California Health Care Foundation

Buprenorphine:
Everything You Need to Know

OCTOBER 2016

Buprenorphine, a medication that is FDA-approved for addiction treatment and pain relief, has also been found to dramatically decrease death rates from opioid overdose. Only 10% of patients needing treatment, however, have access to the medication.

This document provides answers to frequently asked questions about buprenorphine and supplements the California Health Care Foundation (CHCF) webinars **"Expanding Access to Buprenorphine in Primary Care Practices"** and **"Is Buprenorphine for Pain a Safer Alternative to High-Dose or Long-Term Opioid Use?"**[1,2] The clinical information contained in this paper is intended to act as a guideline, not a replacement for onsite medical judgment. Based on information covered in the CHCF webinars, the content was reviewed by addiction specialists Howard Kornfeld, MD, James Gasper, PharmD, and Andrew Herring, MD.

Background

Buprenorphine is an opioid medication approved by the Food and Drug Administration (FDA) for treatment of opioid dependence and for acute and chronic pain. It is a partial opioid agonist, meaning that it acts on certain opioid receptors in the brain, providing potent relief from pain and from opioid withdrawal symptoms, while acting as an antagonist on other opioid receptors, resulting in its unique pharmacology.[3]

Buprenorphine has a "ceiling effect" on respiration; that is, increasingly higher doses do not affect breathing in the same way 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). Some formulations (higher dose sublingual tablet, sublingual film, and implant) are FDA-approved for opioid use disorder, while others are FDA-approved for pain (injectable, patch, and buccal mucoadhesive film).

Per the Drug Addiction Treatment Act of 2000 (DATA 2000), physicians need a waiver to prescribe buprenorphine for addiction; attendance in an eight-hour in-person or online course is required to obtain a waiver. The Comprehensive Addiction and Recovery Act of 2016 allows nurse practitioners and physician assistants to prescribe buprenorphine treatment after 24 hours of certified training. Clinicians are capped at 30 patients the first year and 100 patients per year thereafter. The cap increases 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 care management services, registration with CURES (Controlled Substance Utilization Review and Evaluation System, California's prescription drug monitoring database), and acceptance of third-party insurance. Patients using buprenorphine for pain relief and not addiction are not included in federal cap requirements.

Any provider licensed by the Drug Enforcement Administration (DEA) (e.g., physician, nurse practitioner, physician assistant) can prescribe buprenorphine for pain. As a Schedule III drug, buprenorphine can be ordered by phone or fax, and refills can be included on the original prescription. In contrast, Schedule II drugs, such as hydrocodone, require tamperproof prescriptions and one-month supply limits with no refills.

Treatment with buprenorphine has been proven effective in opioid addiction, decreasing mortality by approximately 50%. Patients treated with buprenorphine show improved social functioning with increased retention in treatment (67% at one year) compared to drug-free treatment (7% to 25% at one year), reduced criminal activity, lower rates of illicit substance abuse, and reduced risk of HIV and hepatitis infection.[4-8]

Buprenorphine is a potent pain reliever with particular advantages for patients with chronic pain or pain complicated by opioid dependence. Although traditional practice has been to discontinue buprenorphine during hospital admissions, new research shows that buprenorphine can be continued when patients are admitted to the hospital, with pain controlled by other opioids used on top of the baseline buprenorphine regimen.[9-11] Studies of patients on high-dose opioids transitioned to sublingual or buccal buprenorphine have shown improved pain control, improved control of psychiatric symptoms, and much lower risk of overdose death.[12,13]

Patients commonly start buprenorphine in a clinician's office after 12 to 48 hours of withdrawal symptoms — a process known as an induction — since sublingual buprenorphine often causes severe withdrawal symptoms if started shortly after use of other opioids. Patients with pain diagnoses can avoid these symptoms, however, by using a fentanyl or buprenorphine patch, which minimizes or eliminates withdrawal symptoms.[14] It should be noted that these patches are FDA-approved for pain, not addiction: A DEA letter clarified that there is no restriction on the use of buprenorphine for pain relief (even for the high-dose sublingual formulations approved for addiction and prescribed off-label for pain).[15] To increase convenience for the patient and decrease the burden on the office practice, home inductions are now in more frequent use; in these cases, the patient is given instructions on when to take the first dose and how to monitor withdrawal symptoms.

California does not have adequate buprenorphine prescribers to meet the growing demand for treatment. As a result, only 10% of those needing opioid addiction treatment with buprenorphine are able to access it. Buprenorphine remains inaccessible to most patients with addiction or chronic pain due to many obstacles: not enough waivered physicians, lack of understanding about its use, the paperwork burden from health plan authorization requirements and from tracking patients to stay under the cap limit. To overcome these obstacles, in 2015 Medi-Cal removed authorization requirements from buprenorphine sublingual and patch formulations.

