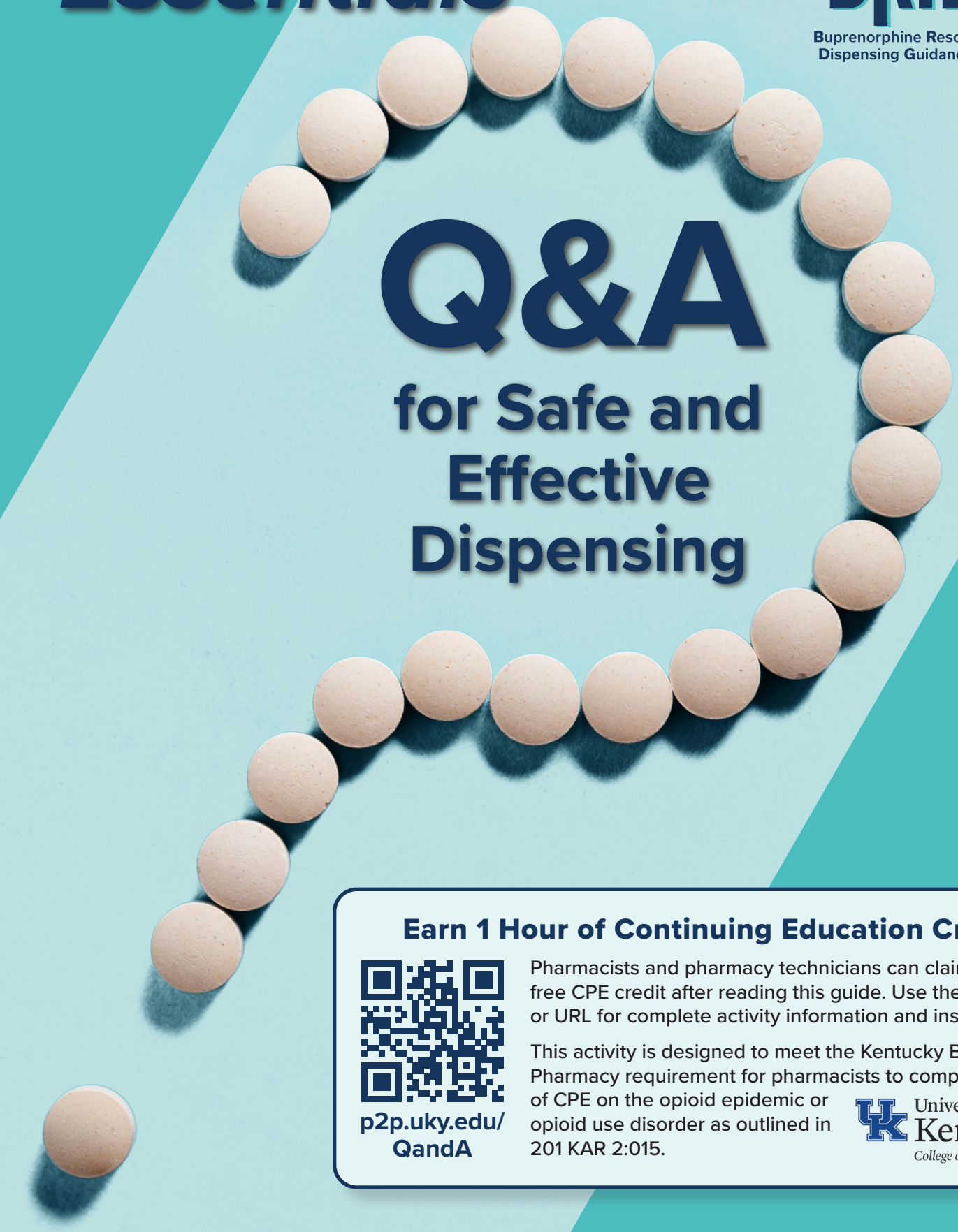
Buprenorphine Essentials

P2P BRIDGE

Buprenorphine Resource Initiative for Dispensing Guidance and Education



Q&A

for Safe and Effective Dispensing

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Pharmacists and pharmacy technicians can claim 1 hour of free CPE credit after reading this guide. Use the QR code or URL for complete activity information and instructions.

This activity is designed to meet the Kentucky Board of Pharmacy requirement for pharmacists to complete 1 hour of CPE on the opioid epidemic or opioid use disorder as outlined in 201 KAR 2:015.

University of Kentucky College of Pharmacy

Buprenorphine Essentials: Q&A for Safe and Effective Dispensing

Learning Objectives

Pharmacists

- Explain the pharmacology and role of buprenorphine in treating opioid use disorder (OUD).
- Review guidelines for buprenorphine induction, maintenance, and monitoring along with key counseling points for buprenorphine therapy.
- Analyze emerging trends in OUD treatment and buprenorphine prescribing.
- Interpret state and federal regulations related to buprenorphine to ensure legal compliance and effective patient care.

Pharmacy Technicians

- Review the role of buprenorphine in treating OUD.
- Identify state and federal regulations related to buprenorphine dispensing.
- List elements of evidence-based care for OUD that can be provided in the pharmacy.

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Disclaimer

The information in this document is intended to be general and educational in nature. Clinical and dispensing decisions should be made based on individual patient and prescription circumstances. This document is not legal advice. Licensed professionals are individually responsible for complying with all laws and regulations related to their practice.

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Acronyms

APRN = advance practice registered nurse

ASAM = American Society of Addiction Medicine

COWS = Clinical Opiate Withdrawal Scale

DATA = Drug Addiction Treatment Act of 2000

DEA = Drug Enforcement Administration

ER = extended release

FDA = Food and Drug Administration

HHS = U.S. Department of Health and Human Services

KAR = Kentucky Administrative Regulations

KBML = Kentucky Board of Medical Licensure

KBN = Kentucky Board of Nursing

MOUD = medications for opioid use disorder

NABP = National Association of Boards of Pharmacy

NCPA = National Community Pharmacists Association

NOWS = neonatal opioid withdrawal syndrome

OUD = opioid use disorder

PA = physician assistant

PHE = public health emergency

REMS = Risk Evaluation and Mitigation Strategy

SAMHSA = Substance Abuse and Mental Health Services Administration

All documents in the "Learn More" boxes are available by scanning the QR code or visiting http://p2p.uky.edu/links

