



Issue Brief

Buprenorphine: An Overview for Clinicians

Buprenorphine, an FDA-approved medication for addiction treatment and pain relief, cuts opioid overdose death rates in half. Yet nearly 80% of Americans with opioid use disorder (OUD) do not receive buprenorphine or other medication-assisted treatment (MAT).

This document provides answers to frequently asked questions, aiming to increase prescriber comfort with prescribing buprenorphine throughout the health care system.* Once the basics are mastered, buprenorphine can be as straightforward to prescribe as medications for other medical conditions.

About Buprenorphine

Buprenorphine is one of three FDA-approved medications for treatment of OUD and for acute and chronic pain; the others are methadone and long-acting naltrexone. While methadone can be administered only in highly regulated opioid treatment programs¹ (OTPs), buprenorphine and naltrexone can be prescribed in a wide variety of settings.

Buprenorphine is a partial opioid agonist, meaning that it acts on certain opioid receptors in the brain, providing potent relief from pain, cravings, and opioid withdrawal symptoms, while acting as an antagonist on other opioid receptors. Buprenorphine has a “ceiling effect” on respiration: Increasingly higher doses do not decrease breathing to the same extent that other opioids do. Deaths due to buprenorphine overdoses are rare and usually involve multiple medications (e.g., benzodiazepines, alcohol, other opioids) or intravenous use.

RESOURCES

[Overcoming Common Objections to MAT](#) (CHCF)

Practice Guidelines

[National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use](#) (ASAM)

[Treatment Improvement Protocol 63: Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction](#) (SAMHSA)

[Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence](#) (World Health Organization)

[Clinical Practice Guideline for Management of Substance Use Disorder](#) (Dept. of Veterans Affairs)

[Model Policy on DATA 2000 and Treatment of Opioid Addiction in the Medical Office](#) (Federation of State Medical Boards)

Pregnancy

[Medications to Treat Opioid Use During Pregnancy — An Info Sheet for Providers](#) (SAMHSA)

Health Care Settings

- ▶ Rural areas and Native Americans / Alaska Natives: [California MAT Expansion Project](#)
- ▶ Emergency departments and hospitals: [California Bridge Program](#)
- ▶ Primary care: [Addiction Treatment Starts Here Resource Hub](#)
- ▶ Jails and the court system: [MAT in County Criminal Justice](#)
- ▶ Treatment centers and SUD counselors: [MAT in residential treatment](#)

*This document was originally published in 2017. It has been updated by Triveni DeFries, MD, MPH, and Scott Steiger, MD, to include more recent evidence and practices. The information is intended to serve as a guideline, not a replacement for individual medical judgment.

Stronger formulations (sublingual tablet or buccal film, injectable, or implant) are FDA-approved for OUD, while weaker formulations are FDA-approved for pain (injectable, patch, and buccal film). Formulations for OUD commonly include naloxone to prevent the medication from being snorted or injected. While the naloxone component is inert and typically will not cause symptoms when used as directed, if snorted or injected, it causes severe withdrawal symptoms. Formulations for pain are not FDA-approved for OUD under the Drug Addiction Treatment Act of 2000 (DATA 2000) and should only be used for patients with a chronic pain diagnosis.

Maintenance treatment with buprenorphine decreases all-cause mortality by approximately 50%. Importantly, short-term buprenorphine “detox” (using medications to manage the brief period of acute withdrawal symptoms) doubles the death rate compared to maintenance, and methadone detox triples the death rate compared to maintenance.² Patients treated with buprenorphine maintenance also show improved social functioning compared to people receiving counseling alone (so-called “detox and rehab”), with reduced criminal activity, lower rates of illicit substance abuse, and reduced risk of HIV and hepatitis infection.³

Buprenorphine Compared to Methadone and Naltrexone

A report from the National Academies advises that providers in any care setting should offer patients any of the three FDA-approved treatments for OUD.⁴ Patients and providers may use an [online decision tool](#) published by the Substance Abuse and Mental Health Services Administration (SAMHSA) to help patients make their decision.

Buprenorphine and methadone have both been proven effective in reducing all-cause mortality for patients with OUD.⁵ Methadone had a slightly higher retention rate in treatment both in randomized control trials and in community effectiveness studies. In the US, however, methadone maintenance treatment can only be provided by licensed OTPs, which have restrictive regulations

governing their care delivery. The OTP setting may be better suited to patients who have psychiatric instability, use of multiple substances, or other conditions that require close monitoring.