Published Studies on Buprenorphine

The following are important studies on buprenorphine's effectiveness in treating opioid addiction:

- A randomized, **controlled study from Sweden** compared detox plus placebo to detox plus maintenance buprenorphine: 4 out of 20 (20%) died of overdose in the first year in the placebo group, compared to 0 deaths in the buprenorphine group.[16]
- Patients on opioid maintenance therapy (buprenorphine or methadone) are less likely to contract **hepatitis C** and **HIV**.[17,18]
- More than **9 of 10 people** continue to use opioids after an overdose event. An overdose should be a signal that the patient is at high risk of death, immediately triggering a plan to taper to a safer regimen of prescribed opioids, offer take-home naloxone, or consider addiction treatment (buprenorphine or methadone) when appropriate.[19]
- The Prescription Opioid Addiction Treatment Study **(POATS) trial** evaluated short- and long-term buprenorphine treatment. Of those patients tapered off at 12 weeks, 9% reported abstinence compared to 50% of those continuing treatment. Patients using buprenorphine were more than twice as likely to report abstinence at 18 months compared to those who were not using buprenorphine (80% versus 37%); the difference persisted at 42 months (80% versus 51%).[20]

California does not have adequate buprenorphine prescribers to meet the growing demand for treatment.

Clinical Questions

Induction Options

Should patients be induced in a clinic or at home? Induction is the process of switching to buprenorphine from other opioids; physicians typically require that patients experience 12 to 48 hours of withdrawal symptoms before starting buprenorphine. Clinical trials on buprenorphine have been performed with observed (in-office) inductions, and many clinic protocols are based on this practice. However, home induction is increasingly used, both to improve clinic workflow and to increase convenience for the patient. Some clinics do home inductions exclusively; others adapt the strategy to the needs of the patient, using home inductions for stable patients and clinic inductions for those needing closer monitoring (e.g., psychiatric instability).

What are induction clinics? Induction clinics relieve primary care practices of the intensity and frequency of visits for patients newly starting on buprenorphine. These clinics can devote time and staff resources to intake, assessment, evaluation of options, education, induction, and early monitoring. The patients can be transferred back to primary care when they are stable on monthly prescriptions. This approach has been used successfully for over 10 years in San Francisco at the Office-Based Opioid Treatment Induction Clinic. A similar **"hub and spoke" model** is used in Vermont, where complex patients go to the hub (an opioid treatment program) and stable patients are managed at the spokes (primary care practices).[21]

What is a buprenorphine or fentanyl patch induction? A buprenorphine or fentanyl patch can bridge a patient from their current opioid treatment to sublingual buprenorphine, without requiring the patient to experience 12 to 48 hours of withdrawal symptoms. *Buprenorphine and fentanyl patches are not FDA-approved for addiction under DATA 2000 and should only be used for patients who have been diagnosed with chronic pain.*

The following guidelines, based on Dr. Kornfeld's research and practice, are not intended to replace medical judgment.[22,23] Patients should be assessed every 1 to 2 days, and adjustments made as needed. Expert advice is widely available (see accompanying sidebar).

Where Can Clinicians Get Training and Support?

Buprenorphine trainings are offered at several locations and websites. The training takes about eight hours and can be attended in person, online, or a combination of both. Buprenorphine waiver training can be valuable to any clinician (medical or behavioral) as it covers the basics of opioid addiction and how buprenorphine works.

Clinicians can only prescribe buprenorphine for addiction after receiving certified training and a Drug Enforcement Administration (DEA) waiver. However, any DEA-licensed clinician can prescribe buprenorphine for pain.

Training opportunities are posted on the following websites: Substance Abuse and Medical Health Services Administration (**SAMHSA**),American Academy of Addiction Psychiatry (**AAAP**), American Osteopathic Academy of Addiction Medicine (**AOAAM**), and Providers' Clinical Support System (**PCSS**).[24-27] Some sites also offer other tools and resources. PCSS offers online mentorship, and Project ECHO[28] offers video telementoring and monthly case review.

The **Clinicians Consultation Center** at UCSF offers expert clinical advice, Monday through Friday, 7 a.m. to 3 p.m. PST.[29]
Substance Use Warmline: (855) 300-3595.