What is buprenorphine?[1–3]

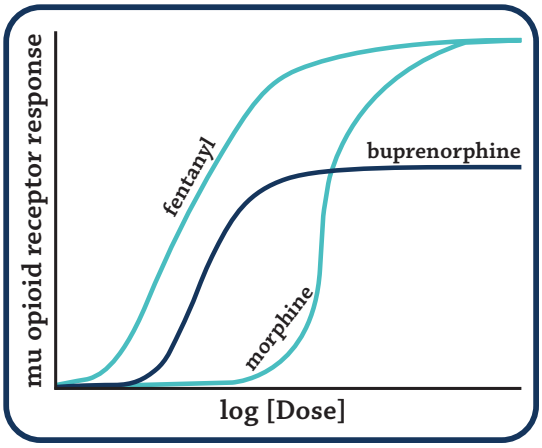
Buprenorphine is a potent semi-synthetic opioid that primarily acts as an agonist at the mu opioid receptor. It is defined by the DEA as a Schedule III opioid, with lower potential for misuse than other opioid agonists such as morphine or hydrocodone.

Key characteristics of buprenorphine's interaction with the mu receptor include:

Partial agonism: Although buprenorphine produces therapeutic opioid effects at typical doses, the maximum achievable effect is lower for buprenorphine than for full-agonist opioids. This "ceiling effect" gives buprenorphine a safety advantage, with low likelihood of respiratory depression or euphoria even at high doses. Despite its partial agonism, buprenorphine's analgesic efficacy is comparable to that of common full-agonist opioids.

High affinity: Buprenorphine is difficult to displace, with a receptor affinity more than 5 times the affinity of morphine. Buprenorphine can therefore rapidly replace other opioids and, due to its partial agonism, precipitate withdrawal symptoms in patients who are physically dependent on full-agonist opioids. This effect does not occur in reverse. A patient who is stable on long-term buprenorphine therapy can be given full-agonist opioids for acute pain with appropriate monitoring. Full agonists bind unoccupied receptors to provide analgesia, but buprenorphine's high affinity provides some protection against overdose.

Slow dissociation: Slow dissociation from the mu receptor contributes to buprenorphine's long duration of action for suppressing opioid withdrawal and the efficacy of once-daily dosing for opioid use disorder (OUD). The analgesic effect of buprenorphine, however, is shorter than its receptor occupancy, so dosing every 6–8 hours may be appropriate when treating co-occurring OUD and pain.



Adapted from Coe, et al.[1]

Did You Know?

Early research on buprenorphine occurred at the Addiction Research Center, located at what is now the Federal Medical Center in Lexington, KY. Buprenorphine's potential as an OUD treatment was identified as early as 1978, but it wasn't approved by the FDA for OUD until 2002.[1]

Buprenorphine also acts as an agonist at opioid receptor-like 1 and an antagonist at the delta and kappa opioid receptors. These receptor interactions may contribute to buprenorphine's unique pharmacologic profile, including a lower potential for addiction, enhanced spinal analgesia, reduced dysphoria and depression, and less impact on GI motility compared to full-agonist opioids.

Buprenorphine pharmacokinetics depend on the formulation. Some key points are:

Bioavailability: Sublingual bioavailability is 28–51% and varies among individuals and products. Oral bioavailability is very low due to extensive first-pass metabolism.

Half-life: Buprenorphine is highly lipophilic and demonstrates a half-life of 24 hours or longer when administered sublingually. Newer injectable depot formulations are also available, which allow for weekly or monthly dosing.

Metabolism: Buprenorphine is primarily metabolized via CYP3A4 and glucuronidation. Metabolites are not thought to contribute to the clinical effects of buprenorphine.

Why use buprenorphine to treat opioid use disorder?

Buprenorphine saves the lives of people with OUD.

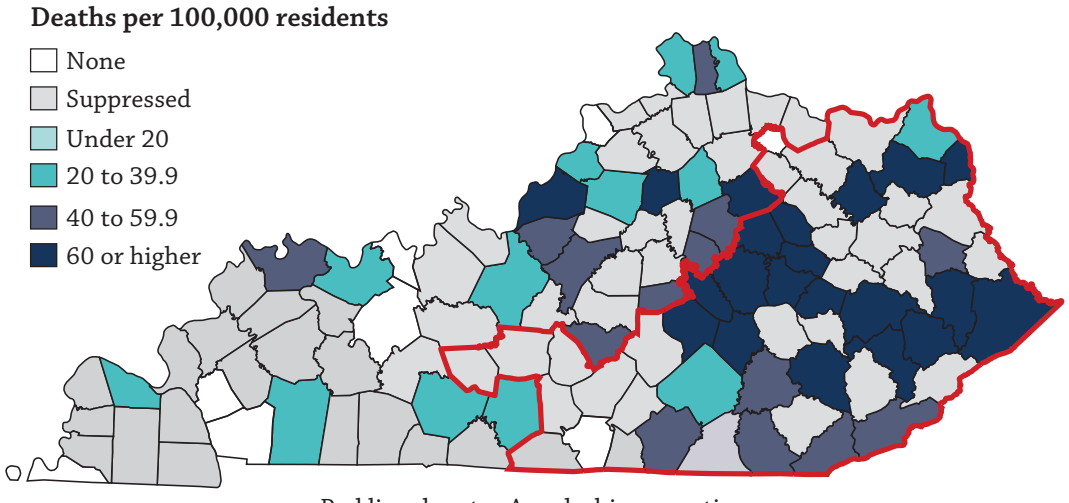
In Kentucky, 1,984 people died of a drug overdose in 2023.[4] Although this is a 9.8% decrease compared to 2022, annual overdose deaths remain well above the numbers recorded in years prior to the COVID-19 pandemic. In 2023, fentanyl, primarily illicitly manufactured fentanyl, was identified in 79% of overdose deaths.[4]

Nearly 160,000 Kentuckians aged 18 to 64 were estimated to have OUD in 2019, with prevalence surpassing 7% in Appalachian counties.[5] Nationally, only about one-third of patients with OUD receive any treatment (including medical and behavioral interventions) and only about 1 in 5 receive medication.[6]

Studies estimate that treatment with an opioid agonist (buprenorphine or methadone) is associated with a greater than 50% lower risk of all-cause mortality, drug-related death, and suicide in persons with OUD.[7]

