeds that for car accidents, the White House has declared the opioid epidemic a national emergency. The epidemic is changing rapidly and medical practice is shifting in response. Earlier, prescription opioids were thought to fuel the crisis. That shifted to heroin in 2010. Since 2019, higher potency opioids like fentanyl have surged (50-100x more potent than heroin).

The approach to opioid use disorder (OUD) is *harm reduction*, where the main aim is to reduce the negative consequences of drug exposure. This requires some changes in our thinking. For example, when prescribing stimulants in ADHD the risk is that an unsuspected substance use disorder will arise and the patient will misuse the drug. If the evidence is strong enough, we taper off the controlled substance.

With OUD, we already assume substance misuse, and the risk is that the use will worsen or the patient will overdose. We minimize those risks by prescribing a maintenance addiction therapy (MAT). This is similar to using lithium to prevent mood disorders. Just as we don't stop the lithium when a patient gets depressed, we don't stop buprenorphine because the patient has relapsed into addiction.

When buprenorphine was first approved for OUD in 2002 there were fears that this replacement therapy would cause another opioid epidemic. Several measures were taken to prevent that:

- Buprenorphine was combined with naloxone, an opioid antagonist. This reduces the risk of diversion with the drug, but does not alter its therapeutic effects because the naloxone component is only minimally absorbed when taken orally. In other words, naloxone makes the medicine less desirable by preventing a high from snorting or injecting the drug.
- Prescribers needed a special license to prescribe buprenorphine, and there were limitations on the number of patients they could treat.

Buprenorphine has not lead to a second epidemic as feared. Instead, the epidemic of opioid use has exploded, moving from prescription opioids to heroin to fentanyl. In January 2023, the DEA recognized that the restrictions on buprenorphine were hamstringing the medical response to the epidemic. They removed the X-waiver so that all clinicians with a DEA license can prescribe buprenorphine.

They also went one step further, requiring clinicians to learn how to use buprenorphine through focused CMEs. This, in effect, has enrolled all prescribing clinicians in the fight against the opioid epidemic. When a patient presents with OUD, we all must know how to start the first-line therapy (buprenorphine). Not doing so could be fatal, and clinicians can no longer avoid that responsibility by claiming that they are not qualified to treat it.

Treatment Setting

In an outpatient settings we often use home induction, although we may refer patients who cannot start it this way to a higher level of care. This may be started at the first visit or during ongoing care. In the latter case, we may not be able to obtain all the items in the diagnostic evaluation below, but should not let that get in the way of starting buprenorphine. Schedule time to gather those later.

Diagnostic Evaluation

In addition to the usual psychiatric/social history we conduct on every patient, pay special attention to:

- Time of last opioid use and type of opioid
- Social factors that reduce or worsen substance use
- Medical and dental consequences of substance use
- History of drug overdose and withdrawal problems
- Evidence of sedatives or controlled substances in the Prescription Drug Monitoring Program (PDMP)
- Urine drug screen (UDS)
- Consider other lab tests, eg urine test for alcohol (ethyl glucuronide), liver enzymes, serum bilirubin, serum creatinine, pregnancy, hepatitis B and C and HIV.
- Providers should not delay buprenorphine treatment while awaiting lab results.

Consider inpatient care for patients who have active suicidal ideation or other evidence of dangerousness. For example, if severe psychiatric symptoms, polysubstance abuse, cognitive impairment, medical problems, or social problems make MAT adherence unlikely and drug-related fatality likely, consider hospitalization or a partial hospital program.

Prescription Standards

Co-prescribe an overdose reversal agent such as naloxone (it is also available over the counter). If possible, involve family and educate them on naloxone use.

Document a diagnosis of opioid use disorder. Buprenorphine should not be prescribed without this documentation.

Check the Prescription Drug Monitoring Program regularly. Irregularities (eg not filling buprenorphine, filling undisclosed controlled substances) usually will prompt therapeutic interventions and discussion rather than buprenorphine discontinuation.