Buprenorphine Transdermal (Patch) Induction

STEP 1. Taper off methadone. Because methadone exits the body slowly, especially at high doses, most addiction treatment protocols advise a gradual taper to ≤30 mg of methadone, followed by abstinence for 48 hours or longer, before administration of sublingual buprenorphine. Unlike patients with addiction alone, patients with an accompanying diagnosis of chronic pain can use buprenorphine patches and other opioids for an easier transition and fewer withdrawal symptoms.

First, convert methadone to a different long-acting opioid (morphine, oxycodone, hydromorphone, hydrocodone, or oxymorphone). 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.

- *<50 mg methadone*: Use long-acting opioid for 3 to 4 days before starting the buprenorphine patch.
- *50 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 (overlapping or cross-taper).
- *>100 mg methadone*: Use the cross-taper method in three or more steps.
- After appropriate time on long-acting opioid, proceed to step 2.

STEP 2. Buprenorphine patch induction for patients on long-acting opioids. Before the induction day, prescribe the following medications and ask the patient to bring all to the office:

- Buprenorphine patches (one 20 mcg/hour, two 10 mcg, or four 5 mcg patches. (One box contains four patches, though pharmacists sometimes dispense less than a box.) Each patch lasts one week. Usually, transdermal buprenorphine is only needed for a few days to a week during the induction phase.
- Buprenorphine sublingual 2 mg #12-30 (amount depends on patient stability). The buprenorphine mono product — without naloxone — is less expensive with similar efficacy, though many clinicians use the combination product, buprenorphine/suboxone, to prevent diversion and injection use (the evidence is unclear whether this combination product prevents diversion).[30-32]
- Four days of short-acting opioids (30% to 50% less than the current long-acting opioid dose). Options include immediate release forms of morphine, oxycodone, hydrocodone, or hydromorphone.

Instruct the patient to stop taking long-acting opioids the night before the induction. Short-acting opioids can be used as needed for pain.

Simultaneously (on the first day of the induction):

- Place 20 mcg/hour of buprenorphine patch (10 mcg/hour for very low dose conversions). Keep patch on for 3 to 4 days.
- Continue short-acting opioids as needed for pain.

STEP 3. Start sublingual buprenorphine.

- After 3 to 4 days on the patch, discontinue the short-acting opioids the night before starting sublingual buprenorphine. Keep the patch in place.
- Give 1 mg (half-tablet) buprenorphine in the office; have the patient wait for 30 minutes to observe the effect before going home (observed induction is recommended for pain patients). The patient can take another 1 mg dose later that day.
- Increase dose by 2 to 4 mg every 3 days, as needed to control pain and cravings, to a maximum of 24 mg. Some physicians titrate up at a faster pace, though many patients 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.

Fentanyl Transdermal (Patch) Induction

- Transition patients from their current opioid regimen to fentanyl 25 or 50 mcg; continue for 3 to 7 days.
- Discontinue any short-acting opioids (if used) at least 24 hours prior to sublingual buprenorphine.
- Remove fentanyl patch and give 1 to 2 mg sublingual buprenorphine; observe for 20 minutes.
- Increase to 8 mg if needed to manage withdrawal symptoms on the first day, and up to 24 mg over 3 to 7 days, as needed.

Behavioral Health and Other Addiction Treatments

What behavioral health treatments are required by the DEA waiver? The standard of care for opioid use disorder requires that patients be offered medications and behavioral health treatment. Although the waiver mandates clinicians to offer referrals to behavioral health services, patients are not required to accept them, and these services do not have to be located onsite or delivered in-person.

Two studies are reassuring for communities with insufficient behavioral health resources: One randomized controlled trial showed that buprenorphine is effective even without behavioral counseling.[33] A 2016 American Society of Addiction Medicine (ASAM) review found mixed support in the literature for behavioral health interventions for opioid addiction.[34] Nevertheless, most experts recommend a comprehensive (medical and behavioral) approach where available. Addiction is a chronic illness that requires lifestyle changes. Behavioral and social therapies, as a supplement to medication treatment, can increse success in recovery.

How long do patients have to be in treatment before they are considered drug-free? Patients participating in buprenorphine treatment while simultaneously avoiding other illicit substances are considered clean and sober by addiction specialists. Addiction specialists now consider opioid use disorder to be a chronic disease, and this perspective informs treatment. Instead of discontinuing treatment when the patient has relapses or slips, an appropriate response is now to increase the intensity of monitoring.

How does buprenorphine compare to methadone? Buprenorphine and methadone have both been proven effective in opioid addiction.[35] Methadone has been shown to have a slightly higher retention rate in treatment, but it is unclear if this result is due to the medication or due to the wrap-around behavioral health services and the close monitoring that are components of methadone programs.

