Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction

A Treatment Improvement Protocol

TIP 40
5 Special Populations

Overview

The presence of certain life circumstances or comorbid medical or psychosocial conditions warrant special attention during the evaluation and treatment of opioid addiction with buprenorphine. Patients with circumstances or conditions that require special attention include those with certain medical comorbidities (e.g., AIDS, tuberculosis), concurrent mental disorders, or concurrent alcohol or other substance abuse disorders, as well as pregnant women, adolescents, geriatric patients, patients under the jurisdiction of the criminal justice system, and healthcare professionals who are addicted. Because of the unique issues presented by these circumstances, addiction treatment for these patients may require additional training or specialty care and consultation. Before treating individuals with these circumstances for opioid addiction in an office setting, physicians should consider whether patient needs can be met with the resources at hand or if referral to specialized treatment programs or to addiction specialists is indicated.

Patients With Medical Comorbidities

Patients addicted to opioids who present for treatment often have other comorbid medical problems. These conditions are often a consequence of high-risk behaviors, including injection drug use (intravenous, intramuscular, or subcutaneous), or of the direct toxic effects of the active and inert ingredients in illicit drugs. The prevalence of infectious diseases (e.g., HIV/AIDS, hepatitis B and C, tuberculosis, skin and soft tissue infections, syphilis and other sexually transmitted diseases [STDs]) is increased in these patients and should be screened for, as outlined in chapter 3. Other comorbid conditions (e.g., seizure disorders, valvular heart disease secondary to endocarditis, pulmonary hypertension secondary to talc granulomatosis, lymphedema, pseudoaneurysms of the neck and groin secondary to...
thrombophlebitis, and renal insufficiency secondary to heroin-associated nephropathy) also are seen in this population and may require special attention. Patients with a history of endocarditis need antibiotic prophylaxis before certain dental procedures. Patients with a history of hepatitis C may require hepatitis A and B vaccinations and may be intolerant of potentially hepatotoxic medications. One retrospective study found that liver function tests were significantly elevated in patients treated with buprenorphine who also had a history of hepatitis, suggesting that liver function tests should be monitored in these patients on a regular basis during buprenorphine treatment (Petry et al. 2000). A detailed discussion of medical comorbidities in addiction is beyond the scope of this chapter and is reviewed extensively elsewhere (Cherubin and Sapira 1993; Stein 1990).

Treatment of opioid addiction in patients with comorbid medical conditions is likely to result in better outcomes for the comorbid conditions than would be achieved in the absence of treatment of the substance use disorder. Moatti et al. (2000) found that patients on buprenorphine tended to be more compliant with highly active antiretroviral therapies (HAART) than patients who were not treated concurrently for opioid addiction.

Pharmacological treatments of comorbid medical disorders may have important drug interactions with buprenorphine due to shared pharmacokinetic properties. Although Carrieri et al. (2000) found no detrimental short-term effect of buprenorphine treatment on the effect of HAART on viral load, buprenorphine is metabolized by the hepatic cytochrome P450 3A4 enzyme system and will likely interact with other medications metabolized by the same system. Certain antiretrovirals may occupy the cytochrome P450 3A4 system and thus inhibit the metabolism of buprenorphine. Other drugs that induce the cytochrome P450 3A4 system (e.g., certain antituberculosis, anticonvulsant, and antiretroviral medications) may decrease serum concentrations of buprenorphine, resulting in opioid withdrawal or decreased effectiveness. Because the interactions of most medications with buprenorphine have not been systematically studied, physicians should monitor for any signs or symptoms of opioid side effects, loss of effectiveness, or withdrawal after a patient starts any new medications. Buprenorphine dose adjustments may be necessary after starting new medications, even for patients who have been on a stable maintenance dose.

Other potential, and as yet unknown, drug interactions include the possibility of buprenorphine increasing or decreasing metabolism of medications used in treating comorbid medical conditions. Informing patients of potential drug-drug interactions, especially sedation or precipitated opioid withdrawal, is important to prevent jeopardizing adherence with medical treatment and/or precipitating relapse to illicit opioid use.

In summary, it is important to screen for and manage common comorbid medical conditions in patients being treated with buprenorphine for opioid addiction and to anticipate known and potential drug interactions. For additional information on drug-drug interactions with buprenorphine, refer to chapter 2.