Visit Frequency

Home Induction: Follow up at approximately 3 days with a tele-health visit to manage the induction, and again 4-7 days after that 2nd visit depending on the severity of the case. See

the patient weekly until they are stable (ie, the level of buprenorphine is controlling their cravings and withdrawal is stabilized).

For routine follow-up, patients on buprenorphine should be seen at least monthly, either in person or by telehealth. More frequent visits are needed until the patient is stabilized (eg weekly, see MAT agreement).

These are ideal frequencies, and we understand reality may get in their way. Have the patient see a colleague or update you through the portal in those cases. Keep your eyes on the goal, which is to make this successful for the patient and improve their chance of sticking with treatment.

Urine Drug Screens (UDS)

A Urine Drug Screen (UDS) is used to assess the diagnosis (i.e: What substances are involved?) and monitor progress (i.e: Is the buprenorphine working?). A UDS should be obtained as close to buprenorphine initiation as possible but in all cases within 30 days of initiation.

It is well known that clients with OUD use other drugs on a regular basis. Medical Assisted Therapy (MAT) improves retention in treatment and results in sustained decreases in other drugs used. However, abstinence from all drugs all the time is an unrealistic goal in the first 3 years of treatment. In fact, 75% of clients will continue to use other drugs (cannabis, alcohol, cocaine, amphetamine, anxiolytics) even while they remain abstinent from opioids.

Record UDS results in the EMR along with any relevant clinical observations. If recreational drugs are detected in the UDS, this should prompt a judgment-free conversation about treatment using the motivational interview. Document those recommendations (see section on *Increasing Level of Care*).

For a missed UDS, make sure the patient understands that the UDS is used to assess recovery and that problems on the UDS are not going to result in discontinuation of buprenorphine. The approach is similar to a patient with mood disorders who doesn't complete rating scales or misses metabolic labs on an antipsychotic.

Treatment Agreement

Review the agreement to buprenorphine treatment and have the patient sign it.

Psychotherapy

Psychotherapy is encouraged but not required for a patient in MAT. Options include 12-step, group, family, and individual therapy. For some addictions, therapy is the main treatment and medication is optional (eg, alcohol use disorder). For opioids, it is the reverse.

Agreement to Buprenorphine Medication-Assisted Treatment (MAT)

I agree to the following for buprenorphine office-based opioid addiction treatment:

Visit frequency. Initially I will have weekly office visits until I am stable. Visits are typically monthly when stable.

Drug screens. Random urine drug testing is a treatment requirement.

Medication misuse. I will take buprenorphine as prescribed and will speak to my provider if I want to change my dose. Taking more than prescribed, or snorting or injecting buprenorphine may result in supervised dosing at the office, referral to a higher level of care, or change in medication.

Storage. I will keep buprenorphine in a safe and secure place away from children (e.g., in a lock box).

Lost medication and missed appointments. If I miss an appointment or lose my buprenorphine, I understand that I will not get more medication until my next office visit. I will be on time for appointments.

Other meds. I understand that people have died by mixing buprenorphine with other drugs like alcohol, benzodiazepines, and sedatives (Valium, Klonopin, and Xanax). I agree not to obtain or take prescription opioid medications prescribed by any other clinicians. If I am going to have a medical procedure that will cause pain, I will let my provider know in advance so that my pain will be adequately treated. I will keep my provider informed of all my medications (including herbs and vitamins) and medical problems.

Do not share meds. I understand that it is illegal to give away or sell my medication – this is diversion. If I do this, my treatment may require referral to a higher level of care or referral to a center that providers supervised dosing.

Be respectful. I will be respectful to the office staff and other patients. Violence, threatening language or behavior, or participation in any illegal activity at the office will result in treatment termination from our clinic.

Rescue med. I have been educated about the use of naloxone as a rescue medication in the case of opioid overdose.

Buprenorphine withdrawal. I understand that I may experience opioid withdrawal symptoms when I go off buprenorphine.