A 2020 study compared treatment modalities — including opioid agonists, behavioral health, inpatient services, and naltrexone — and found that opioid agonists were the only pathway in which patients were less likely to experience an overdose compared to no treatment, with reductions in overdose of 76% at

Age-Adjusted Rates of Drug Overdose Deaths by County of Residence, 2023



Red line denotes Appalachian counties

Rates based on counts greater than zero but less than 10 were suppressed

Adapted from Kentucky Justice and Public Safety Cabinet[4]

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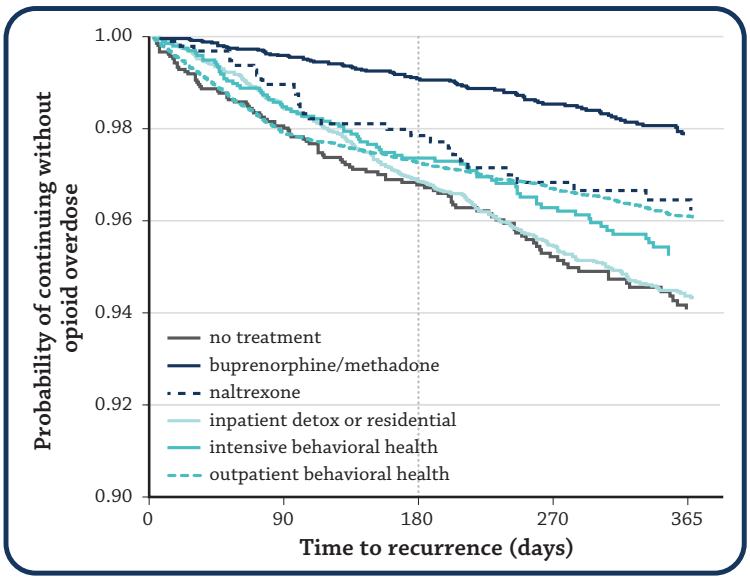
National Academies: *Medications for Opioid Use Disorder Save Lives*

2023 Overdose Fatality Report for Kentucky

3 months and 59% at 12 months.[8]

Opioid agonist treatment has also been shown to reduce injection drug use, improve social functioning, reduce the risk of hepatitis C and HIV infection, and improve quality of life compared to patients with OUD who are not in treatment.[9]

Draft guidelines from the National Association of Boards of Pharmacy (NABP) and the National Community Pharmacists Association (NCPA) note the crucial role of pharmacists in ensuring access to treatment. It recommends that "Pharmacists should maintain a sufficient supply of buprenorphine in their pharmacies and be willing to dispense buprenorphine to patients with OUD." The guideline goes on to note that declining a buprenorphine prescription is "a measure of last resort."[10]



Adapted from Wakeman, et al.[8]

What prescription products contain buprenorphine?

Ingredients	Dosing Frequency	Name	Dosage Form	Strengths
OUD				
Buprenorphine and Naloxone	Daily*	Suboxone and generics	Sublingual film	2-0.5, 4-1, 8-2, 12-3 mg
		Generics	Sublingual tablet	2-0.5, 8-2 mg
		Zubsolv	Sublingual tablet	0.7-0.18, 1.4-0.36, 2.9-0.71, 5.7-1.4, 8.6-2.1, 11.4-2.9 mg
Buprenorphine	Daily*	Generics	Sublingual tablet	2, 8 mg
	Weekly	Brixadi†	Subcutaneous injection	8, 16, 24, 32 mg
	Monthly	Brixadi†	Subcutaneous injection	64, 96, 128 mg
		Sublocade†	Subcutaneous injection	100, 300 mg
Pain				
Buprenorphine	Daily or q 12 hr	Belbuca	Buccal film	75, 150, 300, 450, 600, 750, 900 mcg
	Weekly	Butrans and generics	Transdermal patch	5, 7.5, 10, 15, 20 mcg/hr
	Multiple times a day	Generics	Solution for injection	0.3 mg/mL

*More frequent dosing may be appropriate based on individual patient needs.
†Only available via restricted REMS program; must be administered by a certified healthcare provider.
Note: Bioavailability differences between Suboxone and Zubsolv result in non-interchangeable doses. When switching between these products or their generics, refer to the conversion table in the Zubsolv prescribing information.
Source: UpToDate Lexidrug, accessed May 25, 2024.

What should you know about ER injectable buprenorphine?[11–15]

Two extended release (ER) injectable formulations of buprenorphine offer patients broader treatment options. These products must be administered by a health care professional to prevent harm or death from intravenous administration. Distribution is restricted through a Risk Evaluation and Mitigation Strategy (REMS) program to ensure the product is never dispensed directly to a patient.

Because of the slow-release nature of the subcutaneous injections, some patients may require supplemental sublingual buprenorphine products, especially near the end of the dosing interval. Though results from head-to-head comparisons to sublingual buprenorphine products are not yet available, ER injectables have been found to be safe and effective for moderate to severe OUD.

What about adverse effects, drug interactions & special populations?[3,16]

Adverse Effects

Buprenorphine products are generally well tolerated, with adverse effects similar to other opioids or related to opioid withdrawal. Common adverse effects include headache, constipation, nausea, pain, sweating, and anxiety. The FDA also warns of possible tooth decay or other oral issues associated with the use of transmucosal products. Local injection site reactions are possible with the depot formulations of buprenorphine.

Drug Interactions

The major drug interaction of concern is the combination of buprenorphine with other sedating medications or concurrent substance use. The combined use of sedating drugs increases the risk of serious adverse effects, but the risks related to untreated OUD may outweigh the risk of adverse effects.

Patients should be monitored closely if combining buprenorphine with CYP3A4 inhibitors or inducers, antiretrovirals, or serotonergic drugs due to the possibility of drug interactions.

Pregnancy and Breastfeeding

The standard of care for pregnant patients with OUD is treatment with buprenorphine or methadone. Buprenorphine monoproducts are appropriate in pregnancy to prevent naloxone exposure; however American Society of Addiction Medicine (ASAM) guidelines note that buprenorphine-naloxone combinations are frequently used in this population. Buprenorphine is associated with less severe neonatal opioid withdrawal syndrome (NOWS) than methadone.

Patients can safely breastfeed while on buprenorphine or methadone. Treatment should not be discontinued during pregnancy or after delivery. Breastfeeding while on buprenorphine has also been shown to have favorable effects on NOWS.