Methadone is better suited for patients who have psychiatric instability, addiction to multiple substances, or other conditions that require close monitoring. Buprenorphine has several advantages: It is available in primary 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 recent review of the evidence for treatment options, see the Vancouver Health Authority **Opioid Addiction Guidelines**, which recommends buprenorphine as first-line treatment and methadone for patients failing trials of buprenorphine.[36]

Conversion, Tapers, and Dosage

How should patients be converted from buprenorphine to another opioid and vice-versa? Buprenorphine is a very potent opioid. As a precautionary measure, a factor of 30:1 to 90:1 (morphine milligram equivalents to buprenorphine) is used when converting from other opioids to buprenorphine. Conversion from buprenorphine to other opioids must also be approached cautiously, at a much lower conversion ratio. Buprenorphine leaves the body slowly. If a full agonist treatment is used, it should be started at a low dose and increased gradually, as the buprenorphine wears off. When treating addiction with buprenorphine, the target maintenance dose is 16 mg per day and does not use a conversion factor — the dose

"We have to adopt a different perspective. For pain meds, we don't refill early, and we try to cut doses down. For addiction, we may do early refills and dose increases if craving and symptoms are not controlled. Likewise, we don't cut people off buprenorphine when they use marijuana or other drugs — we shouldn't stop an effective treatment because the patient has more than one problem."

— Gary Pace, MD, medical director, Alexander Valley Medical Center

is based on the need to control cravings and prevent relapse, and the opioid dose used during active addiction is not relevant.

Should patients always be tapered off buprenorphine? Although buprenorphine can be used in short-term detoxification programs, addiction experts increasingly discourage this approach and instead encourage continuing buprenorphine long-term.[37] Patients who stop buprenorphine during the first few months of their treatment experience high rates of relapse, even with intensive behavioral support.[38] 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.[39] Without long-term treatment, patients often return to the drug to which they were addicted, and the dose (or fraction of the dose) their bodies tolerated prior to treatment can lead to overdose death. Detoxification and tapering with buprenorphine is still superior to providing no medication-assisted treatment at all, and can be considered in circumstances where timely follow up for continuation of buprenorphine is not available, or the patient specifically desires detoxification.

How does a physician taper a patient off buprenorphine? When tapering, smaller doses can be used by dividing 2 mg tablets into smaller segments. If a patient has an addiction by no chronic pain diagnosis, the smallest fraction that can be realistically achieved is ½ (1 mg) and ¼ (0.5 mg) of a tablet. Buprenorphine tablets have much lower bioavailability when swallowed compared to when they are absorbed sublingually, so swallowed buprenorphine tablets can be used in the latter stages of a taper to achieve lower doses. If the target condition is pain, then buprenorphine can be compounded by a specialty 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 to 0 in a pain patient.

Should physicians discontinue buprenorphine treatment for patients who are using marijuana, methamphetamine, or other drugs? Marijuana use has not been shown to worsen outcomes for patients on buprenorphine for opioid use disorder.[40] The California Society of Addiction Medicine recommends continuing buprenorphine and treating patients for marijuana use disorder,

Table 1: Buprenorphine Formulations and Dosages

FORMULATION	DOSES AVAILABLE	INDICATION
Parenteral (Buprenex)	0.3 mg IV/IM q 30 minutes, duration 6 to 8 hours Analgesic equivalent = 10 mg IV morphine for opioid naïve	Pain
Transdermal patch (Butrans)	buprenorphine: 5, 7.5, 10, 15, and 20 mcg/hour, every 7 days	Pain
Low-dose buccal mucoadhesive film (Belbuca)	buprenorphine: 75, 150, 300, 450, 600, 750, 900 mcg, twice daily	Pain
High-dose buccal film (Bunavail)	buprenorphine/naloxone, daily: 2.1 mg/0.3 mg, 4.2 mg/0.7 mg, and 6.3 mg/1 mg	Addiction Pain (off-label)
Sublingual tablets (generic subutex, generic suboxone, generic zubsolv)	Dosed daily for addiction; divided doses for pain Generic subutex: buprenorphine: 2 mg, 8 mg Generic suboxone/zubsolv: buprenorphine/naloxone: 2 mg/0.5 mg, 8 mg/2 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	Addiction Pain (off-label)
Sublingual film (Suboxone)	buprenorphine/naloxone: 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg	Addiction Pain (off-label)
Implant	80 mg (equivalent to <8 mg sublingual daily)	Addiction Pain (off-label)
Compounded	Many options from low to high doses	Pain

if present. Patients may have more than one addiction: Buprenorphine may successfully treat opioid use disorder, while patients continue to need behavioral treatments for other active addictions to drugs, such as methamphetamine or cocaine. Patients with addictions to multiple substances may benefit from the intensive treatment of an opioid treatment program, if available. If such programs are not available, these patients will be less likely to overdose, contract an infection, or have another negative outcome if treated with buprenorphine than they would be on other opioids or street alternatives (common pathways when opioid treatment is abruptly discontinued).