Pregnancy. If female, I have been educated about the effects of poor diet, illicit opioid use, use of dirty needles/sharing injection equipment, physical and mental trauma, and lack of pre-natal medical, substance use and mental health care during pregnancy and how these things can adversely affect my health and my current or future fetus/newborn's health. I understand that neonatal abstinence syndrome can occur when taking illicit opioids and that neonatal abstinence syndrome (NAS) is less severe, but can still occur, when pregnant

women take methadone or buprenorphine as prescribed/dispensed in substance use disorder treatment. Cigarette smoking can make the severity of NAS worse and cause pre-term birth and small babies. Alcohol use can cause significant cognitive/brain damage in fetuses and newborns.

Counseling. I understand that treatment of opioid addiction involves more than just taking my medication. I agree to comply with my provider's recommendations for additional counseling or for help with other problems.

Duration of treatment. I understand that there is no fixed time for being on buprenorphine and that the goal of treatment is to stop using all illicit drugs and become successful in all aspects of my life.

_____	_____	_____
Name (print)	Signature	Date

How to Use Buprenorphine

Formulations

There are a lot of formulations of buprenorphine out there (see the Buprenorphine Formulation table). Breaking them down into a few simple categories can help you keep them straight:

Dose. High-dose formulations are used to treat OUD. They come as sublingual tablets or films each containing 2 mg or 8 mg of buprenorphine. Low-dose formulations are only approved for the treatment of chronic pain. They are available as transdermal patches (Butrans) and buccal films (Belbuca), each of which contain < 2 mg of buprenorphine.

Naloxone content. Naloxone is added to some sublingual formulations in order to deter misuse. The reasoning is that naloxone causes withdrawal if snorted or injected, but its poor sublingual bioavailability ensures that someone taking it properly won't feel naloxone effects. Versions without naloxone (*monoproduct*) are preferred for pregnant women and patients with naloxone allergy.

Duration of action. Sublingual tablets and films have a half-life around 36 hours and are typically taken daily or several times a day. There are two long-acting injectable forms; Sublocade, which is given every 1-2 months, and Brixadi, which is given weekly or monthly in the office or at a pharmacy.

Start with an oral naloxone mix like generic Suboxone to minimize diversion. If this does not reduce the substance use, consider an injectable agent.

Tips for sublingual (SL) tablets and films

- They can be cut/split to achieve lower doses
- They take up to 10 min to dissolve completely (no talking, smoking, or swallowing at this time)
- Absorption is better with moistened mouth

Buprenorphine Induction

In outpatient centers, we start buprenorphine as home induction, although we may refer patients who cannot start it this way to a higher level of care.

Buprenorphine can cause *precipitated withdrawal* by displacing other opioids from the mu opioid receptor. The result is opioid withdrawal symptoms like muscle aches, anxiety, nausea, diarrhea, sweating, tremor, and restlessness. Although not directly dangerous, they can make patients give up on treatment which itself could have fatal consequences.

Careful timing of the first few buprenorphine doses minimize this risk—a process called induction. The basic strategy is to start buprenorphine as the opioid of abuse is leaving their system and their opioid withdrawal symptoms are starting to peak. This varies by opioid (eg, 48-72 hours since last use for long-acting opioids like methadone; 12 hours for short-

acting opioids like heroin), but has become much more variable in the fentanyl age (ranging from 1-6 days).

If your patient was using street drugs, assume they were laced with fentanyl. Approximately 80% of street opioids are (as are many non-opioids). Fentanyl withdrawal is more variable because it is slowly released by fat cells that soak up the lipophilic molecule. Fentanyl withdrawal is also more severe because it is highly potent but easily displaced by buprenorphine (ie, low receptor affinity).

Many patients know what works best for them in terms of dose and timing based on past experience with induction. If the patient is not able to tolerate outpatient induction, refer to an acute care setting where they can induce under observation and monitoring (emergency department).

Two rating scales can guide the timing by measuring withdrawal severity: the Clinical Opioid Withdrawal Scale (COWS) or the patient-rated version, the Subjective Opioid Withdrawal Scale (SOWS). Start buprenorphine when the COWS ≥ 8-10 or SOWS ≥ 11-13. There is also a free app (Buprenorphine Home Induction by Amston Studios).

However, these are just rough guides. Best to err on the side of waiting longer and tell the patient, "The goal is to wait as long as they can tolerate before starting it, that is, until you can't stand the withdrawal anymore."