Long-acting naltrexone is a monthly injection that blocks the effects of opioids; it has been found to be superior to a placebo for treatment of OUD, with similar retention rates compared to buprenorphine in two short-term trials.⁶ However, trials have been limited by high drop-out rates, and the required one week of abstinence prior to initiating naltrexone can pose a major challenge to its use. Risk of overdose after discontinuation is also a concern, due to loss of tolerance. Studies of naltrexone show better results in patients with strong social supports and a high level of motivation for abstinence,⁷ and some patients prefer a nonopioid option. Oral naltrexone is effective for alcohol use disorder, but should not be used for OUD, as it was found to have a greater than threefold risk of overdose compared to buprenorphine or methadone in Australian studies (and a greater than sevenfold risk of overdose after discontinuation).⁸

Buprenorphine has several advantages: It is available in primary care and other health care settings, it can be given to stable patients with follow-up once a month or every three months, and its partial agonist properties help prevent overdose death. For a good review of the evidence for treatment options, see the [British Columbia opioid addiction guidelines](#), which recommends buprenorphine as first-line treatment, and methadone for patients failing trials of buprenorphine.⁹

Accessibility Obstacles

Nearly 80% of Americans with OUD do not receive treatment. Office-based treatment has increased, but availability does not meet the demand.¹⁰ Barriers to wide adoption include federal training requirements (clinicians must obtain a DEA waiver to use buprenorphine for addiction),¹¹ lack of knowledge and training, concern about paperwork burdens and prior authorization requirements, and stigma.

To overcome these obstacles, in 2015, Medi-Cal (California's Medicaid program) removed authorization requirements from buprenorphine sublingual and patch formulations; in response, buprenorphine prescriptions in Medi-Cal nearly quadrupled in four years.¹² In addition, the State of California launched the [MAT Expansion Project](#) in 2017, providing funding and technical assistance to integrate MAT into emergency departments (EDs), hospitals, primary care clinics, mental health clinics, jails, prisons, outpatient OTPs, syringe services organizations, street medicine programs, and beyond.

How to Start a Patient on Buprenorphine

Initial Assessment

Standard OUD care is moving toward a “medication-first” model, where patients are started on medications without extensive assessments, just as patients with psychosis are started on medications to stabilize them before starting behavioral health therapy.

After shared decisionmaking with the patient, a focused assessment can include the following:¹³

- ▶ History that establishes diagnosis of OUD using DSM-5 criteria; the frequency, amount, and routes of opioid use; and other drug or alcohol use
- ▶ History of drug treatment and discussion of treatment options — that is, buprenorphine vs. methadone vs. naltrexone
- ▶ Significant medical and psychiatric history (including suicidality), and active medication list and allergies

- ▶ Physical exam that is performed, referred for, or recently recorded, with attention to signs and symptoms of withdrawal or intoxication
- ▶ Laboratory testing is not required, but the following should be considered, initially or later in treatment: urine drug testing, pregnancy testing, liver function testing, hepatitis and HIV serologies
- ▶ State prescription drug monitoring program database ([CURES](#) in California) checked for controlled substances

Start-Up Strategies

Strategies for starting buprenorphine (“induction”) vary based on the patient's circumstances; the goal is to increase the patient's chances of success with the medication by making the process as comfortable and rapid as possible. Induction generally involves switching to buprenorphine from other opioids. Several protocols are available as guides (e.g., from [California Bridge](#)¹⁴ or the [Providers Clinical Support System](#)¹⁵).

Buprenorphine patches can be used to alleviate withdrawal symptoms during the transition; since patches are only FDA-approved for pain, they can only be used for patients with chronic pain diagnoses (with or without OUD), and not for those with only an OUD.¹⁶ See Appendix A for more detail.

Behavioral and social services are typically offered as part of treatment. However, medications may be started prior to a complete behavioral health assessment and consult, and without awaiting laboratory or urine test results, in order to lower barriers to treatment.

Initial Dosage

A starting dose of buprenorphine can vary based on the setting and circumstance, generally between 2 mg and 8 mg. Buprenorphine generally alleviates opioid withdrawal symptoms within 20 to 40 minutes after the first dose.

After the first dose, the patient should receive subsequent doses over the next 1 to 3 days, find an optimal dose, and reach a suitable maintenance dose within 1 to 2 weeks. (See the “Dosage, Duration, and Monitoring”

section for more information on maintenance.) Doses can be titrated based on withdrawal symptoms, cravings, additional opioid use, and side effects (see sidebar). Blood levels stabilize in 3 to 7 days.

Common Bumps in the Road

Nausea or headache. Dose may be too high; consider a dose reduction trial. Taste may be causing nausea; switch formulations. Inert components of the medication may be the cause of nausea or headache; consider switching formulation.

Difficulty taking sublingually. Remind patients not to swallow but to allow the medication to fully dissolve under the tongue. Films may dissolve faster; consider switching formulations.

Persistent withdrawal symptoms and cravings.

Explore how the patient is using the medication, pain or other triggers, and consider a dose increase. Note that some patients with high opioid tolerance require doses in the 16 to 24 mg range, and occasionally higher doses, to prevent relapse.

Managing Withdrawal Symptoms

Patients typically go 12 to 48 hours without other opioids before starting buprenorphine to avoid precipitated withdrawal symptoms. The [Clinical Opioid Withdrawal Score \(COWS\)](#) can help assess the patient's withdrawal severity.¹⁷

Medications such as nonopioid analgesics, antihistamines, anti-nausea medications, clonidine, and loperamide can be provided to the patient to increase comfort during the period of withdrawal. Buprenorphine patches can be used for patients with chronic pain diagnoses (see Appendix A).

Harm Reduction

Overdose prevention education and a prescription for naloxone (in case of overdose) should be provided to all patients considering or receiving buprenorphine, in case of return to use. They should be provided again if the patient discontinues medication treatment.