Adolescents

Buprenorphine is FDA-approved for the treatment of patients aged 16 years and older, and studies have not included adolescents under 16 years. ASAM

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Buprenorphine REMS programs

guidelines state "Clinicians should consider treating adolescents who have opioid use disorder using the full range of treatment options, including pharmacotherapy," but note that federal laws and FDA approvals should be considered.[3]

Hepatic Impairment

Both buprenorphine and naloxone are metabolized in the liver, and patients with moderate to severe hepatic impairment show a higher plasma level and longer half-life for both drugs. Naloxone-containing buprenorphine products should be avoided in severe hepatic impairment and considered carefully in moderate hepatic impairment, as withdrawal symptoms may occur even with transmucosal administration.

What's the Naloxone For?

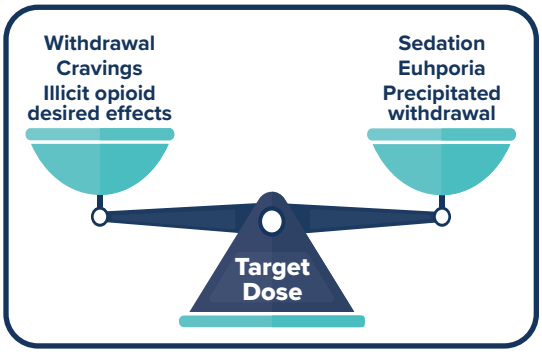
Formulations of buprenorphine for OUD often include naloxone in a 1:4 ratio to deter misuse. Taken sublingually, naloxone is only about 3% bioavailable. If the product is snorted or injected, however, higher bioavailability makes the naloxone more likely to cause withdrawal.[1] Guidelines recommend buprenorphine-naloxone for most patients with OUD but note that the small amount of naloxone absorbed sublingually may cause withdrawal symptoms.[3] Recent commentary suggests that a small subset of non-pregnant patients (less than 5%) may experience intolerable adverse effects from buprenorphine-naloxone products that may warrant a trial of buprenorphine alone.[17]

How is buprenorphine treatment initiated?[18]

Initiation or induction is the process of initial dosing until the patient reaches a state of stability. For sublingual buprenorphine, this most often involves beginning with a low (2 to 4 mg) dose and gradually increasing the dose over a few days until the patient reaches a dose tailored to their specific needs.

Induction can occur in the prescriber's office or in a community setting such as the patient's home. Both options are effective. The choice should be based on the patient's needs, preferences, experience with buprenorphine, and ability to manage initiation. Office-based induction can be a barrier to treatment. Induction outside of clinical settings is becoming more common.

Most patients should be in mild to moderate opioid withdrawal to receive

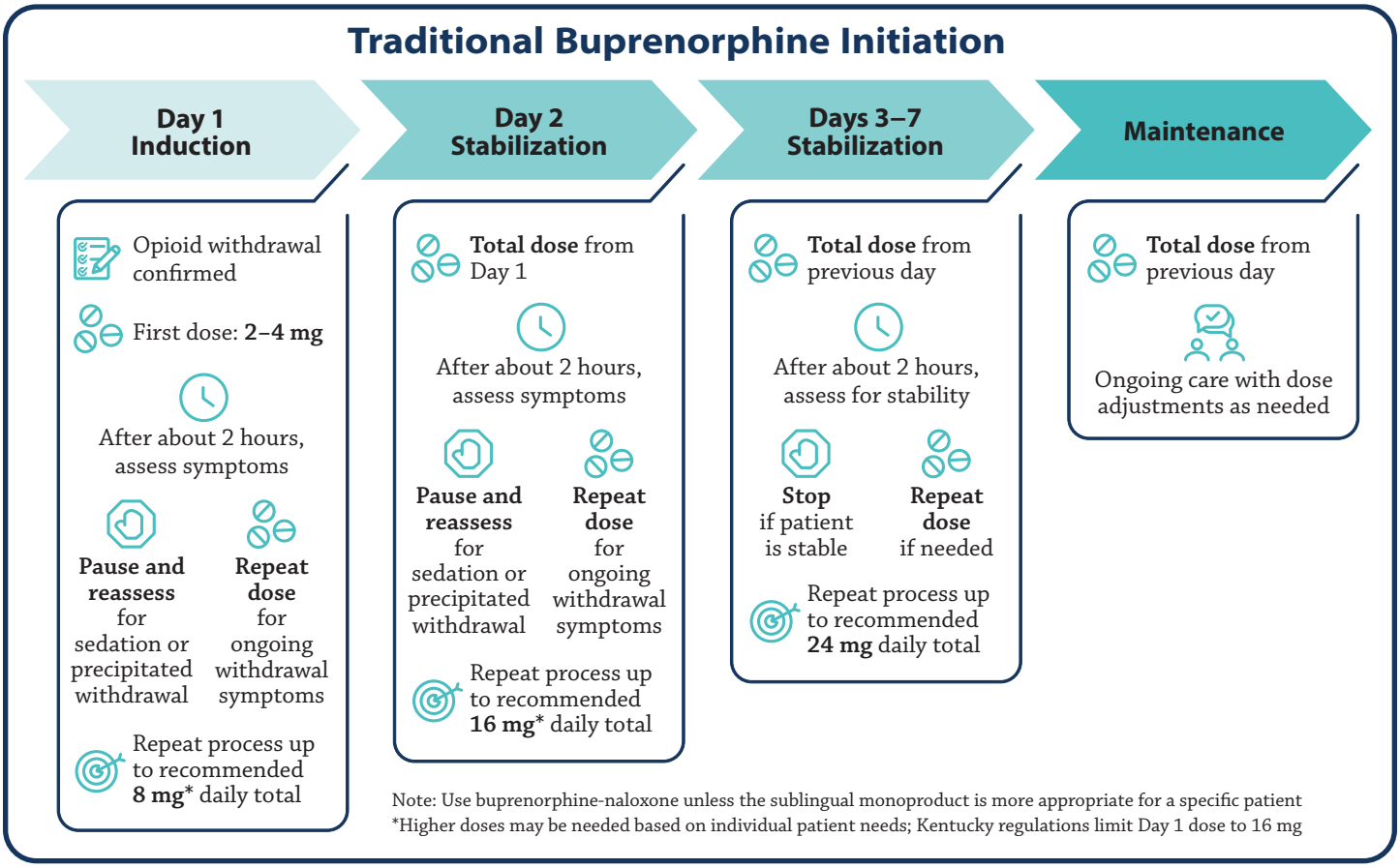


their first dose of buprenorphine to avoid precipitated opioid withdrawal. This is determined by observing the patient exhibit clear signs of opioid withdrawal or using an instrument such as the Clinical Opiate Withdrawal Scale (COWS).[19] The dose of buprenorphine a patient requires can depend on the severity of withdrawal symptoms, the last opioids used, and the timing of the last opioid use.[20]

The goal is to determine the daily dose that will provide adequate withdrawal symptom relief without causing sedation or other undesired effects. Additional doses can be given approximately every 2 hours as needed up to the recommended maximum dose or an individualized necessary dose with appropriate documentation.