Until recently most people used the standard induction, but in the fentanyl age many experts start at a hig dose – macroinduction – to prevent withdrawal:

Macroinduction. Once the timing is right (based on rating scales or intuition):

- Give 4-8 mg oral, wait 30-60 minutes
- As long as there is no withdrawal, give a single dose of 16-24 mg
- Follow up with daily dosing, equivalent to the amount given in the last step (16-24mg)

Standard induction. This was common before the fentanyl age. Here, a medium dose of buprenorphine is given once the patient is in moderate opioid withdrawal, and the dose is escalated over two to three days. Start when the rating scales or withdrawal symptoms are right.

- Day 1: give 2-4 mg, repeat every hour up to 12 mg or until withdrawal is relieved
- Day 2: give the total taken on Day 1, then give additional doses up to a total of 16 mg or until cravings are relieved
- Day 3: give the total take on Day 2, then give additional doses up to a total of 24 mg or until cravings are relieved

Most patients will require 16-24 mg to relieve withdrawal symptoms and cravings.

Microinduction. This is used in observed settings like the ED and not suited for home induction (it starts with low doses).

Induction App

Buprenorphine Home Induction by Amston Studios is a free app that guides patients through home induction.

Transitioning from Naltrexone

Patients on naltrexone should wait for this opioid antagonist to clear before starting buprenorphine (1 day for oral naltrexone or 28 days for extended-release injectable naltrexone).

Transitioning from Methadone

Patients on low doses of methadone (30–40 mg per day or less) generally tolerate the transition to buprenorphine with minimal discomfort, but higher doses can make transition difficult. Monitor closely as stable methadone patients may become unstable when changing to buprenorphine.

Stimulants and Benzos

When other controlled substances are in the patient's medication list it raises the risk of continued substance misuse. With the benzo-opioid combination, we also worry about potentially fatal respiratory suppression. Fortunately the risk of respiratory suppression is lower with buprenorphine, but it could be high if the patient takes opioids off the street.

Earlier, the guidance was to stop all other controlled substances, but several large studies have found worse outcomes with this approach, including higher rates of overdose deaths. Now the standard is to weigh the risk of continuing other controlled meds against the risk that the patient will leave treatment or get them on the street if they are stopped. Make your judgment call and document the risk-rationale.

A good approach is to stabilize the patient's OUD with buprenorphine before attempting to taper off another substance. Once stabilized, lower the doses to the minimum needed and attempt to switch the benzo to one with a lower overdose risk such as lorazepam or oxazepam.

Consider non-stimulants for ADHD, or for anxiety consider silexan or pregabalin (which has a lower overdose risk than benzos). Document if there is a rationale for continued use like ADHD or panic disorder, and that alternative treatments have been attempted such as therapy and SSRIs.

Buprenorphine Maintenance

After induction, continue buprenorphine as a daily medication. You may gradually reduce the dose, but do so with care. Dose reduction does not supersede the higher goals of safety and recovery, and patients who experience cravings or withdrawal after dose reduction will usually need to resume their prior dose.

Dose. Typically 8-24mg daily, though overall, patients to do better with higher doses. Only when the daily dose is ≥16mg does buprenorphine work as well as methadone (Mattick RP et al, *Cochrane Database Syst Rev* 2014(2):CD002207). There can be variability however, so ask if your patient is experiencing opioid cravings. If they say "yes," increase the dose. When dosed properly, buprenorphine should suppress cravings.

Frequency. Buprenorphine can be taken once, twice, or three times daily. Its analgesic properties tend to be relatively short-lived, so patients with co-morbid chronic pain may do better with smaller doses more frequently.

Formulation. Sublingual buprenorphine/naloxone is the most widely available formulation, and therefore the default first-line choice. Buprenorphine alone, or "monoproduct" (without naloxone) can be used in pregnancy or for patients sensitive to naloxone. Buprenorphine/naloxone and the buprenorphine monoproduct are interchangeable in terms of dosing.

