

# Narrative Review: Buprenorphine for Opioid-Dependent Patients in Office Practice

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The profile of opioid dependence in the United States is changing. Abuse of prescription opioids is more common than that of illicit opioids: Recent data indicate that approximately 1.6 million persons abuse or are dependent on prescription opioids, whereas 323 000 abuse or are dependent on heroin. Despite this prevalence, nearly 80% of opioid-dependent persons remain untreated. One option for expanding treatment is the use of buprenorphine and the buprenorphine–naloxone combination. Buprenorphine is a partial opioid agonist that can be prescribed by trained physicians and dispensed at pharmacies.

This article addresses the clinical presentation of a patient with

opioid dependence and describes the relatively new practice of office-based treatment with buprenorphine–naloxone. The different components of treatment; the role of the physician who provides this treatment; and the logistics of treating this growing, multifaceted patient population are also examined.

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**A** 35-year-old woman returns for a follow-up appointment for management of diabetes mellitus and depression. In reviewing her chart, you notice that she has received prescriptions for oxycodone from your colleagues for the past 6 months and has requested early refills. You originally prescribed oxycodone for a wrist fracture last year, but nothing indicates that she should continue to require this medication.

She seems uncomfortable when you express concern. She admits to excessive use of oxycodone, despite the healing of her fracture. She feels pain “all over” once the oxycodone wears off and notes that opioids give her energy. She visited various physicians and emergency departments in the past 6 months to obtain opioids and has stolen morphine from her mother.

*Is this patient opioid-dependent? How common is addiction to prescription opioids?*

Diagnosing opioid dependence is challenging, especially in patients who take prescription opioids and report pain (1). Some behaviors (although none have been validated) can alert clinicians to potential misuse of controlled substances, such as losing, stealing, or adulterating prescriptions; using other sources to obtain medications (for example, obtaining prescriptions from other physicians or purchases from non–medical professionals); requesting early refills; and urine toxicology results inconsistent with prescriptions (2, 3). Anxiety symptoms, fair or poor health, misuse of another class of prescription medications, heroin use, and initiation of substance use before age 13 years are more common in patients who misuse prescription opioids and have a diagnosis of opioid abuse or dependence (4).

See also:

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The criteria for opioid dependence in the *Diagnostic and Statistical Manual of Mental Disorders IV-R* (5) include physical dependence and behaviors that constitute addiction (Table 1). Physical dependence occurs after short periods of opioid use and is characterized by tolerance and withdrawal (6, 7). Opioid dependence (addiction) is a chronic, relapsing disease characterized by impaired control over drug use that persists despite harms (5).

Neurobiological changes occur during development of opioid dependence. Opioid use leads to neuronal adaptations in various regions of the brain. Adaptations in G-protein–coupled receptors, upregulation of cyclic adenosine monophosphate second messenger pathways, and changes in transcription and translation (8) result in tolerance, withdrawal, and craving.

Prescription opioids dominate the profile of opioid dependence in the United States. Data from the 2006 National Survey on Drug Use and Health, a federally administered sample that may underreport the prevalence of opioid dependence in general because of undersampling in marginalized populations, stated that 3.7 million persons reported lifetime heroin use and more than half a million reported heroin use in the past year (9). Approximately 323 000 persons met criteria for heroin abuse or dependence. More than 12 million persons reported nonmedical use of prescription opioids (9). Of these, 1.6 million met criteria for prescription opioid abuse or dependence; 73% were employed, 77% had completed high school, 41% had an annual income greater than \$40 000, and 61% were insured (4). Most persons do not receive treatment. In 2005, only 331 000 persons entered treatment for opioid dependence (10). The discrepancy between the scope of the problem and the number of persons receiving treatment creates a need to expand access.