What dosage formulations are available? Buprenorphine is a Schedule III drug (refills can be called in or faxed). Table 1 lists the formulations and dosages available. (See page 6.)

Buprenorphine for Pain (Outpatient and Inpatient)

Under what circumstances can buprenorphine be prescribed for pain? Any buprenorphine formulation can be used for a patient with a pain diagnosis by any DEA-licensed clinician without a 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 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."[41]

If a patient has an addiction diagnosis but no diagnosis of pain, the physician must have a DEA waiver and can only prescribe tablets, sublingual film (either buprenorphine alone or buprenorphine with naloxone), or the implant.

Compared to other opioids used for pain relief, what are the advantages of buprenorphine? Buprenorphine provides excellent pain control, with no ceiling effect below 300 mg morphine equivalents. It has an excellent safety profile, due to a ceiling effect on respiratory suppression. Buprenorphine's onset of action is 30 to 60 minutes, and it typically provides 8 hours of pain relief, so it is usually given in divided doses when used for pain unless the patch formulation is used.

Buprenorphine, unlike other long-acting opioids, 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.[42] 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 is finding improved pain relief on buprenorphine after conversion from other long-acting opioids.[43-46] For example, one study of 35 patients found a mean decrease in pain score from 7.2 to 3.5, with 34 out of 35 patients reporting a pain decrease.[47] A Cochrane meta-analysis of cancer pain found that buprenorphine was superior to other opioids (5 out of 11 studies) or at least equivalent to other opioids for pain relief (3 out of 11 studies).[48]

How do physicians convince patients to transition from other opioids to buprenorphine? Education about the medical side effects of opioids used over a long period of time often helps patients understand the rationale for change. Patients may be unaware that some of their medical problems are due to chronic opioid use and that these issues may resolve after the transition: Sedation, mood disorders (depression and anxiety), sleep apnea, and erectile dysfunction are some of the more distressing problems for patients. Education about hyperalgesia and the common experience of withdrawal symptoms between doses may convince patients to make the change. Some patients can be tapered off of antidepressants and neuroleptic drugs. Other patients are motivated by the fact that buprenorphine is a Schedule III medication (refills can be called in), which mitigates patients' bureaucratic inconvenience in obtaining the drug.

Should buprenorphine be prescribed for the elderly? For elderly patients already on 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. For elderly patients *not* currently taking opioids, the lowest dose of the buprenorphine-naloxone sublingual tablet formulation (2 mg) can be equivalent to 60 to 180 mg oral morphine a day, depending on the patient's metabolism, and would be too high a dose. Buprenorphine products

in the form of a transdermal patch or buccal film come in much lower doses and can therefore be used for treating elderly patients with no opioid tolerance.

How should patients on buprenorphine be managed perioperatively or in the hospital? Some perioperative protocols still require buprenorphine to be discontinued, but this approach puts patients at risk for longer lengths of stay and subjects patients to a risk of relapse and the need for re-induction. Continuing buprenorphine, with additional analgesia when needed, has been shown in recent studies to be an effective way of managing inpatient and perioperative pain.[49] Additional doses of buprenorphine, or other opioids, can be given simultaneously with maintenance buprenorphine for satisfactory pain relief. In small cohorts, continuing buprenorphine lowered the length of hospital stay with better or equal pain control.[50]

Can patients be induced on buprenorphine in the emergency department (ED)? Gail D'Onofrio, MD, MS, of Yale University, conducted a randomized controlled trial of starting buprenorphine in the ED for addiction and found that those given buprenorphine had twice the 30-day retention rate in treatment (78%) compared with referral to addiction treatment services (37%).[51] 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, by injection (intravenous or intramuscular) while in the ED, or as take-home doses after discharge.

Some California EDs are now performing buprenorphine inductions while the patient is in the ED, or are giving patients instructions for home induction, combined with expedited referral to outpatient treatment. CHCF works with emergency physicians interested in piloting this treatment; for more information, contact CHCF's director of High-Value Care Kelly Pfeifer, MD, at kpfeifer@chcf.org.