Remember that guidelines are evidence-based recommendations that may not be optimal for all patients. Individualization is key. Initiation protocols may vary from one healthcare institution to another based on resources available, location, and community characteristics. Differences may be seen in:[20–22]

- Withdrawal criteria
- Initial dose on day 1
- Starting dose on day 2
- Time of assessment for each dose
- Maximum daily dose during initiation



Adapted from ASAM, prescribing information, SAMHSA, and Kentucky Administrative Regulations. See references 3,16,18,21,23, and 24.

Why are withdrawal and precipitated withdrawal important?[18]

Withdrawal symptoms are described by patients as incapacitating with a sense of urgency to relieve symptoms.[25] Withdrawal can interfere with sustaining housing and employment and influence people to continue or return to opioid use.

Fear of withdrawal, especially precipitated withdrawal, is a deterrent for initiating buprenorphine for OUD. Precipitated withdrawal, when buprenorphine displaces full-agonist opioids, can be rapid and severe, which may lead to illicit substance

use for relief. After this experience, many patients do not want to continue buprenorphine treatment.

Alleviating withdrawal symptoms and avoiding withdrawal symptoms between buprenorphine doses is a goal of treatment to avoid unnecessary pain and suffering for patients and ensure the greatest chance for treatment retention and success.

Reducing the Risk of Precipitated Withdrawal[3]

- Ensure the patient is exhibiting objective signs of mild to moderate opioid withdrawal prior to induction
- Allow sufficient time since last opioid use (12–18 hours after short-acting opioids, 24–48 hours after long-acting opioids, and 48–72 hours after methadone)[20]
- Use a lower initial buprenorphine dose (e.g., 2 mg)
- Use COWS to guide decision making
- Offer office/clinic-based induction to patients with anxiety or negative past experiences
- Explore alternative induction strategies
- Avoid combination products in moderate to severe hepatic impairment
- Avoid buccal administration; exposure to naloxone is higher with buccal rather than sublingual absorption[16]
- Fentanyl may require a modified induction protocol and moderate withdrawal before buprenorphine administration

What are the symptoms of withdrawal?[19]

Diaphoresis	Tachycardia
Restlessness	Muscle aches and cramping
Anxiety	Yawning
Stomach cramping	Rhinorrhea
Diarrhea	Lacrimation
Vomiting	Tremors

Patient Perspective: Precipitated Withdrawal

"I hear that the Suboxone can make you dope sick immediately, so that sounds really scary when you're trying to avoid that.

From what I was told, you have to be really sick to get on it (buprenorphine) and I don't want to be really sick. I don't want to feel that. So that was not for me."

"… I thought I was dying. I was crying and screaming. And I wanted to kill myself.

(Describing precipitated withdrawal in a hospital setting)

Excerpted from Simpson, et al.[25]

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Clinical Opioid Withdrawal Scale (COWS)

How is buprenorphine treatment monitored and maintained?

Buprenorphine maintenance treatment is similar to that of other chronic diseases.

Monitoring is frequent at the beginning of treatment and becomes less frequent as patients become more stable. This is assessed by the clinician and may be specific for each patient. As with other chronic conditions, the level of care may increase or decrease over time based on the patient needs and disease severity.[3]

The maintenance dose of buprenorphine should be the lowest dose that can achieve efficacy (eliminates withdrawal, reduces/eliminates opioid cravings, reduces or blocks illicit opioid desirable effects) and is well tolerated.[18]

The typical range for maintenance in guidelines and prescribing information is 4 mg to 24 mg per day, with a recommended target of 16 mg.[3,16,18] Evidence is accumulating, however, that maintenance doses above 16 mg are associated with improved treatment retention and decreased mortality.[26]

Duration of treatment is not specified under any recommendations.[3,16,21,27]

Maintenance Visits[3,21]

At a typical maintenance visit, several assessments may be used to determine treatment progress:

- Toxicology/drug screening, prescription drug monitoring program review
- Lab testing (e.g., pregnancy, liver function, HIV, hepatitis C)
- Alcohol use screening
- Patient status, including instances of substance use, medical issues or planned surgeries, participation in recovery-based activities, occupational/social/community functioning, quality of life[19]
- Medication adherence and administration technique
- Assess for acute/chronic pain

The prescriber and patient review the treatment plan and discuss aspects such as difficulties obtaining buprenorphine, adverse effects, cravings, and withdrawal symptoms. Medication adjustments or other changes are made as needed.

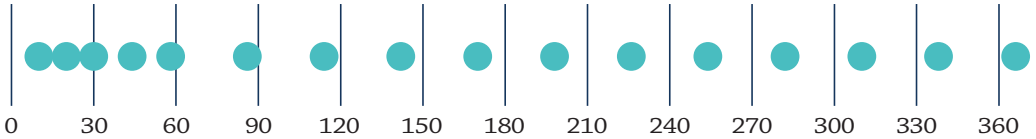
What should patients know about sublingual administration?[16,27]

- Abstain from tobacco products before buprenorphine (can decrease absorption)[18]
- A dose can take 3 to 10 minutes to dissolve
- After buprenorphine has completely dissolved, take a sip of water, swish gently around the teeth and gums, and swallow
- Wait for at least one hour after dose before brushing teeth
- Allow to dissolve. Do not swallow films or tablets
- Do not talk while buprenorphine is dissolving

Monitoring Timeline[23,24]

- First appointment no later than 10 days after induction
- Visit intervals of no more than every 10 days for the first month
- Visit intervals of no more than every 14 days for the second month
- If patient demonstrates signs of positive treatment progress, visits can occur monthly after the second month
- If patient demonstrates signs of positive treatment progress for 2 years, visits can occur every 3 months

Visit Timeline for Year 1



● = visit required under 201 KAR 9:270 and 201 KAR 20:065

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The ASAM National Practice Guideline

Why should patients stay on buprenorphine long-term?