*The patient becomes teary and admits to snorting heroin to relieve withdrawal symptoms. She injected heroin once, last*

*New Year's Eve. You refer her to a local clinic for methadone. She states that she knows too many people and cannot be seen in a drug treatment clinic. She requests a referral for "detox" so she can "be off of everything."*

*Is detoxification the right treatment option for some patients?*

Patients may express a desire to be "off of everything." Studies of detoxification are often limited by lack of long-term follow-up (11). Good-quality evidence shows that the outcomes of ongoing medication treatment (maintenance) with methadone (opioid agonist) or buprenorphine (partial agonist) are better than those of detoxification (12). A meta-analysis revealed that methadone retained patients in treatment (relative risk [RR], 3.05 [95% CI, 1.75 to 5.35]) and decreased heroin use (RR, 0.32 [CI, 0.23 to 0.44]) more effectively than detoxification (13). Good-quality evidence reveals similar outcomes with buprenorphine detoxification. Findings in patients randomly assigned to individual counseling and either buprenorphine maintenance or a 6-day buprenorphine detoxification showed that 75% of the maintenance group and 0% of the detoxification group were in treatment at 1 year ( $P < 0.001$ ) (14). Four patients in the detoxification group died during follow-up, and none remained in treatment after 50 days. In another study of buprenorphine detoxification, only 15 of 37 patients (14%) had 2 or fewer opioid-positive urine tests and were retained in treatment for 12 weeks (15).

Some studies demonstrate reasonable short-term treatment retention with detoxification (16, 17). A trial of detoxification, along with counseling, may be appropriate for patients who have been dependent for only a short period and have a low level of dependence (16, 18). Physicians should warn patients who attempt detoxification that if they resume opioid use at their predetoxification levels, they will have decreased tolerance and risk overdose and death (19).

### Key Summary Points

A trained physician can prescribe buprenorphine–naloxone, a medication used to treat opioid dependence, providing increased access to treatment. Although buprenorphine–naloxone is less effective than methadone in retaining patients in treatment and decreasing illicit opioid use, it can be prescribed by office-based physicians and dispensed at pharmacies.

Patients who have no substantial, untreated psychiatric conditions or who do not abuse substances other than opioids; have no history of office-based treatment failure; and can adhere to office guidelines are probably good candidates for office-based buprenorphine–naloxone treatment.

Physicians can qualify to prescribe buprenorphine–naloxone by completing an 8-hour course on the treatment of opioid dependence. The U.S. Drug Enforcement Administration issues a new registration certificate code to the physician, which is needed on all prescriptions written for buprenorphine–naloxone.

Office-based treatment of opioid dependence gives physicians the opportunity to care for and treat opioid-dependent patients. It also allows patients to view their addiction as a manageable medical condition.

*The patient undergoes a 14-day detoxification. One week later she reports that she is again abusing oxycodone. She wants to know if you can provide treatment from your office. You indicate that you received training and have begun providing a new medication, buprenorphine–naloxone, for opioid dependence.*

*What are the important differences between buprenorphine–naloxone and methadone treatment?*

**Table 1. Criteria for Opioid Dependence\***

Use of opioids in a maladaptive pattern that leads to clinically significant impairment or distress, manifested by  $\geq 3$  of the following (occurring at any time in the same 12-month period):

Tolerance, defined by 1 of the following:

- Needing markedly increased amounts of opioids to achieve intoxication or desired effect
- Experiencing a markedly diminished effect with continued use of the same amount of opioids

Withdrawal, manifested by 1 of the following:

- Experiencing the characteristic withdrawal syndrome for opioids
- Taking opioids (or a closely related substance) to relieve or avoid withdrawal symptoms
- Using larger amounts of opioids or taking them for a longer period than intended
- Persistent desire or unsuccessful efforts to reduce or control use
- Spending a great deal of time on activities necessary to obtain opioids (for example, visiting multiple physicians or driving long distances), using opioids, or recovering from their effects
- Reducing or giving up important social, occupational, or recreational activities because of opioid use
- Continuing opioid use, despite knowledge that opioids are probably causing or exacerbating a persistent or recurrent physical or psychological problem (for example, opioid use despite recognition of opioid-induced depression)

\* Adapted from reference 5.

Buprenorphine is a partial agonist at the  $\mu$  opioid receptor (Table 2). It has low potential for abuse and diversion (25), especially when combined with the antagonist naloxone, and has a low risk for respiratory depression or overdose (26). It is a sublingual tablet, usually taken daily. Although good evidence demonstrates reduced treatment retention (RR, 0.79 [CI, 0.62 to 1.01]) and reduced ability to suppress illicit opioid use (standardized mean difference, 0.27 [CI, 0.05 to 0.50]) in trials comparing buprenorphine with methadone (27), buprenorphine and buprenorphine–naloxone may be prescribed by physicians and dispensed at pharmacies, whereas methadone must be dispensed from opioid treatment programs (28).