Lab testing for HIV and hepatitis, and immunization and treatment for hepatitis A, B, and C are especially important

for patients who have ever injected drugs, as are sterile needles for those at risk of ongoing injection drug use.

Just as many smokers require 30 or more quit attempts before they quit for good, multiple quit attempts may be required before a patient reaches full sobriety.¹⁸ Clinicians should treat a return to use with compassion, as part of the typical course of a chronic relapsing and remitting disease. In no case should patients be dismissed from treatment due to return to use or positive drug screens, nor should they be dismissed from treatment for using other substances (such as THC or methamphetamine); this only puts the patient at risk of overdose or other harm. Buprenorphine is effective for OUD and should not be discontinued only because the patient has other use disorders. Returns to use or ongoing positive urine screens may indicate the patient needs a higher level of care, and clinicians or their staff should develop relationships with opioid treatment programs to facilitate these transfers of care.

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Contraindications

Contraindications to starting buprenorphine include a demonstrated drug allergy, or active sedation or intoxication. Based on a case report, the inactive naloxone component of combined products may build up in patients with moderate to severe hepatic impairment, so buprenorphine monoprodut (without naloxone) may be preferred in advanced cirrhosis.¹⁹ The buprenorphine monoprodut is commonly used in pregnancy, but pregnancy is not a contraindication to the combined product.²⁰ There are no other absolute contraindications to buprenorphine use.

Where Can a Patient Start Buprenorphine?

Buprenorphine can be started in a wide variety of settings, including primary care clinics, specialized induction clinics, at home, EDs, hospitals, correctional institutions, residential facilities, OTPs, and via telehealth. Some details follow.

Primary Care

Primary care clinics can provide the most accessibility and continuity for many patients. Some settings offer specialized clinics for addiction and/or pain and for induction. Some are connected to “bridge” programs that link patients from other settings, such as emergency departments, to ongoing services.²¹

Induction Clinics

Specialized clinics devote time and staff resources to intake, assessment, evaluation of options, education, medication starts, and monitoring. These clinics relieve primary care practices of the intensity and frequency of visits associated with patients newly starting on buprenorphine. The patients can be transferred back to primary care when they are stable on monthly prescriptions. This approach has been used successfully for over 15 years in San Francisco at the [Office-Based Buprenorphine Induction Clinic](#). A similar hub and spoke model is used in Vermont and California, where complex patients go to the hub (an opioid treatment program), and stable patients are managed at the spokes (typically primary care practices).²²

Home Starts

To increase convenience for the patient and decrease the burden on the office practice, home inductions are increasingly common and can be offered from primary care or the ED. SAMHSA and most recent literature support either the clinic- or home-based approach.²³ With a home start, the patient is given instructions on how to monitor withdrawal symptoms and when to take the first dose (see examples of low-literacy patient materials in [English](#) and [Spanish](#)). Education, frequent office visits, and telephone or text outreach can maximize support for the patient during the transition period. Clinic-based starts or referral to opioid treatment programs could be used for those needing closer monitoring (e.g., psychiatric instability).

ED and Hospital Settings

Patients who are identified with OUD or who overdose in the ED or hospital can be started on buprenorphine or methadone (see the [ED-Bridge](#) website for resources and tools). Any licensed provider in any setting, including the ED, can administer buprenorphine to a patient with opioid use disorder for up to three consecutive days without a DEA waiver (*administration* is defined as giving a medication under observation, as opposed to *prescribing*, defined as giving a prescription to be filled at a pharmacy).²⁴ There is no three-day limit for patients admitted to the hospital for medical conditions — they can be treated with buprenorphine or methadone by any licensed provider, without a DEA waiver, to prevent withdrawal from complicating their medical condition.²⁵

EDs and hospitals are increasingly recognizing their role in treating the root cause of opioid-related injury and illness by starting MAT and then expediting referral to outpatient treatment. Peers or substance use treatment navigators can help ensure patients are linked to treatment and recovery programs.

If opioids are indicated for pain, buprenorphine can be a safer choice for patients with active or historical substance use, and can be administered sublingually, by patch, or by injection (intravenous or intramuscular) while in the ED. Formulations indicated for pain are weaker

DEA Waiver Exceptions

Clinicians do not need a DEA waiver to provide buprenorphine in these circumstances:

- ▶ **When treating a patient for pain.** Any formulation — whether FDA-approved for addiction or pain — can be prescribed to any patient with a pain diagnosis.
- ▶ **When treating a patient hospitalized for a medical condition.** Both buprenorphine and methadone can be ordered to prevent withdrawal from complicating the medical condition.
- ▶ **When managing withdrawal while facilitating entry into treatment.** For at most three days, and as long as the buprenorphine is administered (given under observation) as opposed to prescribed.

Source: “Special Circumstances for Providing Buprenorphine,” SAMHSA, last modified March 4, 2019, www.samhsa.gov.

than those used in addiction and are unlikely to prevent cravings and return to use in patients with OUD. Providers with DEA waivers can also prescribe buprenorphine to be filled at a pharmacy and taken at home.

Correctional Facilities and Residential Treatment

Correctional facilities and residential treatment facilities also can start patients on MAT. See these resource pages about [MAT in corrections](#)²⁶ and [MAT in residential treatment](#)²⁷ for more information and tools. Some OTPs also provide buprenorphine as an option in addition to methadone.