Pregnant Women and Neonates

The continued use of heroin during pregnancy, with its attendant risks of infection, overdose, and intrauterine withdrawal, is life threatening to both the woman and the fetus. Research on the safety and efficacy of buprenorphine in pregnant women and neonates is scarce, however. If a patient is pregnant or is likely to become pregnant during the course of opioid addiction treatment, the physician must consider whether buprenorphine is an appropriate option for treatment. Physicians should weigh all the risks and benefits of treatment with buprenorphine against all the risks associated with the continued use of illicit opioids. Methadone is currently the standard of care in the United States for the treatment of opioid addiction in pregnant
Methadone is currently the standard of care in the United States for the treatment of opioid addiction in pregnant women. Methadone has been shown to be safe and effective for both pregnant women and neonates.

The FDA classifies buprenorphine as a Pregnancy Category C drug. The FDA Pregnancy Labeling Task Force, whose long-term goal is to determine how animal toxicologic information contributes to clinically meaningful information in pregnancy, assigns a human prescription drug to Pregnancy Category C (1) if animal reproduction studies have shown an adverse effect on the fetus, (2) if there are no adequate and well-controlled studies in humans, and (3) if the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks. In addition to considering the FDA warnings pertaining to the use of buprenorphine in pregnant women, physicians also must consider the risks of infectious diseases and lifestyle issues (e.g., poor nutrition, lack of prenatal care) when addressing the needs of these patients.

Effects of Buprenorphine in Pregnancy

Data on the pharmacokinetics of buprenorphine in pregnant women and neonates are extremely limited (Johnson et al. 2003a; Marquet et al. 1997). Likewise, data are limited regarding the clinical use of buprenorphine for the maintenance treatment of opioid addiction in pregnant women. The literature in this area generally consists of case reports and a small number of prospective studies; there have been no controlled clinical trials. In case reports from European and Australian sources on the use of buprenorphine in opioid-addicted pregnant women, doses have ranged from 0.4 to 24 mg per day. In these limited reports, pregnancies have generally progressed normally, with low rates of prematurity or other problems. Maternal clinical laboratory data in these reports generally have been within normal limits; or were deemed either clinically nonsignificant at levels expected during pregnancy, when outside normal limits, or were due to factors other than the medication. For a complete review of the published literature on the use of buprenorphine in the treatment of opioid addiction in pregnant women, see Johnson et al. 2003a.

Infants of Mothers Treated With Buprenorphine

Buprenorphine and its metabolite norbuprenorphine have been found in high concentrations in the blood, urine, and meconium of the neonates of women maintained on buprenorphine (Johnson et al. 2003a; Marquet et al. 1997).

The published literature includes information on at least 309 infants born to women maintained on buprenorphine treatment. Although not systematically studied, a neonatal abstinence syndrome (NAS) has been reported in 191 of these 309 infants, with approximately one-half of those with NAS requiring treatment. In more than 40 percent of the cases, however, evaluation of the abstinence syndrome was confounded by other drug use by the mothers. Overall, although no randomized controlled trials have been reported, the NAS associated with buprenorphine has been reported to be less intense than that observed with methadone. One prospective open-label study (Fischer et al. 2000) found signs of NAS in 7 of 15 neonates exposed to buprenorphine in utero. Of these 15 neonates, 3 had moderate signs of NAS that required treatment, 4 had mild signs of NAS that required no treatment, and 8 had no signs of NAS. A second prospective open-label study (Johnson et al. 2003a)
reported NAS in 3 of 3 neonates; however, none required treatment with medications.

NAS from buprenorphine generally appears within the first 2 days of life, peaks within 3 or 4 days, and lasts for 5 to 7 days. Few infants were reported to have had a withdrawal syndrome for 6 to 10 weeks.

Similar to the treatment of NAS following exposure to methadone, several different medications (including chlorpromazine, phenobarbital, benzodiazepine, paregoric elixir, and morphine drops) have been used successfully to treat the NAS associated with buprenorphine. The American Academy of Pediatrics recommends tincture of opium as the medication of choice for treatment of neonatal opioid withdrawal symptoms (American Academy of Pediatrics Committee on Drugs 1998).