In the United States, the ratio of buprenorphine to naloxone in the combination tablet is 4 to 1 (29–34). This combination may reduce the potential for abuse compared with buprenorphine alone (35, 36). Buprenorphine is well absorbed sublingually, and naloxone absorption is limited (37, 38); however, when naloxone is injected, it is rapidly bioavailable and can precipitate withdrawal in patients who are opioid dependent (39). Physicians should use the buprenorphine–naloxone combination instead of buprenorphine monotherapy, except for directly observed treatment or during pregnancy (40).

Women receiving buprenorphine–naloxone who become pregnant should switch to buprenorphine alone or methadone (40). Current data indicate that buprenorphine

may be safe in pregnancy (41). To our knowledge, there are no studies on the safety of naloxone during pregnancy (42).

*What is required for a physician to prescribe buprenorphine–naloxone for opioid dependence? What training and support are needed?*

The Drug Addiction Treatment Act of 2000 (43) allows qualifying physicians to use approved medications to treat opioid dependence (Table 3). Most physicians can qualify by completing an 8-hour course on the treatment of opioid dependence. Information on training is available at [www.buprenorphine.samhsa.gov](http://www.buprenorphine.samhsa.gov). In 2005, 56% of physicians eligible to prescribe were non-addiction specialists (25). As of January 2008, 13 095 U.S. physicians were trained.

Once qualified, a physician must notify the Center for Substance Abuse Treatment of their intent to practice under the Drug Addiction Treatment Act of 2000. Notification forms are available at [www.buprenorphine.samhsa.gov](http://www.buprenorphine.samhsa.gov). Subsequently, the Drug Enforcement Administration issues a second registration certificate code, which is needed on all prescriptions for buprenorphine–naloxone for opioid dependence.

To assist physicians unaccustomed to providing treatment for addiction, the Center for Substance Abuse Treatment provides a practice guideline (40) and funds the Phy-

**Table 2. Comparison of Buprenorphine or Buprenorphine–Naloxone and Methadone for the Treatment of Opioid Dependence**

Characteristic	Buprenorphine or Buprenorphine–Naloxone	Methadone
Pharmacologic action at $\mu$ opioid receptor	Buprenorphine (partial agonist) and naloxone (full antagonist)	Full agonist
Clinical indication	Pharmacologic withdrawal, maintenance therapy	Pharmacologic withdrawal, maintenance therapy
Route of administration	Sublingual*	Oral
Dose	Buprenorphine, 2–32 mg† (20); naloxone, 0.5–8 mg*	20–120 mg†
Frequency of administration	Daily or 3 times weekly	Daily
Primary side effects (unrelated to withdrawal syndrome)	Headache, nausea, sweating, constipation, rhinitis (21–23)	Cardiac dysrhythmia, hypotension, diaphoresis, constipation, nausea, vomiting, asthenia, dizziness, lightheadedness (24), sedation
Contraindications	Need for ongoing full opioid agonist medications to obtain pain relief; hypersensitivity to either compound	Hypersensitivity
Use in pregnancy	Category C: Buprenorphine–naloxone is not recommended in pregnancy and should be replaced with methadone or buprenorphine alone	Category C: Methadone is considered current standard of care for treatment in pregnancy because there are more data on its safety in pregnant patients
Location of prescribing and dispensing treatment of opioid dependence	A physician's office or opioid treatment programs	Opioid treatment programs
Regulations on prescribing and dispensing treatment	Physicians can prescribe only with a special registration certificate code issued from the Drug Enforcement Administration; 30-patient census per prescriber in first year and 100-patient census thereafter; pharmacies can dispense up to a 30-day supply on the basis of schedule III	Physicians can prescribe methadone only to patients with opioid dependence for up to 72 hours as a bridge to treatment entry; only licensed opioid treatment programs can dispense methadone; federal regulations govern frequency of medication dispensing (e.g., daily, 3 times weekly, weekly)
Insurance coverage	Variable, depending on insurance plan	Variable, depending on insurance plan

\* Naloxone is not well absorbed sublingually, resulting in a primary buprenorphine effect. Naloxone is added to discourage injection misuse.

† Lower doses typically reflect dose initiation or dose tapering in stabilized patients.