Telehealth

Telehealth MAT is an alternative to in-person treatment and is growing in response to widespread demand for more-convenient and private options. At the time of publication, the Ryan Haight Online Pharmacy Consumer Protection Act of 2008 requires one initial in-person visit prior to prescribing buprenorphine (and other controlled substances) through telehealth, followed by another in-person visit every 24 months. The 21st Century Cures Act of 2016 directed the FDA to amend the law to decrease barriers to care; at the time of publication, these regulations had not yet been defined. In the meantime, several MAT telehealth companies are providing virtual individual and group services after an initial in-person visit. For information, see [Innovation Landscape: Telehealth MAT](#)²⁸ and [Using Telehealth to Provide Medication-Assisted Treatment in Medi-Cal](#)²⁹ on the unique challenges and opportunities in providing telehealth in California's Medicaid program.

Dosage, Duration, and Monitoring

Maintenance Dosage

The optimal dose to promote recovery and prevent return to use is different for every patient and generally varies between 4 and 32 mg daily (based on the bioavailability of the commonly used buprenorphine or buprenorphine/naloxone sublingual tablets and film). Greater rates of retention in treatment and suppression of illicit opioid use have been found at doses of 16 mg or greater. The maximum dose is generally considered to be 32 mg, although the FDA package insert states that doses higher than 24 mg have not been demonstrated to have a clinical advantage in the treatment of OUD. Some states and settings have imposed regulations on the upper limit of dosing.

Buprenorphine can be dosed one to three times a day. Because of its long-acting properties, it can also be dosed three times a week under observation. Daily dosing may enhance adherence, but taking buprenorphine every six to eight hours provides better pain management for patients with chronic pain. Because buprenorphine is a Schedule III drug, refills can be called in or faxed. Appendix B lists the formulations and dosages available.

Treatment Duration: Detox, Maintenance, Tapering

Addiction specialists now consider opioid use disorder to be a chronic disease, and this perspective informs treatment. Although buprenorphine can be used in short-term detoxification programs, addiction experts increasingly discourage this approach and instead advise continuing buprenorphine long-term, attempting tapers only after one to two years if strongly desired by the patient and if the patient can be closely monitored for return of cravings or opioid use.³⁰ Patients who stop buprenorphine during the first few months of their treatment experience high rates of return to use, even with intensive behavioral support.³¹ In a 2015 long-term treatment study, only 9% of patients remained abstinent after buprenorphine taper, while 80% of patients reported abstinence at 18 months and 42 months if they continued daily

buprenorphine treatment.³² Without long-term treatment, patients often return to illicit opioid use, and if they have been abstinent for a period of time, tolerance to opioids is lost: the amount of drug tolerated prior to abstinence can be enough to cause overdose death. A large meta-analysis showed that overdose death rates double after buprenorphine discontinuation, and they triple after methadone discontinuation.³³

Detoxification and tapering with buprenorphine or methadone is still superior to providing no medication at all and can be considered in circumstances when well-informed patients specifically desire detoxification after counseling about risks and options.

The DSM-5 criteria define remission as at least 12 months without meeting criteria for OUD other than craving.³⁴ For patients in remission wanting to stop medications, the American Society of Addiction Medicine (ASAM) recommends tapering slowly over several months. When tapering, smaller doses can be used by dividing 2 mg tablets or films into smaller segments. The smallest fraction that can be realistically achieved is one-half (1 mg) and one-quarter (0.5 mg) of a 2 mg tablet or film. Lower doses of buprenorphine approved for pain are available for patients who also have a pain diagnosis. Patients who are discontinuing the medication should be offered additional support, such as follow-up visits, overdose prevention counseling, and naloxone.

Ongoing opioid use is common in patients on maintenance treatment. Over time, opioid use typically decreases; however, return to use may still occur and should be addressed therapeutically and not punitively. Instead of discontinuing treatment when the patient returns to use, an appropriate response is to increase the dose of buprenorphine to better control cravings, while increasing the intensity of monitoring: either observed dosing in the office or at the pharmacy, or decreasing the prescribed supply. Some patients will need daily dosing, and arrangements can be made with the pharmacist to dispense one day at a time. If the patient returns to active addiction, consider the possible need for a higher level of care (such as an opioid treatment program). Transitions between providers and treatment settings are high risk, and efforts should be made to coordinate transitions to ensure no interruption in treatment.

Monitoring and Diversion

Patients should have follow-up visits that entail regular urine drug screens including urine buprenorphine testing. In most patients who are regularly taking buprenorphine, the norbuprenorphine-to-buprenorphine ratio should be greater than one. If the ratio is less than one, or if no norbuprenorphine (or buprenorphine) is detected, the patient may not have been taking the medication regularly. In some cases, extremely high buprenorphine levels indicate that patients have tampered with the urine specimen. When discrepancies are found, patients should be given the benefit of the doubt and approached in a compassionate and caring way. There may very well be understandable explanations, and urine toxicology is only one method of treatment monitoring.