Breast Feeding While on Buprenorphine Treatment

The limited human pharmacokinetic data show that buprenorphine passes into the breast milk of lactating women at a plasma-to-milk ratio of approximately 1. As a result, and because of the poor oral bioavailability of buprenorphine, the nursing infant will be exposed to only 1/5–1/10 of the total amount of buprenorphine available.

The literature includes reports on approximately 40 to 50 women who were maintained on buprenorphine and who breastfed after delivery (Johnson et al. 2003a; Lejeune et al. 2001; Loustauneau et al. 2002; Marquet et al. 1997). These reports indicate that buprenorphine present in breast milk does not appear to suppress NAS. Additionally, NAS has not been observed after the cessation of breastfeeding by women who were maintained on buprenorphine (Loustauneau et al. 2002).

Although the Subutex® and Suboxone® package inserts state that breastfeeding is not advised in mothers treated with these medications, it is the consensus of the panel that any effects of these medications on the breastfed infant would be minimal and that breastfeeding is not contraindicated. However, given the limited literature in this subject area, physicians are advised to use their professional judgment in their recommendations.

The Buprenorphine/Naloxone Combination in Pregnancy

The panel notes that there is a question whether the buprenorphine/naloxone combination is or is not recommended for use in pregnancy. Naloxone is labeled by FDA as a Pregnancy Category B drug. The FDA Pregnancy Labeling Task Force assigns a human prescription drug to Pregnancy Category B (1) if animal reproduction studies have failed to demonstrate a risk to the fetus and (2) if there are no adequate and well-controlled studies in pregnant women. Despite the fact that naloxone is classified as a Pregnancy Category B drug, it should be used with caution in pregnant women who are addicted to opioids. Because both mother and fetus will be dependent on the opioids used by the mother, administration of naloxone could precipitate withdrawal in both.

If it is determined that buprenorphine is the only acceptable option for the treatment of a pregnant woman, and she understands the issues and risks, then she should be treated with buprenorphine monotherapy so as not to risk fetal exposure to naloxone. It should be noted that use of buprenorphine monotherapy, because of its greater potential for abuse, necessitates more frequent monitoring of patients and of their medication supplies. To prevent abuse and diversion of the buprenorphine monotherapy formulation, quantities of take-home supplies and quantities provided via prescription should be smaller compared to treatment with the buprenorphine/naloxone combination formulation.
Summary

Buprenorphine is classified by FDA as a Pregnancy Category C drug. Data from controlled studies on the use of buprenorphine in pregnant women are needed. The available evidence does not show any causal adverse effects on pregnancy or neonatal outcomes from buprenorphine treatment, but this evidence is from case series not from controlled studies. Methadone is currently the standard of care in the United States for the treatment of heroin addiction in pregnant women. Pregnant women presenting for treatment of opioid addiction should be referred to specialized services in methadone maintenance treatment programs. If such specialized services are refused by a patient or are unavailable in the community, maintenance treatment with the buprenorphine monotherapy formulation may be considered as an alternative. In such circumstances, it should be clearly documented in the medical record that the patient has refused methadone maintenance treatment, or that such services were unavailable; that she was informed of the risks of using buprenorphine, a medication that has not been thoroughly studied in pregnancy; and that she understands those risks.

Adolescents/Young Adults

The use of buprenorphine for the treatment of opioid addiction in adolescents has not been systematically studied. It is known, however, that patients younger than 18 years of age, with relatively short addiction histories, are at particularly high risk for serious complications of addiction (e.g., overdose deaths, suicide, HIV, other infectious diseases). Many experts in the field of opioid addiction treatment believe that buprenorphine should be the treatment of choice for adolescent patients with short addiction histories. Additionally, buprenorphine may be an appropriate treatment option for adolescent patients who have histories of opioid abuse and addiction and multiple relapses but who are not currently dependent on opioids. Buprenorphine may be preferred to methadone for the treatment of opioid addiction in adolescents because of the relative ease of withdrawal from buprenorphine treatment. Because adolescents often present with short histories of drug use, detoxification with buprenorphine, followed by drug-free or naltrexone treatment, should be attempted first before proceeding to opioid maintenance. Naltrexone may be a valuable therapeutic adjunct after detoxification. Naltrexone has no abuse potential and may help to prevent relapse by blocking the effects of opioids if the patient relapses to opioid use. Naltrexone has been a valuable therapeutic adjunct in some opioid-abusing populations, particularly youth and other opioid users early in the course of addiction. Naltrexone is most likely to be effective for patients with strong support systems that include one or more individuals willing to observe, supervise, or administer the naltrexone on a daily basis. In those adolescent patients in whom detoxification is followed by relapse, buprenorphine maintenance may then be the appropriate alternative. Refer to chapter 4 for buprenorphine maintenance and detoxification procedures.