**Table 3. Criteria for Physicians to Qualify to Prescribe Medications Under the Drug Addiction Treatment Act of 2000**

Licensed physician who meets 1 of the following criteria:

- Completion of an 8-hour course provided by the American Society of Addiction Medicine, American Academy of Addiction Psychiatry, American Osteopathic Association, American Psychiatric Association, or American Medical Association
- Board certification in addiction psychiatry
- Certification in addiction medicine by the American Society of Addiction Medicine or American Osteopathic Association
- Served as an investigator in a buprenorphine clinical trial leading to the U.S. Food and Drug Administration approval
- Training or experience determined by state medical licensing board
- Other criteria established through regulation by the Secretary of Health and Human Services

sician Clinical Support System ([www.pcssmentor.org](http://www.pcssmentor.org)), which provides mentoring services by e-mail, telephone, or onsite visits to prescribers of buprenorphine–naloxone.

*You discuss with the patient that opioid dependence is a medical condition. You note that it is a chronic and relapsing disorder that may need treatment with medication, counseling, and lifestyle modification. She agrees to try buprenorphine–naloxone.*

*What are the features of office-based buprenorphine–naloxone treatment? What does a physician need to provide this care?*

Office-based treatment emphasizes a medical approach to opioid dependence. **Table 4** outlines the important features of office-based buprenorphine treatment. Not all patients should receive treatment from an internist. Research demonstrates that patients who have no substantial, untreated psychiatric conditions or who do not abuse substances other than opioids can do well in this setting (44–47). Patients in whom office-based treatment has failed in the past; those with severe psychiatric illness, comorbid substance use, or high levels of physical dependence; and those who cannot adhere to office guidelines may do poorly (40).

History and physical examination aid in patient selection. The history should confirm the diagnosis of opioid dependence. Documentation should include the effect of dependence on daily function, substance use history, past treatments, psychiatric history, and injection-related diseases. Appropriate testing and vaccinations should be provided (48–50). Laboratory assessments should include liver function tests (51) and a complete blood count and standard chemistries, as indicated. Buprenorphine–naloxone seems to pose minimal risks for liver toxicity when taken sublingually. Liver function tests should be conducted at baseline and periodically, if indicated (52).

Monitoring by means of urine toxicology is important because patients may deny drug use. Once a patient has begun maintenance treatment, urine testing can be conducted weekly to monthly (40). Urine immunoassay testing can infrequently give false-positive and false-negative results due to interference from contaminants (53, 54). For further analysis, physicians can use chromatography or

mass spectrometry. Repeated urine sample testing can also increase accuracy. Standard urine analyses detect naturally occurring opioids and their metabolites (for example, morphine and heroin). Physicians should request testing for synthetic or semisynthetic opioids (oxycodone, methadone, hydrocodone). Standard urine assays detect recent use of heroin or morphine (1 to 3 days), some benzodiazepines ( $\leq 30$  days), cocaine (1 to 3 days), methadone (2 to 4 days), marijuana (chronic use,  $\leq 30$  days; occasional use, 1 to 3 days), and oxycodone (1 to 2 days) (55). The response to positive results on a urine test should take into account the overall clinical picture, type of drug found, and stage of treatment. Responses include increasing the frequency of visits, changing the dose, initiating or increasing the level of counseling, or transferring to another form of care (for example, methadone or inpatient).

The patient and provider should agree on the terms of treatment before the first prescription is written. Resources to assist physicians in discussing buprenorphine–naloxone induction and maintenance, medication adherence, and examples of patient–provider agreements are available ([www.csam-asam.org/resources-buprenorphine\\_info.vp.html](http://www.csam-asam.org/resources-buprenorphine_info.vp.html)). Information for patients and their families about buprenorphine–naloxone treatment is also available (56).

*Are there medication interactions to consider?*

Buprenorphine is metabolized to norbuprenorphine by the cytochrome P450 3A4 (CYP3A4) isoenzyme. In theory, CYP3A4 inhibitors may increase and CYP3A4 inducers may decrease plasma concentrations of buprenorphine, and providers should consider adjusting the buprenorphine–naloxone dose accordingly. However, clinical experience suggests otherwise—few reports of interactions exist. Empirical studies focus on protease inhibitors (57). These data indicate that although some pharmacokinetic changes may lead to sedation in a few patients receiving atazanavir and buprenorphine, most interactions do not seem to be clinically significant (58–60).