Prescription drug monitoring programs (CURES in California) should be checked regularly (California law requires one check for new patients and then checks every four months).³⁵ Patient opioid use, cravings, and withdrawal symptoms should be assessed. As in follow-up for any chronic disease, providers should assess medication adherence, benefits, and adverse effects.

Buprenorphine is occasionally diverted — given or sold — to people who are not prescribed the medication. Sharing medication often occurs in areas with limited access to treatment. Strategies to address diversion can include discussion with patients and their social supports, pill counts, shorter-duration prescriptions, urine testing, and avoiding doses >24 mg. Both mono- and coformulated (with naloxone) buprenorphine are diverted, most often to people actively addicted to opioids who are self-managing their withdrawal.³⁶

ASAM has created several documents to help members and other physicians understand best practices to prevent diversion:

- ▶ [Sample Diversion Policy](#) (PDF)³⁷
- ▶ [Sample Treatment Agreement](#) (PDF)³⁸
- ▶ [Adherence, Diversion and Misuse of Sublingual Buprenorphine](#) (PDF)³⁹

Substance Use

Many patients with OUD have other concurrent substance use disorders. Stabilizing OUD with medications provides the opportunity to address other substance use disorders, and each disorder merits its own treatment plan. Use of substances such as marijuana, methamphetamine, benzodiazepines, cocaine, or other drugs should not preclude treatment of OUD with buprenorphine, according to ASAM.⁴⁰ Some patients with multiple substance use disorders may benefit from the intensive treatment of an OTP setting.

Cannabis use has not been shown to worsen outcomes for patients on buprenorphine for OUD.⁴¹ The California Society of Addiction Medicine recommends continuing buprenorphine for patients using cannabis and treating patients for marijuana use disorder, if present.

Studies have shown that patients using other drugs, like cocaine, have similar success with buprenorphine compared to patients without other drug use.⁴²

Buprenorphine should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system, according to the FDA⁴³ and SAMHSA (Treatment Improvement Protocol 63: “Some patients may have taken appropriately prescribed benzodiazepines for years with limited or no evidence of misuse. For such patients, tapering benzodiazepines may be contraindicated and unrealistic.”)⁴⁴ While acknowledging that use of benzodiazepines or alcohol with buprenorphine or methadone increases the risk of side effects, the FDA notes that risk of overdose is highest when people are not on medications to treat OUD. Use of these substances should be discussed with patients, and when a use disorder is present, it should be treated.

Loss of control is common for patients with chronic disease, whether diabetes, hypertension, or OUD. The provider should address return to use as a part of the treatment course. Additional counseling and support, dose adjustments, increased monitoring and frequency of visits should be offered to patients who return to using opioids. Return to use should not be used as a basis for dismissal from treatment and discontinuing buprenorphine, but rather for intensification of treatment.⁴⁵

Patients frequently relapsing on buprenorphine treatment should be considered for a higher level of care, such as at an OTP.

Behavioral Health Treatments

Many — but not all — people with OUD benefit from additional counseling or mental health services.⁴⁶ These do not need to be provided by the prescribing provider. Per SAMHSA, the standard of care requires that a provider be able to refer patients on buprenorphine to behavioral health treatment but does not mandate that they do so, nor does it specify the type of treatment.⁴⁷ Patients are not required to accept referrals to behavioral health services, and these services do not have to be located on-site or delivered in person. Providers should not hesitate to initiate and/or continue buprenorphine for patients who are not engaged in special counseling or psychosocial services.⁴⁸

Two studies are reassuring for communities with insufficient behavioral health resources, and for patients who decline psychosocial treatment. One randomized controlled trial showed that buprenorphine is effective even without behavioral counseling beyond the usual care provided by good primary care providers.⁴⁹ A 2016 ASAM review found mixed support in the literature for behavioral health interventions for opioid addiction, and it may be reasonable to consider a step-up approach, with more-intensive behavioral management for the patients who need it.⁵⁰

Buprenorphine for treatment of opioid use disorder should not be withheld from patients who do not participate in behavioral health services. Extensive evidence demonstrates that routine visits with a medical provider doing regular medication management may be all that some patients need to attain stability and regain control over their lives. At the same time, many patients will be helped by supports such as motivational interviewing by a clinic provider, peer support groups, case management, social supports, vocational training, counseling, and cognitive behavioral therapy. Contingency management techniques (small incentives, such as bus passes, movie tickets, or gift cards, tied to healthy behaviors) have been consistently demonstrated to improve adherence to

medication and to decrease drug use. Options can be offered and tailored to the individual patient.⁵¹

Pain Management with Buprenorphine

Buprenorphine is a potent pain reliever with particular advantages for patients with chronic pain or pain complicated by OUD. Any provider licensed by the DEA (e.g., physician, nurse practitioner, physician assistant, midwife, clinical pharmacist) can prescribe buprenorphine for pain without a DEA waiver. The DEA clarified that “limitations and requirements [relating to addiction treatment] in no way impact the ability of a practitioner to utilize opioids for the treatment of pain when acting in the usual course of medical practice. Consequently, when it is necessary to discontinue a pain patient’s opioid analgesic therapy by tapering or weaning doses, there are no restrictions with respect to the drugs that may be used. This is not considered detoxification as it is applied to addiction treatment.”⁵² If the target condition is pain, then buprenorphine can be compounded by a compounding pharmacy to create low doses, or low doses of the buccal and patch formulations can be used. For example, one month of each strength of the buprenorphine patch (20, 15, 10, 7.5, and then 5 mcg/hour) is one effective method of gradually tapering buprenorphine in a patient with a pain diagnosis. Buprenorphine in formulations for pain cannot be used for patients with addiction and without a pain diagnosis due to FDA restrictions.