ASAM defines addiction as a ***treatable, chronic medical disease*** and states that "there is no recommended time limit for pharmacological treatment with buprenorphine."[3] Guidelines discourage clinicians from using buprenorphine for withdrawal management without ongoing treatment. The standard of care for treating OUD is "ongoing maintenance medication in combination with psychosocial treatment appropriate for the patient's needs."[3] Both ASAM and the FDA, however, have stated that "provision of medication should not be made contingent upon participation" in counseling or other services.[3,28]

Early discontinuation of opioid agonist treatment is associated with higher rates of both relapse and overdose.[8] In one meta-analysis, all-cause mortality was 6 times higher in the first 4 weeks after treatment discontinuation than during a stable period of treatment.[7]

Despite risks related to discontinuation, only about half of patients continue receiving buprenorphine beyond 6 months, a treatment duration associated with substantial reductions in overdose and opioid-related acute care.[8,29] Factors that have been associated with increased retention include higher doses, low-barrier clinical approaches, and initiation in hospitals or criminal justice settings.[29,30] The addition of behavioral therapy to buprenorphine treatment was not associated with retention in care in three randomized trials.[29]

Common Maintenance Meds

Opioid agonists for OUD
More than **50%** lower risk of all-cause mortality, drug-related death, and suicide[6]

ACE inhibitors in hypertension
Reductions of **13%** in all-cause mortality and **17%** in cardiovascular mortality[31]

GLP-1 agonists in diabetes
25% reduction in all-cause mortality risk among elderly patients with T2DM[32]

Statins in cardiovascular and other disease states
30% lower risk of all-cause mortality[33]

How is buprenorphine tapered when patients choose to discontinue?

Do *not* discontinue abruptly.

Though there is no set duration of buprenorphine treatment, some patients may wish to taper or discontinue treatment.[21] It is important to keep in mind that this is a patient-centered decision that requires thoughtful discussion. Patient behaviors such as continued substance use are not sufficient reasons to discontinue buprenorphine treatment.[3] These patients should be referred to a higher level of care.

What should be discussed when considering a taper?

- Response to treatment, including OUD remission
- Psychosocial supports to maintain recovery
- Reason for tapering
- Expectations for tapering
- Risks and benefits of tapering
- Withdrawal symptoms

No specific algorithm or prescriptive guidelines are available for buprenorphine tapering or discontinuation.[34] Resources agree that tapering should be done slowly, over several months with close monitoring.[3,18] Monitoring should continue after discontinuation of buprenorphine.[21] Many patients who taper off buprenorphine return to treatment. Continued monitoring can facilitate rapid re-engagement.[34]

The period following buprenorphine discontinuation can be vulnerable for patients. Proper education is necessary to reduce the risk of harm.

What should be discussed when tapering?

- Risk of opioid overdose, overdose prevention, and naloxone
- Increased risk of relapse
- Decreased tolerance if the patient returns to opioid use
- Risk of infections with drug use
- Treatment alternatives (methadone, naltrexone)
- Tapering can be stopped or paused at any time[21]
- Returning to buprenorphine treatment is not a failure[34]

How is buprenorphine treatment changing?

New methods are necessary to overcome patient barriers to buprenorphine initiation (e.g., opioid withdrawal) and treatment retention and to address challenges faced with fentanyl and other high-potency synthetic opioids.[35]

Rapid High-Dose Buprenorphine Initiation

Rationale: Increasing initial doses rapidly during induction will increase mu-opioid receptor activation and strengthen opioid blockage, reducing withdrawal quickly.[35] This may be beneficial in patients with high levels of opioid dependence. Initial studies do not report increased precipitated withdrawal with this strategy. If precipitated withdrawal occurs, it may improve with buprenorphine doses of 32 to 64 mg.[35,36]

Example: When patient is in mild withdrawal, titrate to 16–32 mg in 1 or 2 doses.[35]

Low-Dose Buprenorphine with Opioid Continuation

Rationale: Continuation of full-agonist opioids (prescription or illicit) maintains the level of mu-opioid receptor activation needed to match a patient's baseline opioid tolerance during buprenorphine initiation.[35] Small doses of buprenorphine should not precipitate withdrawal but will accumulate and slowly replace the full agonist at the receptor.[37,38] It is not necessary for patients to be in withdrawal. Stabilization may require 3 to 10 days.

Bernese Method: Very small initial doses of transmucosal buprenorphine (e.g., 0.125–0.5 mg) are followed by daily incremental increases in dose and frequency.[37]

Transdermal patches (not indicated for OUD) have been used to deliver very low doses consistently in inpatient settings.[39]

Example: Methadone 30 mg daily + buprenorphine 0.25–1 mg starting dose.

Note: Emerging strategies are provided for educational purposes only. No specific dosing guidelines are available, and current literature is not from outpatient settings.

Higher Doses in Stabilization and Long-Term Treatment

- Patients exposed to fentanyl and other high-potency synthetic opioids may benefit from higher buprenorphine doses.[35]
- Improved treatment retention, reduced opioid use, and lack of adverse events has been shown in studies of buprenorphine 16–32 mg per day.[26,35,38,40]
- Expanded plasma volumes and adipose store may necessitate higher buprenorphine doses in pregnancy.[35]

Who can prescribe buprenorphine for OUD?

Any DEA-registered practitioner with prescriptive authority for Schedule III controlled substances can write for buprenorphine to treat OUD. There are no limits to the number of patients an individual prescriber can treat with buprenorphine.[41]

In Kentucky, practitioners must see patients taking buprenorphine for OUD at specific intervals based on their progress in therapy. After 2 years of treatment, patients with positive treatment progress may be seen as little as every 3 months.[23,24]

Schedule III controlled substances like buprenorphine cannot be filled or refilled more than 6 months after the date issued, and practitioners are subject to the following limits:

Physicians: No days' supply limit, no more than 5 refills

APRNs: 30-day supply, no refills

PAs: 30-day supply, no refills

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Letter from DEA and HHS

What Happened to X Waivers?