The treatment of patients younger than 18 years of age can be complicated due to psychosocial considerations, the involvement of family members, and State laws concerning consent and reporting requirements for minors. Ancillary counseling and social services are important to support cooperation and follow through with the treatment regimen.
Parental Consent

Parental consent is a critical issue for physicians who treat adolescents addicted to opioids. In general, adult patients with “decisional capacity” have the unquestioned right to decide which treatments they will accept or refuse, even if refusal might result in death. The situation for adolescents is somewhat different, however. Adolescents do not have the legal status of adults unless they are legally “emancipated minors.” Adolescents’ rights to consent to or to refuse medical treatment differ from those of adults. Rules differ from State to State regarding whether an adolescent may obtain substance use disorder treatment without parental consent. Some State statutes governing consent and parental notification specify consideration of a number of fact-based variables, including the adolescent’s age and stage of cognitive, emotional, and social development, as well as issues concerning payment for treatment and rules for emancipated minors.

More than one-half of the States permit individuals younger than 18 years of age to consent to substance use disorder treatment without parental consent. In States that do require parental consent, providers may admit adolescents to treatment when parental consent is obtained. In States requiring parental notification, treatment may be provided to an adolescent when the adolescent is willing to have the program communicate with a parent. Histories of neglect or abuse may be revealed during the care of adolescent patients, and physicians must be aware of reporting requirements in their State. Mandatory child abuse reporting takes precedence over Federal addiction treatment confidentiality regulations, according to Title 42, Part 2 of the Code of Federal Relations (42 C.F.R. Part 2).

Additional difficulties may arise when adolescents requesting treatment refuse to permit notification of a parent or guardian. With one very limited exception, the Federal confidentiality regulations prohibit physicians (or their designees) from communicating substance abuse treatment information to any third parties, including parents, without patient consent. The sole exception allows a “program director” (i.e., treating physician) to communicate “facts relevant to reducing a threat to the life or physical well-being of the applicant or any other individual to the minor’s parent, guardian, or other person authorized under State law to act in the minor’s behalf,” when the program director believes that the adolescent, because of extreme youth or mental or physical condition, lacks the capacity to decide rationally whether to consent to the notification of his or her parent or guardian (42 C.F.R. Part 2, Subpart B, Section 2.14d 2001). The program director must believe the disclosure to a parent or guardian is necessary to cope with a substantial threat to the life or physical well-being of the adolescent applicant or someone else. In some cases, communication with State child protection agencies or judicial authorities may be an acceptable alternative, or the required course of action, if the physician believes neglect or abuse has already occurred.

Treatment Setting

The more intensive a proposed treatment is, the more risk a program assumes in admitting adolescents without parental consent. Outpatient programs may have a better justification for admitting adolescents without parental consent than do intensive outpatient or residential programs.

Summary

Buprenorphine can be a useful option for the treatment of adolescents who have opioid addiction problems. The treatment of addiction in adolescents is complicated by a number of medical, legal, and ethical considerations, however. Physicians intending to treat addiction in adolescents should be thoroughly familiar with the laws in their State regarding parental consent. Physicians who do not specialize in the treatment of opioid addiction or adolescent medicine should strongly consider consulting with, or referring adolescent
addiction patients to, such specialists. Additionally, State child protection agencies can be a valuable resource when determining the proper disposition for adolescent patients.

**Geriatric Patients**

Literature on the use of buprenorphine in geriatric patients is extremely limited. Because of potential differences in rates of metabolism and absorption compared to the nonelderly, care should be exercised in the use of buprenorphine in elderly individuals. Particular care should be exercised during buprenorphine induction both because of differences in body composition and because of the possibility of medication interactions.