Should buprenorphine be used for pain in the ED? Buprenorphine used to treat pain (sublingual, buccal, transdermal, intravenous, or intramuscular forms) can be used in the ED by clinicians without a waiver. Advantages of buprenorphine as a first-line opioid analgesic, when opioids are indicated, include: lower abuse potential, lower risk for respiratory depression, and longer duration of pain relief.

Buprenorphine may be a better choice for people with active or historical substance use disorders requiring opioid analgesia, as it would be less likely to trigger relapse. As with all opioid analgesics, buprenorphine should be used sparingly for pain after both nonpharmacologic interventions and nonopioid analgesics have failed. Buprenorphine can be administered or prescribed for pain by any clinical provider with DEA opioid-prescribing authority.

Administrative Questions

Where can patients find buprenorphine-waivered clinicians? Visit the SAMHSA treatment finder.

How do physicians get buprenorphine approved by medical insurance companies or Medi-Cal? What is a Treatment Authorization Request (TAR)? **Medi-Cal does not require the physician to obtain prior authorization (TAR) when prescribing buprenorphine for addiction or the buprenorphine patch for pain.** When prescribers include their x-number and "Dx: Opioid Dependence" on the prescription, buprenorphine will be covered by fee-for-service (FFS) Medi-Cal without an authorization review. Pharmacies should not send the prescription forms to the managed Medi-Cal plan, as buprenorphine is not covered by managed Medi-Cal. Prescribers starting their patients on buprenorphine should confirm that their local pharmacy stocks buprenorphine and that the pharmacist knows the procedure for billing Medi-Cal directly.

Medi-Cal does not require a TAR for the buprenorphine patch, but all other buprenorphine formulations for pain require a TAR. The prescriber can write the justification on the prescription, such as: "chronic pain due to ___ diagnosis; at high risk, currently on ___ regimen; buprenorphine is indicated for pain and for a more favorable safety profile." The pharmacist will use this information to complete a TAR and send it to FFS Medi-Cal for review. Medi-Cal will approve sublingual, transdermal, and buccal formulations for pain.

As of April 2016, Medicare Part D plans are required to cover buprenorphine, but may require justification (in the form of 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.

What is the Drug Medi-Cal Organized Delivery System (DMC-ODS) Waiver? The DMC-ODS changes the way Medi-Cal substance use treatment services are delivered. Instead of providers contracting directly with the state, for counties that "opt-in" providers contract with the county. The county is responsible for offering the continuum of care for patients with substance use disorder, modeled on ASAM criteria. The program is launching in phases through 2020 in these regions: Bay Area (Phase I), Southern California (Phase II), Central Valley (Phase III), Northern California (Phase IV), and the Tribal Delivery System (Phase V). For more information, see the Department of Health Care Services **website**.[52]

How do federal regulations and California state law affect documentation requirements in primary care? Both federal regulations (at 42 C.F.R. Part 2) and California law (Cal. Civil Code Section 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 and the sources of funding. For more information, see CHCF's ***Fine Print: Rules for Exchanging Behavioral Health Information in California***; and resources from the **ASAM** and **SAMHSA**.[53-55]

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.

For more information, visit **www.chcf.org**.