Advantages of Using Buprenorphine for Chronic Pain

Buprenorphine provides excellent pain control. It has an excellent safety profile due to a ceiling effect on respiratory suppression (meaning higher doses will not stop breathing and only rarely cause overdose). Buprenorphine’s onset of action is 30 to 60 minutes, and it typically provides eight hours of pain relief, so it is usually given in divided doses when used for pain unless the patch formulation is used.

Like any opioid, buprenorphine should be used sparingly, and only when the benefit outweighs the risk.

Buprenorphine can be a safer analgesic choice than other opioids for:

- ▶ Patients with severe acute pain and who have current or historical substance use disorders, especially in ED or hospital settings where patient histories are unavailable
- ▶ Patients dependent on long-term opioids for pain, especially for those either experiencing negative effects from long-term opioid use or taking opioids at potentially unsafe doses

Unlike other long-acting opioids, buprenorphine has relatively few drug/drug interactions and does not accumulate in patients with renal impairment. Due to long half-life, partial agonist activity at the mu receptor, and antagonism at the kappa receptor, common medical problems resulting from other long-acting opioids arise less frequently with buprenorphine.⁵³ These problems include sleep apnea, low testosterone, sexual dysfunction, osteopenia, opioid-induced hyperalgesia, mood disorders (depression and anxiety), and dysregulation of the hypothalamic pituitary adrenal axis. A growing body of literature shows improved pain relief on buprenorphine after conversion from other long-acting opioids.⁵⁴

While some patients may be hesitant to switch to a medication associated with addiction treatment, the potential for relief of the common side effects of full agonist opioids described above can be compelling. Other patients are motivated by the fact that buprenorphine is a Schedule III medication (refills can be called in) as compared to Schedule II medications.

Elderly Patients with Chronic Pain

For elderly patients using long-term opioids, transitioning to buprenorphine lowers the risk of accidental overdose and potentially lowers the risk of medical complications (e.g., sleep apnea and hypogonadism). For this reason, buprenorphine may be a safer choice for elderly patients already on daily opioid treatment.

Treating Pain in the Emergency Department and Hospital

Buprenorphine can be effectively used for pain management by ED and inpatient clinicians without a DEA waiver. Advantages of buprenorphine as a first-line opioid analgesic, when opioids are indicated, include lower abuse potential, lower risk for respiratory depression, longer duration of pain relief, and (for patients with OUD) potential lower risk of triggering return to use. As with all opioid analgesics, buprenorphine should be used sparingly for pain after both nonpharmacologic interventions and nonopioid analgesics have failed.

Hospitalized and Perioperative Patients on Buprenorphine

Discontinuing methadone or buprenorphine in the hospital puts patients at risk for pain exacerbation, return to use, and longer lengths of stay; in addition, patients face logistical challenges starting back on buprenorphine after discontinuation.⁵⁵ SAMHSA now recommends maintaining buprenorphine in the perioperative period.⁵⁶

Continuing buprenorphine, with additional analgesia when needed, has been shown in recent studies to be an effective way of managing inpatient and perioperative pain, and may lower length of stay compared to buprenorphine discontinuation.⁵⁷ Additional doses of buprenorphine or other opioids can be given simultaneously with maintenance doses for satisfactory pain relief.

A DEA waiver is not required to administer or dispense buprenorphine or methadone for hospitalized patients admitted for a primary medical problem other than opioid dependency.⁵⁸

Prescribing Buprenorphine in Medi-Cal

OUD. Medi-Cal does not require prior authorization (Treatment Authorization Request, or TAR) when prescribing buprenorphine for addiction. Prescribers should include their DEA waiver number (the provider's DEA number preceded by an "x") and "Dx: Opioid Dependence" or "Dx: OUD" on the prescription. Pharmacies should send the claim to fee-for-service Medi-Cal, not the managed Medi-Cal plan, as all buprenorphine products are carved out from managed care.

Pain. Medi-Cal does not require a TAR for the sublingual, transdermal, and buccal buprenorphine formulations for pain; all other formulations for pain require a TAR. Prescribers should write a justification on the script about why other covered drugs are not appropriate (e.g., inadequate response to other opioids or the buprenorphine patch, or improved safety over full agonists.) The pharmacist will use this information to complete a TAR and send it to FFS Medi-Cal for review.