Side effects

Besides precipitated withdrawal, potential buprenorphine side effects include oral numbness, constipation, tongue pain, oral mucosal erythema, vomiting, intoxication, problems with attention, palpitations, insomnia, sweating, and blurred vision.

Management strategies:

- Constipation. We recommend all patients on buprenorphine get a standing bowel regimen. Avoid bulk formers, such as psyllium, which can worsen constipation. Use the approach outlined in the Recommended Bowel Regimen Table.
- Dental problems. Certain forms of buprenorphine (buccal films and the sublingual tablets and films) are associated with potentially serious dental problems (cavities, abscesses, and infections). To reduce this risk, patients should wash out their mouth with water right after taking buprenorphine and avoid eating, drinking, or teeth brushing for one hour. Whenever possible, ensure regular dental follow-up.
- Naloxone sensitivity. Very little naloxone is absorbed sublingually, but some patients may experience headache, nausea, anxiety, or flushing. If your patient reliably develops these symptoms immediately after taking a dose of buprenorphine/naloxone, consider switching to the monoproduct (without naloxone).
- Sedation. This is usually not a problem, though some patients will feel tired after taking buprenorphine. It tends to go away after a few weeks, but if not, consider minimizing other sedating medications and switching buprenorphine to evening.
- Sweating (hyperhidrosis). Consider clonidine (which has evidence in both OUD and hyperhidrosis), or glycopyrrolate, oxybutynin, terazosin, benztropine.

Bowel Regimen for Constipation on Buprenorphine

For all Patients: Start Docusate/Sennosides 2 tabs BID standing
If ineffective...
Increase to Docusate/Sennosides 3 tabs BID standing
If ineffective...
Add Polyethylene Glycol 17g (one capful or packet) dissolved in liquid, daily
If ineffective…
Add Magnesium based laxative as needed: o Magnesium Citrate solution- 5-10oz daily o Magnesium Hydroxide (Milk of Magnesia)- 30-60mL
If ineffective…
Suppository as needed: o Bisacodyl suppository "Magic Bullet" o Glycerin suppository

Special populations

Pregnancy. May require higher or more frequent dosing due to volume of distribution. Switch to monoproduct (without naloxone) to minimize medication exposure to the fetus. Buprenorphine is safer in pregnancy than methadone, and safer than a relapse into OUD.

Chronic pain. Pain can be treated with buprenorphine in patients with OUD. However, they usually require more frequent dosing, so divide the dose BID or TID instead of QD. If they need to switch to a version that is FDA approved for pain and not MAT, this should be managed by a pain clinic. The DEA does not allow prescription of unapproved products for MAT.

Long-acting Injectable (Sublocade, Brixadi)

Long-acting injectable buprenorphine is usually recommended for patients with poor adherence, though we don't have studies showing this definitively. There are two long-acting options, both subcutaneous injections; Sublocade and Brixadi. How these compare to each other remains to be seen. For more about long-acting injectable buprenorphine, and a detailed guide on how to use Sublocade, see "What to Know About Injectable Buprenorphine" in *The Carlat Addiction Treatment Report*, January 2023.

Addressing Partial or non-Response

Relapse into opioids or other drugs of abuse is common during MAT, especially in the first few years of treatment. Here the risk-benefit consideration usually favors continuation of buprenorphine while implementing steps to address the problem, which may include but are not limited to:

1. Motivational interviewing (during your sessions) to decrease use
2. Dose adjustments of buprenorphine for clients who have cravings or withdrawal
3. Direct treatment for the co-occurring substance use with therapy or medication (including augmentation strategies for opioids such as clonidine)
4. Referral to 12-step or other community support groups

5. Treatment of co-occurring mental health problems that may be contributing to substance use (trauma, chronic anxiety, depression, insomnia), including psychotherapy in treatment options
6. Naloxone prescription and education
7. Family involvement if appropriate and agreeable to client
8. Long-acting injectable forms of buprenorphine (Sublocade, Brixadi) if adherence to MAT is inconsistent
9. Referral to methadone treatment if buprenorphine does not reduce opioid use
10. More frequent visits if the use of other substances is associated with deteriorating psychosocial functioning such as reckless behaviors, loss of employment, disrupted relationships, or criminality. A higher level of care such as residential treatment should be considered in these cases. However, if they cannot get to a higher level of care, giving buprenorphine is usually better than no treatment.
11. Given the high risk of fatality with the availability of high potency synthetic opioids like fentanyl, discontinuation of buprenorphine is very rarely a desirable step when drug use is discovered on UDS. The risk benefit equation has shifted to favor continued treatment with MAT even when individuals continue to use other drugs.