Endnotes

1. "Expanding Access to Buprenorphine in Primary Care Practices," CHCF webinar, April 28, 2016, **www.chcf.org**.
2. "Opioid Safety Coalitions: Is Buprenorphine for Pain a Safer Alternative to High-Dose or Long-Term Opioid Use?" CHCF webinar, June 8, 2016, **www.chcf.org**.
3. A substantial portion of this Background section is derived from page 18 of "Changing Course: The Role of Health Plans in Curbing the Opioid Epidemic." CHCF report, June 2016, **www.chcf.org**.
4. Thomas CP, et al., "Medication-Assisted Treatment with Buprenorphine: Assessing the Evidence," *Psychiatric Services*. 2014; 65(2):158-170. doi:10.1176/appi.ps.201300256.
5. Kimber J, et al. "Mortality Risk of Opioid Substitution Therapy with Methadone Versus Buprenorphine: A Retrospective Cohort Study." *Lancet Psychiatry*. 2015;2(10):901-908.
6. Degenhardt L, et al. "The Impact of Opioid Substitution Therapy on Mortality Post-Release from Prison: Retrospective Data Linkage Study." *Addiction*. 2014;109(8):1306-1317.
7. Pierce M, et al. "Impact of Treatment for Opioid Dependence on Fatal Drug-Related Poisoning: A National Cohort Study in England." *Addiction*. 2016;111(2):298-308.
8. Schuckit MA. "Treatment of Opioid-Use Disorders." *New Engl J Med*. 2016;375(4):357-368.
9. Tigerstedt I, and Tammisto T. "Double-Blind, Multiple-Dose Comparison of Buprenorphine and Morphine in Post-Operative Pain." *Acta Anaesth Scand*. 1980; 24(6):462-468. doi:10.1111/j;1399-6576.1980.tb01584.x.
10. Carl P, et al. "Pain Relief After Major Abdominal Surgery: A Double-Blind Controlled Comparison of Sublingual Buprenorphine, Intramuscular Buprenorphine, and Intramuscular Meperidine," *Anesth & Analg*. 1987; 66(2): 142-146. doi:10.1213/00000539-198666020-00008.
11. Kornfeld H and Manfredi L. "Effectiveness of Full Agonist Opioids in Patients Stabilized on Buprenorphine Undergoing Major Surgery: A Case Series," *Am J Ther*. 2010;17(5):523-528.doi:10.1097/MJT.0b013e3181be0804.
12. Daitch J, et al. "Conversion of Chronic Pain Patients from Full-Opioid Agonists to Sublingual Buprenorphine," *Pain Physician*. 2012;15(3Suppl): ES59-ES66, **www.painphysicianjournal.com**; Daitch D, et al. "Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients." *Pain Medicine*. 2014. 15 (12):2087-2094, doi:10.1111/pme.12520; Baron and McDonald, "Significant Pain Reduction."
13. Berland DW, et al. "When Opioids Fail in Chronic Pain Management: The Role for Buprenorphine and Hospitalization. *Am J Ther*. 2013; 20(4):316-321. DOI: 10.1097/MJT.0b013e31827ab599.
14. Kornfeld H, Reetz H. "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," *Am J Ther*. 2015;22(3): 199-205. doi:10.1097/mjt.0b013e31828bfb6e.
15. Heit HA, Covington E, and Good PM. "Dear DEA." *Pain Medicine*. 2004;5(3):303-308. doi:10.1111/j.1526-4637.2004.04044.x.
16. Kakko J, et al. "1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomized, placebo-controlled trial." Lancet. 2003;361:662-668.
17. Highleyman L. "Young Drug Injectors on Opioid Maintenance Therapy Have Lower Risk of Hepatitis C Infection." *Infohep*. November 11, 2014, **www.infohep.org**.
18. "Methadone reduces risk of HIV transmission in people who inject drugs, say experts." *Br Med J* press release, October 4, 2012, **www.bmj.com**.
19. Larochelle MR, et al. "Opioid Prescribing After Nonfatal Overdose and Association with Repeated Overdose: A Cohort Study." *Ann Intern Med*. 2016;164(1):1-9.
20. Weiss RD, et al. "Long-term outcomes from the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study." *Drug Alcohol Depend*. 2015;150:112-119.
21. "Substance Abuse Treatment Services Objective and Performance Measures." Report to Vermont Legislature. September 11, 2014, **legislature.vermont.gov** (PDF).
22. Dr. Kornfeld is a nationally known researcher and addiction and pain specialist with a practice in Marin County, California. He is on faculty at UCSF and was the founding medical director of an integrated pain and addiction clinic at Highland Hospital for low-income patients.
23. Kornfeld H, Reetz H. "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," *Am J Ther*. 2013;22(3), Doi: 10.1097/MJT.0b013e31828bfb6e, **recoverywithoutwalls.com** (PDF).
24. "Buprenorphine Training for Physicians." Substance Abuse and Medical Health Services Administration. July 2016, **www.samhsa.gov**.
25. "Buprenorphine Waiver Training." American Academy of Addiction Psychiatry. 2016, **www.aaap.org**.
26. "PCSS-MAT and the Office-Based Treatment of Opioid Dependence (Waiver Eligibility Trainings." American Osteopathic Academy of Addiction Medicine, **www.aoaam.org**.

27. "Providers' Clinical Support System for Medication Assisted Treatment." PCSS, **pcssmat.org**.

28. "Project ECHO." Weitzman Institute, **weitzmaninstitute.org**.

29. Substance Use Resources." UCSF Clinician Consultation Center, **nccc.ucsf.edu**.

30. Bruce RD, et al. "Lack of Reduction in Buprenorphine Injection after Introduction of Coformulated Buprenorphine/Naloxone to the Malaysian Market." *Am J Drug and Alcohol Abuse*. 2009;35(2)68-72.

31. Larance B, et al. "The Diversion and Injection of a Buprenorphine-Naloxone Soluble Film Formulation." *Drug and Alcohol Dependence*. 2014;36:21-27.