**Patients With Significant Psychiatric Comorbidity**

The association of psychopathology and opioid addiction is well established. Psychiatric symptoms and disorders may be drug-induced, independent, or interrelated. Substance use and addiction can mimic, exacerbate, or precipitate psychiatric symptoms and disorders. Most substances of abuse produce moderate-to-severe psychiatric symptoms, and there is a complex association between substance use and psychiatric status.

A study of rates of psychiatric disorders among 716 patients addicted to opioids seeking treatment with methadone (Brooner et al. 1997), found a lifetime rate of 47 percent, and a current rate of 39 percent. Of note, patients in this study were stabilized in treatment for 1 month before the psychiatric evaluation. Other, earlier studies have reported higher rates of depression, antisocial personality characteristics, schizophrenia or schizotypal features, manic symptomatology, and alcoholism in opioid-addicted patients. For example, in a study of 533 opioid-addicted patients in treatment for their drug problems, Rounsaville and colleagues (1982) found that 86.9 percent met diagnostic criteria for some psychiatric disorder (including personality disorders) in their lifetimes, and 70.3 percent met criteria for a current psychiatric disorder. It should be noted, however, that, although the rates of major depressive disorder, alcoholism, antisocial personality, minor mood disorders, and anxiety disorders in this group exceeded those found in the general population, the rates of schizophrenia and mania did not.

Although the etiological significance of psychiatric disorders in the genesis of opioid addiction is not established, it is known that treatment for both conditions is necessary for substance abuse treatment to be effective. Therefore, the presence and severity of comorbid psychiatric conditions must be assessed in patients who are opioid addicted before, or while, initiating buprenorphine treatment, and a determination must be made whether referral to specialized behavioral health services is indicated.

Untreated or inadequately treated psychiatric disorders can interfere with the effective treatment of addiction. Polysubstance use and psychiatric problems are both associated with negative treatment outcomes unless they are identified and treated appropriately. For example, patients with major depression or dysthymia are more likely to use illicit drugs during treatment than patients who do not suffer from depression. Assessment is critical to determine whether psychiatric symptoms represent primary psychiatric disorders or substance-induced conditions. Primary
psychiatric disorders may improve but do not dissipate with abstinence or maintenance therapies, and these disorders may require additional treatment. The psychiatric disorders most commonly encountered in patients who are opioid addicted are other substance abuse disorders, depressive disorders, posttraumatic stress disorder, substance-induced psychiatric disorders, and antisocial and borderline personality disorders.

The presence of comorbid psychiatric disorders should not exclude patients from admission to opioid addiction treatment. Diagnosis of psychiatric disorders is critical to matching patients to appropriate treatment services. In first encounters with patients, it is essential to evaluate for the presence of suicidal or homicidal ideations, signs or symptoms of acute psychosis, and other acute or chronic psychiatric problems that may render patients unstable. Initiation of antidepressant therapy, in conjunction with treatment for opioid addiction, may be considered in patients presenting with signs or symptoms of depression. If manic behavior is present, attempts should be made to determine whether it is substance induced or whether the etiology is a primary mood disorder.

When psychiatric symptoms are severe or unstable, hospitalization for protection and containment may be appropriate to ensure the safety of the patient and others. Patients who are considered actively suicidal should not receive buprenorphine on an outpatient, prescription basis. Rather, they should be referred immediately for appropriate treatment, which may include psychiatric hospitalization. Those who are not currently suicidal but who have a history of suicidal ideation or attempts should be monitored closely in terms of medication supply and followup.

Psychiatrically stable patients can be readily accepted into treatment and stabilized on buprenorphine; subsequently they may receive additional psychiatric assessment to identify conditions requiring treatment. Patients who present with depression during the maintenance phase of buprenorphine treatment require continued assessment and should be treated appropriately.

Polysubstance Abuse

The abuse of multiple drugs (polysubstance abuse) among individuals addicted to opioids is common. Although polysubstance abuse or dependence may be identified during assessment, physicians should remain alert to their presence throughout the course of addiction treatment.

Pharmacotherapy with buprenorphine for opioid addiction will not necessarily have a beneficial effect on an individual’s use of other drugs. It is essential that patients be referred for treatment of addiction to other types of drugs when indicated. In addition, care must be exercised in the prescribing of buprenorphine for patients who abuse alcohol and for those who abuse sedative/hypnotic drugs (especially benzodiazepines) because of the documented potential for fatal interactions. (See chapter 2 for further information.)