The *Consolidated Appropriations Act, 2023* eliminated the federal system of DATA waivers (X waivers) that were previously required for prescribing buprenorphine to treat OUD. Effective December 29, 2022, prescriptions no longer need to have an X-DEA number.[41]

Although 201 KAR 9:270 still refers to the waiver, the Kentucky Board of Medical Licensure has said that all licensees with a valid KY DEA registration may prescribe buprenorphine as long as they follow the remaining legal requirements.[42]

The DEA and HHS issued a statement acknowledging that this change is likely to increase demand for buprenorphine and supporting "collaboration amongst all DEA registrants to ensure there is an adequate and uninterrupted supply of MOUD products."[43]

Is telemedicine allowed for buprenorphine prescribing?[44–46]

Practitioners must be licensed in Kentucky to treat a patient who is physically located in Kentucky at the time care is provided. Telemedicine is held to the same standards of practice as traditional in-person practice, including establishing a provider-patient relationship, maintaining patient records, and ensuring the patient

is able to follow up with the provider. A Kentucky Board of Medical Licensure (KBML) opinion on telemedicine states that "telemedicine visit prescriptions carry the same professional accountability as prescriptions delivered during an encounter in person."[44]

For the duration of the nationwide opioid public health emergency (PHE), the DEA permits the prescription of buprenorphine for OUD without the practitioner first conducting an in-person medical evaluation of the patient, if the following prescription conditions are met:

- Issued for a legitimate medical purpose by a practitioner acting in the usual course of professional practice
- Issued pursuant to a communication between a practitioner and a patient using a telecommunications system

  The definition of *telecommunications system* includes "audio and video equipment permitting two-way, real-time interactive communication." Audio only is permitted if the patient is not capable of or does not consent to video.
- Consistent with all other requirements of a controlled substance prescription

For all other controlled substances, similar telemedicine flexibilities implemented by the DEA during the COVID-19 PHE have been extended until December 31, 2024.[47]

Learn More

Telemedicine Prescribing Updates

What is low barrier care?[48]

In late 2023, SAMHSA issued an advisory outlining how ***low barrier care*** can engage individuals in substance use disorder treatment and close gaps in treatment access. The advisory defines low barrier care as "a model for treatment that seeks to minimize the demands placed on clients and makes services readily available and easily accessible."[48] Low barrier care has been shown to be both cost-effective and effective for improving treatment.

Compared to high barrier care, which may impose rigid visit schedules, abstinence as the only goal, uniform maximum dosages, and treatment discontinuation for ongoing substance use, low barrier care emphasizes individualized and non-punitive care, with elements like telemedicine or walk-in appointments, home medication initiation, and co-located medical, behavioral, and social services to encourage engagement and retention in treatment.

Learn More

SAMHSA Advisory

When should you seek more info about a buprenorphine prescription?

The Oath of a Pharmacist calls for the consideration of "the welfare of humanity and relief of suffering" as a primary concern, and federal law assigns pharmacists a "corresponding responsibility" for ensuring that controlled substance prescriptions are issued for a legitimate medical purpose in the usual course of professional treatment.[49,50] Pharmacists can meet both of these obligations by understanding clinical guidelines, reviewing state and federal regulations, communicating with prescribers,

documenting details, and placing individual patient outcomes at the center of the decision-making process.

NABP/NCPA draft guidelines remind pharmacists that "all pharmacy staff should approach persons living with OUD with empathy, compassion, and support."[10]

Generally, pharmacists can approach buprenorphine prescriptions using the same standard as typical pharmacy practice. Seek and document more information from a patient or prescriber when a buprenorphine prescription fails to meet technical requirements (e.g., missing information or suspicious format) or when the prescribed therapy does not conform to established evidence-based care.

In Kentucky, state regulations establish professional standards for prescribers of buprenorphine. While only the Board of Pharmacy can regulate pharmacy practice, prescribing regulations can inform pharmacists' decisions. The following elements of the buprenorphine regulations may be relevant:[23,24]

Indication: KBML limits buprenorphine prescribing to FDA-approved indications, with some products approved for pain and others for OUD. The Kentucky Board of Nursing (KBN) regulation does not include this limit.

Mono-Products: Buprenorphine that does not contain naloxone can only be prescribed for OUD under one of the following conditions:

- Administration in a physician's office or other healthcare facility
- Pregnancy
- Demonstrated hypersensitivity to naloxone
- Transition from methadone to buprenorphine (limited to 1 week)

Concomitant Medications: Consultation with a provider certified in addiction medicine, preventative medicine or psychiatry is required when buprenorphine is prescribed with benzodiazepines, sedative hypnotics, stimulants, or opioids. Consultation is not necessary for an extraordinary or acute medical need not exceeding 30 days.

Maintenance Dosing: Doses of buprenorphine are individualized to minimize cravings and withdrawal

Which Regulation Applies?

KBML promulgates regulations for Kentucky physicians and PAs, and KBN promulgates regulations for APRNs and other nurses. Each board has its own buprenorphine regulation, and though they are similar, there are differences between the two. Pharmacists should ensure that they are reviewing the correct regulation – 201 KAR 9:270 for physicians and PAs and 201 KAR 20:065 for APRNs – if they are concerned about a specific buprenorphine prescription. Remember that laws are routinely revised and amended, so use official sources to access the latest version.

Are there Exceptions?

Both 201 KAR 9:270 and 201 KAR 20:065 contain provisions for circumstances in which a buprenorphine prescriber "makes a professional determination that it is not appropriate to comply with a specific standard, based upon the individual facts applicable to a specific patient's diagnosis and treatment." In these circumstances, the prescriber may deviate from the regulation but must document the situation in the patient's record and prescribe in accordance with SAMHSA guidelines.[23,24]

Learn More

201 KAR 9:270

201 KAR 20:065

Note: This section details elements of the law specific to the use of buprenorphine for the treatment of OUD. Other controlled substance regulations are not included but may apply. This document is not legal advice.

without sedation. The goal is improving quality of life and ability to function in the community. Quantity should supply the patient only until the next visit.

Under KBML's regulation, the dose is taken once daily, except up to:[23]

- BID if pregnant
- BID if daily dose is less than 16 mg
- TID if in cancer treatment, hospice or palliative care
- TID for up to 14 days following major surgery or significant physical trauma

KBN's regulation does not impose a once-daily dosing limit on buprenorphine.[24]

How should you handle red flags with buprenorphine prescriptions?