*What instructions should physicians give patients before their first dose of buprenorphine–naloxone?*

Patients should be instructed to abstain from short-acting opioids, such as heroin or oxycodone, for 12 to 24 hours or from long-acting opioids, such as methadone or

**Table 4. Requirements for Physicians to Provide Buprenorphine or Buprenorphine–Naloxone Treatment**

Certification in addiction medicine, psychiatry, or completion of an 8-hour training course qualified under the Drug Addiction Treatment Act of 2000
Receipt of a second registration certificate code from the Drug Enforcement Administration, which needs to be on written prescriptions for buprenorphine and buprenorphine–naloxone
Ability to diagnose opioid dependence
Ability to conduct urine toxicology testing (on-site or referral to outside laboratory)
Ability to conduct basic laboratory assessments
Capacity to establish linkages to mental health professionals and substance abuse treatment programs

sustained-release oxycodone, for 24 to 36 hours before their first dose of buprenorphine–naloxone. This ensures mild-to-moderate opioid withdrawal before they take their first dose. The patient should present for induction in mild-to-moderate withdrawal. Formal opioid withdrawal scales are available to assess the severity of withdrawal (40). Buprenorphine has high affinity for the  $\mu$  opioid receptor but partial agonist activity. It can cause opioid withdrawal by displacing full opioid agonists. The overall decrease in agonist activity that accompanies the abrupt transition from a full agonist to buprenorphine is referred to as “precipitated withdrawal” (61–63).

Scheduling the induction appointment early in the day can decrease the risk for recent opioid use. Starting treatment before the end of the week allows for weekday follow-up.

Transferring patients from methadone to buprenorphine can be difficult because methadone is a relatively long-acting opioid agonist and can be stored in the liver and adipose tissue and released, leading to ongoing agonist activity (64). Data on the optimal dose of methadone for a patient transferring to buprenorphine–naloxone are limited. One guideline recommends less than 30 mg of methadone daily (64). Recent clinical experience suggests that patients should decrease the dose to less than 40 mg/d (65, 66). The appropriate dose of buprenorphine–naloxone for patients who are transferring from methadone is also not clear. One study found that lower doses of buprenorphine–naloxone produced less withdrawal than larger doses in patients stabilized on methadone (67). Induction should be initiated 24 to 48 hours after the last dose of methadone and when the patient is manifesting opioid withdrawal.

Clinicians have developed induction techniques that are compatible with primary care and office-based practice (20, 44–47, 68, 69). One detail to address is how patients will obtain their first dose. Physicians can keep a supply of medication in the office for administration on the induction day (storage must be consistent with regulations for class III controlled substances), they can have the patient fill a prescription for the first day’s dose and bring it to the office, or they can fax the prescription and have the medication delivered. Home inductions have demonstrated feasibility in selected populations (44).

Once withdrawal is documented, a reasonable first dose of combination therapy is 2 mg buprenorphine/0.5 mg naloxone to 4 mg buprenorphine/1 mg naloxone. The

maximum first-day dose typically ranges from 8 mg buprenorphine/2.0 mg naloxone to 12.0 mg buprenorphine/3 mg naloxone. During the induction and stabilization period, the patient should be seen at least weekly. Biweekly or monthly visits can be initiated once the patient has a stable medication dose and is making progress toward abstinence. Key components of these visits include discussion of ongoing drug use, identification of triggers, discussion of urine toxicology results, and potential modifications in medication dosing.

#### *What type of counseling should be provided?*

Counseling can enhance pharmacologic treatment of addiction. Opioid-dependent patients benefit from education and counseling, similar to patients with diabetes and hypertension (70). Some patients continue to use opioids (because of the psychological aspects of their addiction) or develop or manifest use of other substances (for example, alcohol, benzodiazepines, or cocaine). Specific counseling techniques can help address concomitant drug and alcohol use (71, 72). One study of patients who received methadone from a treatment-program demonstrated better abstinence and treatment retention among patients who received more intensive services (73). A systematic review of studies of patients who received methadone from a treatment program demonstrated that counseling was associated with decreased heroin use but no statistically significant improvement in treatment retention (18). Trials with different intensities of counseling for patients who received either buprenorphine or buprenorphine–naloxone report contradictory results (45, 74). Findings from an observational study of buprenorphine–naloxone in a primary care setting showed a positive association between counseling attendance and treatment retention (47). In another study, approximately 50% of patients sought counseling and 25% attended self-help groups (44). A trial of 3 levels of counseling and visit frequency did not detect decreased drug use or improved retention in patients who received 40 minutes of weekly counseling compared with those receiving 20 minutes (45). Less intensive counseling was associated with greater patient satisfaction (75).