Before introducing change, assess their readiness to change. Most clients will not accept all recommendations. More important is to create a non-judgmental atmosphere that encourages honesty and treatment retention. That goal can be threatened when clients feel pressured to accept change they are not ready for.

Your own liability is covered by documenting your recommendations, rather than by whether the client followed them. Use neutral language to document whether the client "accepted" or "declined" (rather than "refused") the intervention. This is no different than the approach we take with clients who decline treatments like ECT for severe depression.

Referral sources: https://findtreatment.gov

Discontinuing Buprenorphine

There is no evidence indicating that there is a safe time to stop buprenorphine. On the contrary, data show that mortality increases six-fold in the month after stopping OUD treatment (Santo T Jr et al, *JAMA Psychiatry* 2021;78(9):979–993) and that longer duration of buprenorphine treatment is associated with better outcomes, at least for the first year (Hasan NM et al, *AM J Drug Alcohol Abuse* 2022;48(4):481–491). Encourage patients who are doing well on buprenorphine to stay on buprenorphine.

Nonetheless, some patients will insist on coming off medication. Most patients will experience withdrawal symptoms when the dose is lowered, so for these patients, prescribe a medication taper. Slower tapers are associated with lower rates of opioid use (Dunn KE, et al., *Drug Alcohol Depend* 2011; 119(1-2):1–9), so we recommend no more than at 20% reduction at any one time. Check in with your patients frequently during the taper process and adjust the taper schedule accordingly.

Reasons to Discontinue Buprenorphine

We stop buprenorphine because it is not working or is dangerous. It is a risk/benefit decision like any other in medicine, and nor a punishment. Factors that lead to discontinuation are usually signs that the patient needs a higher level of care and should be approached in that vein, as a therapeutic discussion.

If the patient declines a higher level of care, we might still continue buprenorphine and document the harm-reduction rationale. Generally it is best to err on the side of continuing treatment, as the risk of death from treatment discontinuation is serious.

Missed appointments, missed UDS's, and even suspicion of buprenorphine diversion are not in themselves reasons to discontinue treatment. In fact, studies find that most buprenorphine diversion is used to treat OUD in people who lack access to care.

Here are situations where you might consider discontinuing treatment:

- Patient is unable to attend appointments at a reasonable frequency for you to safely monitor their treatment (eg, misses 2 visits in a row). Warn the patient about ending care before taking this step and document this.
- Medical contraindications. There are no absolute contrainidications to buprenorphine other than hypersensitivity (allergy) to the medication (see Table 4).

Before acting on this, first remind the patient that they will need a higher level of care if the problem continues. When ending care, notify the patient and give referrals. Unless contraindicated, provide a one month prescription of buprenorphine.

TABLE 4. Contraindications and Precautions for Pharmacotherapy Options[3,63,64]