Historically, the DEA and pharmacists have relied on a patchwork of so-called "red flags" as indications that a controlled substance prescription is not appropriate. The national opioid settlements entered into by several large pharmacy chains have codified specific red flags for controlled substance prescriptions.[51]

Both court cases and the national opioid settlements have established that red flags do not prohibit dispensing of a controlled substance but call for the pharmacist to resolve the red flag prior to dispensing. The national opioid settlements state that "the method of resolution falls within the judgment of the pharmacist," including options like reviewing the patient's profile and history, calling a prescriber, speaking with the patient, relying on pre-existing knowledge of the patient or prescriber, and reviewing the prescription drug monitoring program or other information available to the pharmacist.[51]

When dispensing buprenorphine, it is important to note that many red flags — e.g., traveling long distances, using telemedicine, and paying cash — may be indicative of access barriers to OUD treatment rather than likely diversion or misuse.[52,53] Pharmacists should rely on efficient methods of resolution that take into account the individual patient's circumstances and relative safety of buprenorphine compared to full-agonist opioids. NABP/NCPA draft guidelines caution that "pharmacists should weigh the risks of delaying treatment against the benefits of waiting for the provider to respond to the pharmacist's query," and consider dispensing a partial fill while waiting for clarification from a prescriber.[10]

Learn More

NABP/NCPA PhARM-OUD Guideline

How can pharmacists support treatment with buprenorphine?

In addition to routine patient counseling, pharmacists should address specific safety concerns with patients who take buprenorphine for OUD.

Precautions to Discuss[54]

- Risk of overdose is increased with benzodiazepine or alcohol use.[18]
- Do not inject sublingual or buccal forms of buprenorphine. This can lead to overdose.[18]
- Do not share buprenorphine.[16]
- Abrupt discontinuation can lead to opioid withdrawal and put you at

increased risk for suicide, return to drug use, and opioid overdose.

- Notify healthcare providers if surgery is planned. Buprenorphine schedule adjustments and higher short-acting opioid doses may be required for pain management.[20]
- Notify your health care providers if you become or plan to become pregnant or are breastfeeding.[16]
- Dispose of medication safely. (Visit **http://www.fda.gov/drugdisposal** for more information.)

Questions to Ask[18]

Because patients with OUD face unique challenges and barriers to treatment, pharmacists can initiate conversations to gather information about factors that may influence treatment success and help patients on their path to recovery.

How are you today? How can I help?

- You can be a positive influence on a patient's recovery and remission with simple acts of respect and care.

Do you have naloxone? Do you and the people around you know how to use it?[16]

- The pharmacy can dispense under protocol or request a prescription, provide training, or recommend a community resource for overdose education and naloxone distribution.

Where do you store your medication?[16]

- Safe storage can reduce diversion or unintentional pediatric exposure.

Do you experience sedation (sleepiness, drowsiness) or cognitive impairment (trouble thinking, brain fog)? Do you feel euphoric (high)? Do you have withdrawal symptoms?

- Adverse effects may require a dose adjustment. Inquiries about other medications with CNS depression and administration technique can help guide dose adjustments.

What Else Could Help?

Asking about social determinants of health can help pharmacists dig deeper into barriers faced by patients with OUD:

- Do you have reliable housing and transportation?
- Do you have social support?
- Are you employed?
- Do you have health insurance?
- Do you have reliable child care?

To learn more, read a document from The EveryONE Project at **http://p2p.uky.edu/sdoh**

Patients and families looking for mental health and recovery-related services, naloxone, and community resources can visit **http://www.findhelpnowky.org**

Have you had any changes in your prescription or over-the-counter medicine?

- It is important to have a full medication history and to be aware of changes to prevent drug interactions.

Have you had any instances of substance use?

- Return to drug use or use of other controlled substances can occur in patients being treated for OUD. Substance use during treatment is ***not*** an indication to discontinue buprenorphine but may indicate that a patient needs a dose adjustment or higher level of care.
- Create an environment where patients feel safe sharing their progress.[3]

What are your treatment goals? How is your progress toward meeting your goals?

- Healthcare provider goals may differ from what the patient hopes to gain from treatment of OUD. Find

out what success looks like for the patient and celebrate victories.

Do you smoke or vape? Do you drink alcohol?[18]

- Patients with OUD may use other substances. Screening and offering treatment is important.

Do you have any questions or concerns about withdrawal? Can you tell the difference between withdrawal symptoms and an allergic reaction to buprenorphine?[18]

- Fear of withdrawal based on past experiences can be a barrier to buprenorphine initiation. This may be a good topic for patients who are doing a home/community buprenorphine induction.
- Unpleasant withdrawal symptoms may lead patients to believe that they are having a reaction to buprenorphine. Education can help patients identify a true allergy.

How often do you take buprenorphine? How often do you miss doses of your medication?

- Medication non-adherence is a problem in the treatment of many chronic diseases. A patient taking medication in a manner that is different from prescribed is as important as missed doses. Correct misunderstandings on instructions, explain the importance of consistent drug levels, and try to find out why a patient has made changes. Adjustments in treatment may be beneficial.

Are you up to date on screenings and vaccines? When was your last visit to the dentist?[16,55]

- Treat the whole patient. Ask about other medical conditions and infectious diseases. Recommend screenings and vaccines when appropriate.
- Xerostomia and dental carries can be associated with sublingual and buccal buprenorphine. Monitoring and prevention instructions are important.[55] Gently rinsing with water after administration and waiting an hour before brushing are recommended for prevention.[56]

What questions do you have?

- Patients may be hesitant to ask questions and may not understand standard pharmacy operations, regulations, or medical terminology. Invite questions to help prevent misunderstandings.[21]

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The Buprenorphine Resource Initiative for Dispensing Guidance and Education (BRIDGE) is the first project of the Pharmacist to Pharmacist (P2P) educational outreach initiative.

P2P pharmacists bring evidence-based recommendations to practicing pharmacists to improve practice and health in Kentucky. BRIDGE aims to identify and mitigate pharmacy-level barriers to dispensing buprenorphine for opioid use disorder in 23 counties in Appalachian Kentucky.

To access additional continuing education activities from P2P, visit https://p2p.uky.edu/cpe

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References are abbreviated for space; full list available at http://p2p.uky.edu/QandA.
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