Physicians prescribing buprenorphine–naloxone must be able to access counseling for their patients (43). The actual use of counseling, however, seems to be infrequent. In a study of patient experience, 41% reported no counseling in the first month of treatment (76). The options for

counseling in office-based practices vary by setting. Some practices provide on-site counseling services by allied health professionals, nurses, or social workers. Most settings need to refer patients to local services. Physicians can cultivate relationships with nurses, social workers, mental health counselors, treatment facilities, or local self-help groups. It is useful to review local addiction treatment providers (<http://findtreatment.samhsa.gov>) and those covered by a patient's insurance. Patients with substantial comorbid psychiatric conditions may need to be comanaged with a psychiatrist or transferred to the care of an addiction psychiatrist.

*How does one bill for office-based buprenorphine–naloxone therapy?*

Office-based buprenorphine treatment is new, and the reimbursement system is evolving (77). Private and public insurers have variable coverage. Some insurers cover all services provided by a physician and others do not. Items that need to be covered include office visits (typically weekly during stabilization and biweekly or monthly once the patient is stable), medication, counseling (typically weekly or biweekly during stabilization and monthly once the patient is stable), urine testing (conducted weekly to monthly), and blood tests (at baseline and repeated when clinically indicated) (40). Urine toxicology analyses range between \$5 and \$55, depending on the type of assay and the number of tests done. Daily medication doses generally range from 8 mg to 24 mg and can cost \$4 to \$19 per day (Jones ES, et al. Cost analysis of clinic and office-based treatment of opioid dependence: results with methadone and buprenorphine in clinically stable patients. Under revision.) Some patients may need to pay out-of-pocket for certain items. Physicians should determine how the expenses will be covered before initiating treatment. The International Classification of Diseases, Ninth Revision, code for opioid dependence is 304.0. Providers can use Current Procedural Terminology codes, such as outpatient new patient (99201, 05), outpatient consultation (99241, 45), and outpatient established patient revisit (99211, 15), for office visits.

*How should office staff and colleagues providing coverage be educated?*

It is useful to educate office staff to facilitate a positive experience for the patients, providers, and staff (78). Training for office staff should include general education about addiction and the rationale for medication treatment (45, 70). It may be necessary to educate staff about using a nonjudgmental attitude (79, 80). Staff should know the confidentiality guidelines (81).

Buprenorphine–naloxone providers must assure cross-coverage for their patients. The covering physician needs a special Drug Enforcement Administration registration certificate code only if prescribing the medication. No specific

registration is needed for general medical and psychiatric conditions.

*The patient does well with buprenorphine–naloxone and attends monthly appointments with you and a social worker. Her hemoglobin A<sub>1c</sub> level improves because of better medication compliance. Her depression improves with abstinence, but ultimately a complete response is achieved with a selective serotonin reuptake inhibitor. After several months, your service pages you. The patient is in the emergency department with a kidney stone. She is worried about receiving opioids for pain and is not sure if she should take her buprenorphine–naloxone.*

*What happens if a patient requires pain medication while receiving buprenorphine–naloxone?*

It is appropriate to use opioids to manage pain in opioid-dependent patients; however, clinicians should be cautious to avoid precipitating a relapse to uncontrolled use. One strategy is to discuss this concern with the patient and limit the number of pills and the duration of opioid use. Opioid-dependent patients often require higher doses than patients who are not dependent because of tolerance.

Buprenorphine has high affinity and slow dissociation at the  $\mu$  opioid receptor; as a result, it can be difficult to achieve analgesia in a patient receiving buprenorphine–naloxone. One study reviewed acute pain management in patients receiving methadone and buprenorphine (1). In brief, moderate pain can be managed by continuing the buprenorphine–naloxone and adding nonsteroidal anti-inflammatory agents. If a painful condition is anticipated (for example, elective surgery), the last dose of buprenorphine–naloxone should occur approximately 24 hours before the need for analgesia. For brief pain (8 to 12 hours), short-acting full opioid agonists can be titrated. Alternatively, a case report described the benefits of a temporary increase of buprenorphine–naloxone for analgesia (82).