Medication	Contraindications	Warnings and Precautions
Methadone	1. Hypersensitivity 2. Respiratory depression 3. Severe bronchial asthma or hypercapnia 4. Paralytic ileus	1. Head injury and increased intracranial pressure 2. Liver disease 3. Respiratory insufficiency 4. Cardiac conduction effects 5. Drug interactions with medications metabolized by cytochrome p450 enzymes principally CYP34A, CYP2B6, CYP2C19, and to a lesser extent by CYP2C9and CYP2D6 6. Drugs co-administered with methadone, especially anti-retrovirals (including PrEP), anti-convulsants, and rifampin, should be evaluated for interaction potential 7. Diversion and misuse are possible 8. Physical dependence 9. Risk of life-threatening respiratory depression and death when used in association with benzodiazepines or other CNS depressants including alcohol, other opioid, and illicit drugs 10. Interaction with antidepressants and migraine medicines can cause a serious CNS reaction called serotonin syndrome 11. Addison's disease, a rare, but serious condition in which the adrenal glands do not produce adequate amounts of the hormone cortisol 12. Neonatal withdrawal after use of methadone during pregnancy
Buprenorphine (all formulations)	Hypersensitivity	1. Not recommended for patients with severe hepatic impairment 2. May cause sedation 3. Physical dependence 4. Risk of life-threatening respiratory depression and death when used in association with benzodiazepines or other CNS depressants including alcohol, other opioids, and illicit drugs 5. Precipitated withdrawal if used in patients physically dependent on full agonists opioids before the agonist effects have worn off 6. Interaction with antidepressants and migraine medicines can, in rare cases, cause a serious CNS reaction called serotonin syndrome 7. Addison's disease, a rare, but serious condition in which the adrenal glands do not produce adequate amounts of the hormone cortisol 8. Diversion and misuse are possible 9. Neonatal withdrawal after use of buprenorphine during pregnancy
Naltrexone (oral and injectable formulations)	1. Hypersensitivity reactions to naltrexone, or for injectable previous hypersensitivity reactions to polylactide-co-glycolide carboxymethylcellulose, or any other constituent of the diluent 2. Active hepatitis (hepatitis or if LFTs are > 3x normal) 3. Patients currently physically dependent on opioids, including partial agonists 4. Patients receiving opioid analgesics 5. Patients in acute opioid withdrawal	1. Vulnerability to overdose 2. Injection site reactions associated with injectable naltrexone 3. Precipitated opioid withdrawal 4. Administer IM injections with caution to patients with thrombocytopenia or a coagulation disorder 5. Risk of hepatotoxicity 6. Patient should be monitored for the development of depression and suicidality 7. Emergency reversal of opiate blockade may require special monitoring in a critical care setting 8. Eosinophil pneumonia has been reported in association with injectable naltrexone 9. Insufficient evidence of safety during pregnancy

Buprenorphine Formulations

Short-Acting		
Formulation	**Brand-name**	**Dosage Forms**
Buprenorphine	Subutex, generic	SL tablets 2mg, 8mg
	Butrans*	Transdermal patch 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr
	Buccal film*	Buccal Film 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, 900 mcg
	Buprenex, generic*	IV or IM injection 0.3mg/mL
Buprenorphine/naloxone	Generic	SL tablets 2mg/0.5mg, 8mg/2mg
	Suboxone	SL films 2mg/0.5mg, 8mg/2mg
	Zubsolv	SL tablets 0.7/0.18 mg, 1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg
	Bunavail	Buccal film: 2.1/0.3mg, 4.2/0.7mg, 6.3/1mg
Long-Acting		
Formulation	**Brand-name**	**Dosage Forms**
Buprenorphine	Sublocade	SC injection 100mg, 300mg
	Brixadi	SC injection mg, 16 mg, 24 mg, 32 mg (weekly) and 64 mg, 96 mg, 128 mg (monthly)

* approved for pain only, not OUD

The Bottom Line

Buprenorphine is a first-line treatment for OUD and now can be prescribed by anyone able to write for controlled substances. Patients can start buprenorphine with a carefully timed induction and increase the dose until they are free from withdrawal symptoms and opioid cravings. Consider long-acting injectable formulations for patients with poor adherence. Finally, encourage your patients to stay on buprenorphine.

—Chris Aiken, MD, with assistance from Noah Carpuso, MD and David Sack, MD

Further Learning

Practice guidelines from ASAM:
https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline

Quick guide:
https://www.samhsa.gov/sites/default/files/quick-start-guide.pdf

Psychotherapy for OUD:
https://store.samhsa.gov/sites/default/files/pep23-02-01-003.pdf

CME training

https://pcssnow.org/medications-for-opioid-use-disorder/8-hour-moud-education-options/

https://www.samhsa.gov/medications-substance-use-disorders/training-requirements-mate-act-resources

https://www.netce.com/specials.php

https://tnaap.org/education/mate-dea-training