Legal and Administrative Facts

Laws Regulating Buprenorphine Prescribing

The Drug Addiction Treatment Act of 2000 (DATA 2000) allowed physicians with eight hours of special training to prescribe buprenorphine for addiction. (Prior to that, physicians were prohibited from treating opioid addiction with opioids outside of OTPs.) The Comprehensive Addiction and Recovery Act of 2016 allowed nurse practitioners and physician assistants to prescribe buprenorphine for addiction after completing 24 hours of certified training.⁵⁹ In 2018, the Substance Use–Disorder Prevention That Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act authorized clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives to prescribe buprenorphine as well.⁶⁰

Clinicians may treat a maximum of 30 patients at a time during the first year and 100 patients per year thereafter. The patient cap can increase to 275 patients for physicians board-certified in addiction, or those in practices that meet certain qualifications: 24-hour call coverage,

use of health information technology, provision of case management services, registration with the state prescription drug monitoring database, and acceptance of third-party insurance. Clinicians can submit a notification of intent to SAMHSA in order to expedite treating their first patient before the DEA waiver has been fully processed.

Federal regulations explicitly state that providers do not need a DEA waiver to order buprenorphine to be administered to a patient who is hospitalized, or for a patient with a pain diagnosis. The “three-day rule” also allows buprenorphine administration (not prescription) by any licensed provider in any setting for up to three days while a patient is transitioning into ongoing treatment.⁶¹ The California Department of Public Health released a letter in 2019 advising that no state regulations or statutes prohibit this either.⁶²

Find buprenorphine-waivered clinicians by visiting the **SAMHSA Buprenorphine Practitioner Locator**.

Getting Prescriptions Approved by Health Plans

Medi-Cal, California’s Medicaid program, and many other Medicaid and commercial health plans have removed prior authorization requirements for buprenorphine used for addiction. Prescribers can decrease delays by writing their DEA waiver number (DEA license number preceded by “x”) and the diagnosis (e.g., opioid dependence or OUD) on the prescription. When prescribed for pain, it is helpful to write the pain diagnosis and justification on the script as well.

Prescribers should confirm that their local pharmacy stocks buprenorphine and that, in states where substance use disorder treatment is carved out of managed care, the pharmacist knows the procedure for billing Medicaid. Pharmacies can be partners in addiction treatment by working with prescribing doctors to dispense small supplies of buprenorphine for high-risk patients and by alerting the prescriber when the patient is having difficulty, such as sedation.

Medicare Part D plans are required to cover buprenorphine formulations for addiction but may require prior authorization. Information written on the prescription to justify its use will expedite the pharmacy’s ability to obtain authorization.

Commercial insurance plans have different rules about buprenorphine coverage for pain and addiction and may require the prescriber to contact the plan or submit an authorization form.

Documentation Required by Federal and/or California Laws

Chart documentation for patients on buprenorphine should explain the diagnosis and severity of opioid use disorder by DSM-5 criteria, indications and benefits of treatment, monitoring, and patient’s progress or challenges in treatment.

Informed consent and treatment agreements are often used in practice, but they have not been studied and should not be implemented in a way that increases barriers to treatment (e.g., they should not be used to fire patients from care). They can be used as a tool for communication and education.

Both federal regulations (at 42 CFR Part 2) and California law (Cal. Civil Code § 56.11) include restrictions on disclosure of patient information related to substance use disorder treatment that are stricter than those for other health information. The applicability of these rules varies depending on the type of provider, whether the provider “holds themselves out” as a substance use treatment provider, and the sources of funding. For more information, see the California Health Care Foundation’s *Fine Print: Rules for Exchanging Behavioral Health Information in California* and resources from ASAM and SAMHSA.⁶³

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About the Foundation

The California Health Care Foundation is dedicated to advancing meaningful, measurable improvements in the way the health care delivery system provides care to the people of California, particularly those with low incomes and those whose needs are not well served by the status quo. We work to ensure that people have access to the care they need, when they need it, at a price they can afford.

CHCF informs policymakers and industry leaders, invests in ideas and innovations, and connects with changemakers to create a more responsive, patient-centered health care system.

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Appendix A. Buprenorphine Transdermal (Patch) Transition for Patients with Chronic Pain Diagnosis

The following protocol was developed by Howard Kornfeld, MD. For more information, see “Transdermal Buprenorphine, Opioid Rotation to Sublingual Buprenorphine, and the Avoidance of Precipitated Withdrawal: A Review of the Literature and Demonstration in Three Chronic Pain Patients Treated with Butrans,” *The Use of Transdermal Buprenorphine Patches in Aiding in Opioid Withdrawal: Clinical Effectiveness and Guidelines* and “Transdermal Buprenorphine to Switch Patients from Higher Dose Methadone to Buprenorphine Without Severe Withdrawal Symptoms.”⁶⁴

Background

With changing prescribing practices, many patients taking high-dose opioids for years are being tapered to lower doses or off opioids altogether. However, people with long-term opioid use for pain develop the same neurochemical changes seen in addiction, and opioid discontinuation is poorly tolerated, especially when done abruptly. In a large review study, half of those tapered off opioids were tapered abruptly, and half of these were hospitalized or admitted to the ED for opioid-related diagnoses.⁶⁵

Buprenorphine can be a safer and better-tolerated option for patients with long-time opioid agonist use. Using buprenorphine patches during induction can ease the symptoms of withdrawal during the transition.

Note: This protocol is for patients with pain diagnoses (with or without OUD). The buprenorphine products that are FDA-approved for pain and not addiction cannot be used for patients with OUD and no chronic pain diagnosis. The information is intended to serve as a guideline, not a replacement for individual medical judgment.