For severe pain lasting longer than 12 to 24 hours, buprenorphine–naloxone treatment should be discontinued and replaced with a full-agonist analgesic. Initial doses may be higher than needed on subsequent days to overcome partial blockade of the opioid receptors due to the buprenorphine. Once the pain no longer requires opioids, patients should discontinue the opioid medication, experience withdrawal, and start buprenorphine–naloxone treatment again.

*The patient successfully passes her kidney stone, and buprenorphine–naloxone treatment is started again. She returns to your office 2 weeks later. When asked about her drug use, she hesitates and admits that over the weekend, after drinking with friends, she took some oxycodone. She did not report feeling any euphoria or withdrawal, only guilt.*

*How should episodic drug use be handled?*

Episodic illicit opioid use in previously abstinent patients is common in patients receiving buprenorphine–

naloxone. In 1 trial, only 27% of patients achieved continuous abstinence from opioids for 13 weeks (83). Another study reported 26% of patients achieving 12 weeks or more of continuous abstinence (84). In patients followed for at least 2 years, 9% of urine test results had evidence of illicit opioid use (85). Episodic use does not mean that treatment has failed, but it needs to be addressed to prevent complete relapse. The clinician should ensure that the patient is taking a full dose of medication and allowing adequate time for it to dissolve. The patient should be asked about the circumstances surrounding illicit opioid use (for example, concomitant alcohol use or psychosocial stressors) and symptoms of opioid withdrawal or craving. The dose of medication can be increased in 2- to 4-mg intervals to alleviate craving or withdrawal. The clinician can increase the frequency of urine testing or counseling (for example, every 4 or 7 days) and shorten the duration of prescriptions (for example, 7 or 14 days).

*You increase the frequency of urine testing to weekly for 4 weeks, and the patient experiences no further relapses and continues to see you on a monthly basis. The patient has now been in office-based treatment with you for more than 1 year and is asking about discontinuing buprenorphine–naloxone.*

*How should buprenorphine–naloxone be tapered? How should one educate patients who would like to discontinue pharmacotherapy for opioid dependence?*

Most literature supports the efficacy of maintenance treatment over detoxification. In some cases, detoxification is the end point of long-term opioid agonist treatment with either buprenorphine or methadone. Withdrawal from buprenorphine may be milder than that from other opioids because of its partial agonist properties. Tapering over a period of months is more successful than tapering over a short period. Data from a small study that compared a shorter detoxification schedule (12 days) with a longer detoxification schedule (36 days) showed that gradual reduction in buprenorphine produced less patient-rated opioid withdrawal and illicit opioid use and greater treatment retention than the more rapid detoxification (86).

Physicians should consider ancillary medications to assist with opioid withdrawal symptoms in patients who choose detoxification. One trial of buprenorphine–naloxone detoxification showed that approximately 80% of patients received at least 1 ancillary medication for insomnia (62%), anxiety and restlessness (52%), and arthralgia (54%) (16).

Counseling improves outcomes in detoxification. A systematic review found that counseling increased the number of patients who completed treatment (RR, 1.7 [CI, 1.11 to 2.55]) and remained abstinent (RR, 2.4 [CI, 1.61 to 3.66]). Counseling decreased the number of patients lost to follow-up (RR, 0.48 [CI, 0.38 to 0.59]) (18).

Patients considering buprenorphine–naloxone detoxification should know the risk for relapse to drug use and

overdose once maintenance treatment is discontinued. In addition, the provider should highlight the potential need to increase counseling or increase the monitoring of urine toxicologies during and after tapering.

*After discussing the various treatment options with you, the patient decides to continue treatment but states that she would like to consider the option of slowly tapering off buprenorphine–naloxone in the future.*

In conclusion, physicians are often involved with many of their patients' clinical issues that historically have been delegated to other specialties (for example, depression treatment or end-of-life care). Office-based buprenorphine–naloxone treatment gives physicians the opportunity to participate in the care and treatment of their opioid-dependent patients while providing these patients an opportunity to experience their addiction as a chronic medical condition that responds to treatment and can be addressed by a physician. The new option afforded by buprenorphine–naloxone can result in dramatic changes in a patient's life and satisfaction for their provider.

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