32. Yokell A, et al. "Buprenorphine and Buprenorphine/ Naloxone Diversion, Misuse, and Illicit Use: An International Review." *Current Drug Abuse Reviews*. 2011;4(1):28-41.

33. Fielin DA, et al., "Counseling plus Buprenorphine-Naloxone Maintenance Therapy for Opioid Dependence." *N Engl J Med*. 2006;355(4):365-374.

34. Dugosh K, et al. "A Systematic Review on the Use of Psychosocial Interventions in Conjunction with Medications for the Treatment of Opioid Addiction." *J Addiction Med*. 2016. Doi:10.1097.

35. "A Guideline for the Clinical Management of Opioid Addiction." Providence Health Care and Vancouver Coastal Health, 2015, **www.vch.ca** (PDF).

36. "Opioid Addiction Guidelines." Vancouver Health Authority. **www.vch.ca**.

37. *Public Policy Statement on Rapid and Ultra Rapid Opioid Detoxification*. American Society of Addiction Medicine. April 2005, **www.asam.org**.

38. Bart G. "Maintenance Medication for Opiate Addiction: The Foundation of Recovery." *J Addict Dis.*2012; Doi: 10.1080?10550887.2012.694598.

39. Sarlin E. "Long-Term Follow-Up of Medication-Assisted Treatment for Addiction to Pain Relievers Yields 'Cause for Optimism,'" National Institute on Drug Abuse, November 30, 2015, **www.drugabuse.gov**.

40. Epstein DH, et al., "Does Cannabis Use Predict Poor Outcome for Heroin-Dependent Patients on Maintenance Treatment? Past Findings and More Evidence Against," *Addiction*, 2003;98(3):269-279.

41. Heit H, et al. "Dear DEA." *Pain Medicine*. 2004;5(3):303-308.

42. Davis MP. "Twelve Reasons for Considering Buprenorphine as a Frontline Analgesic in the Management of Pain. *J Support Oncol*. 2012;10(6):209-219.

43. Daitch D, et al., "Conversion of Chronic Pain Patients from Full-Opioid Agonists to Sublingual Buprenorphine." *Pain Physician*. 2012;15(3 Suppl):ES59-ES66.

44. Baron MJ, McDonald PW. "Significant Pain Reduction in Chronic Pain Patients after Detoxification from High-Dose Opioids." *J Opioid Management*. 2006;2(5):277-282.

45. Khanna I, et al. "Buprenorphine: An Attractive Opioid with Underutilized Potential in Treatment of Chronic Pain." *J Pain Res*. 2015;8:859-870. 2015 Dec 4. Doi: 10.2147/JPR.S85951

46. Malinoff, H, et al., "Sublingual Buprenorphine Ins Effective in the Treatment of Chronic Pain Syndrome." *Am J Ther*. 2005;12:378-384. Berland DW, et al. "When Opioids Fail In Chronic Pain Management: The Role for Buprenorphine and Hospitalization." *Am J Ther*. 2013; 20(4):316-321. Doi: 10.1097/MJT.0b013e31827ab599.

47. Daitch D, et al. "Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients," *Pain Medicine*. 2014;15:2087-2094.

48. Schmidt-Hansen M, et al. "Buprenorphine for Treating Cancer Pain." *Cochrane Database Syst Rev*. 2015;(3):CD009596. Doi: 10.1002/14651858.CD009596.pub4.

49. Macintyre, PE, et al. "Pain Relief and Opioid Requirements in the First 24 Hours After Surgery in Patients Taking Buprenorphine and Methadone Opioid Substitution Therapy," *Anaesth Intensive Care* 2013;41:222-230, **www.ncbi.nlm.nih.gov**.

50. Kornfeld H, Manfredi L. "Effectiveness of Full Agonist Opioids in Patients Stabilized on Buprenorphine Undergoing Major Surgery: A Case Series," *Am J Therapeutics*.

51. D'Onofrio G, et al. "Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial." *JAMA*. 2015;313(16):1636-1644.

52. California Department of Health Care Services, Drug Medi-Cal Organized Delivery System, **www.dhcs.ca.gov**.

53. California Health Care Foundation. "Fine Print: Rules for Exchanging Behavioral Health Information in California." July 2015, **www.chcf.org**.

54. Awad S. "Confused by Confidentiality? A Primer on 42 CFR Part 2," August 15, 2013, American Society of Addiction Medicine, **www.asam.org**.

55. Substance Abuse and Mental Health Services Administration, Confidentiality and Regulations: FAQs, **www.samhsa.gov**.