Buprenorphine Patch Induction

STEP 1. If patient is on methadone, first transition to another opioid agonist.

Choose an opioid agonist (morphine, oxycodone, hydromorphone, hydrocodone, or oxymorphone), and calculate the morphine equivalent ([online calculator](#)).⁶⁶ Due to individual variability, use caution when calculating the morphine equivalent dose: Use 30% to 50% less than the dose calculated by any conversion calculator, and prescribe only a small quantity of pills at a time.

- ▶ **Patient on <50 mg methadone.** Replace all methadone with long-acting opioid for 3 to 4 days.

- ▶ **Patient on 50 mg to 100 mg methadone.** Replace half of methadone with long-acting opioid for 3 to 4 days, then replace the other half for 3 to 4 days.
- ▶ **Patient on >100 mg methadone.** Replace one-quarter to one-half of methadone with long-acting opioid for 3 to 4 days and repeat in two to four steps.

STEP 2. Use buprenorphine patch to transition off long-acting opioids.

Prescribe the following medications:

- ▶ **Buprenorphine patches.** Use 20 mcg/hour for patients on MME \geq 100, and 10 mcg/hour for patients on MME <100. (Patches come in 5, 10, and 20 mcg/hour; each box contains four patches; some pharmacists are willing to split up boxes).
- ▶ **Buprenorphine sublingual 2 mg #12.** The buprenorphine mono product (without naloxone) is less expensive than the combination product, with similar efficacy; either can be used.
- ▶ **Four days of short-acting opioid agonists.** 30% to 50% less than the current long-acting opioid dose.

Instruct the patient to use the last long-acting opioid dose at night and place the patch in the morning. Short-acting opioids can be used as needed before and after patch placement.

STEP 3. Start sublingual buprenorphine after 3 to 4 days on the patch.

Note: Home starts on sublingual buprenorphine are appropriate for stable patients with good support, when the office can be contacted for questions; otherwise, the first sublingual buprenorphine doses should be observed in the office.

After 3 to 4 days, instruct the patient to take the last short-acting opioid dose at night and start 1 mg (half-tablet) in the morning. The patient can take another 1 mg dose later in the day.

Increase dose by 2 to 4 mg every 3 days, as needed to control pain and cravings, to a maximum of 24 mg. Unlike those with OUD, many patients with chronic pain do well on lower doses.

The slow onset of the buprenorphine delivered through the patch system should prevent precipitated withdrawal. Once higher doses of sublingual buprenorphine are tolerated, discontinue the patch.

Appendix B. Buprenorphine Formulations, by Type

TYPE/NAME	DOSAGE FORM	ADULT DOSING
Buprenorphine/Naloxone		
Buprenorphine/naloxone (Suboxone, also available as generic)	Sublingual film	2 mg — 0.5 mg, 4 mg — 1 mg, 8 mg — 2 mg, 12 mg — 3 mg
Buprenorphine/naloxone (Bunavail)	Buccal film	2.1 mg — 0.3 mg, 4.2 mg — 0.7 mg, 6.3 mg — 1 mg
Buprenorphine/naloxone	Sublingual tablet	2 mg — 0.5 mg, 8 mg — 2 mg
Buprenorphine/naloxone (Zubsolv)	Sublingual tablet	0.7 mg — 0.18 mg, 1.4 mg — 0.36 mg, 2.9 mg — 0.71 mg, 5.7 mg — 1.4 mg, 8.6 mg — 2.1 mg, 11.4 mg — 2.9 mg
Buprenorphine Monoprodukt (analgesic)		
Buprenorphine (Belbuca)	Buccal film	75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, 900 mcg
Buprenorphine (Butrans, also available as generic)	Transdermal patch, extended release	5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr
Buprenorphine Hydrochloride (Subutex, also available as generic)	Sublingual tablet	2 mg, 8 mg
Injectable/Extended Release		
Buprenorphine (Probuphine)	Intradermal implant	74.2 mg
Buprenorphine Hydrochloride (Buprenex, also available as generic)	Injection solution	0.3 mg/1 mL
<i>Used for analgesia, not for OUD.</i>		
Buprenorphine (Sublocade 100 mg, Sublocade 300 mg)	Subcutaneous solution	100 mg/0.5 mL, 300 mg/1.5 mL

Note: Buprenorphine 8 mg sublingual tablet = buprenorphine/naloxone 8 mg/2 mg sublingual film = buprenorphine/naloxone 4.2 mg/0.7 mg buccal film = buprenorphine/naloxone (Zubsolv®) 5.7 mg/1.4 mg sublingual tablet.

Sources: "Buprenorphine" and "Buprenorphine Hydrochloride," IBM Micromedex, accessed March 28, 2019, www.micromedexsolutions.com (REQUIRES LOGIN); "Buprenorphine" and "Buprenorphine and Naloxone," Lexi-Drugs, accessed April 1, 2019, online.lexi.com (REQUIRES LOGIN); search results for "Buprenorphine," DailyMed, Natl. Library of Medicine, n.d., dailymed.nlm.nih.gov/dailymed; and UCSF, Clinician Consultation Center, www.nccc.ucsf.edu.

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