Patients With Pain

Patients Being Treated for Pain Who Become Dependent on Opioids

Patients who need treatment for pain but not for addiction should be treated within the context of their regular medical or surgical setting. They should not be transferred to an opioid maintenance treatment program simply because they are being prescribed opioids and have become physically dependent on the opioids in the course of their medical treatment.

It can be difficult to distinguish between the legitimate desire to use opioids for pain relief and the desire to procure them for purposes of obtaining a high. This may be especially true in patients who have become physically dependent on opioids in the course of the treatment of a pain condition when that pain has been undertreated and inadequately
Special Populations

Patients Who Are Addicted to Opioids and Who Require Treatment for Pain

Behaviors associated with drug abuse frequently result in the development of acute and chronic pain conditions. These conditions may be caused by the toxic effects of the drug itself, as well as by trauma and infection. Patients receiving addiction treatment also may experience pain due to illness or injury unrelated to drug use. Physicians must manage this pain efficiently and appropriately. Opioids are among the most effective available options for managing pain, but they are often not prescribed to patients receiving treatment for addiction out of fear of “feeding the addiction” or of triggering relapse in currently abstinent patients. State laws governing the prescription of opioids to known substance abusers may place prescribing physicians at risk for prosecution unless the medical record clearly distinguishes between treatment of the addiction and treatment of the pain condition.

**Treatment Approach.** Little clinical experience is documented regarding the treatment of pain in patients receiving buprenorphine. Pain in patients receiving buprenorphine treatment initially should be treated with nonopioid analgesics when appropriate. Although buprenorphine itself has powerful analgesic properties, the once-daily administration of buprenorphine, as used for the treatment of opioid addiction, often does not provide sufficiently sustained relief of pain. Additionally, the onset of action of analgesia with buprenorphine may not be adequate for the treatment of acute pain. In a study of the use of buprenorphine for acute analgesia (Nikoda et al. 1998), the high analgesic activity of buprenorphine was comparable to that of morphine, but the onset of action was found to be inadequate for urgent care.

Patients maintained on buprenorphine whose acute pain is not relieved by nonopioid

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**Figure 5-1**

**Clinical Features Distinguishing Opioid Use in Patients With Pain Versus Patients Who Are Addicted to Opioids**

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Patients With Pain</th>
<th>Patients Who Are Addicted to Opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compulsive drug use</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Crave drug (when not in pain)</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Obtain or purchase drugs from nonmedical sources</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Procure drugs through illegal activities</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Escalate opioid dose without medical instruction</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Supplement with other opioid drugs</td>
<td>Unusual</td>
<td>Frequent</td>
</tr>
<tr>
<td>Demand specific opioid agent</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Can stop use when effective alternate treatments are available</td>
<td>Usually</td>
<td>Usually not</td>
</tr>
<tr>
<td>Prefer specific routes of administration</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Can regulate use according to supply</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
medications should receive the usual aggressive pain management, which may include the use of short-acting opioid pain relievers. While patients are taking opioid pain medications, the administration of buprenorphine generally should be discontinued. Note that, until buprenorphine clears the body, it may be difficult to achieve analgesia with short-acting opioids in patients who have been maintained on buprenorphine, and higher doses of short-acting opioids may be required. Noncombination opioid analgesics are generally preferred to avoid the risk of acetaminophen or salicylate toxicity when combination products are used at the doses that are likely to be required for pain control in patients who have been maintained on buprenorphine. Analgesic dose requirements should be expected to decrease as buprenorphine clears the body.

When restarting buprenorphine administration, physicians should refer to chapter 4 for induction procedures. To prevent the precipitation of withdrawal, buprenorphine should not be restarted until an appropriate period after the last dose of the opioid analgesic, depending on the half-life of the opioid analgesic used.

Patients who are receiving opioids for chronic severe pain may not be good candidates for buprenorphine treatment because of the ceiling effect on buprenorphine’s analgesic properties. This rationale also would be applicable to terminally ill patients. In patients who are maintained on buprenorphine and require end-of-life opioid analgesia, buprenorphine administration should be discontinued, unless the buprenorphine provides adequate analgesia or the patient prefers buprenorphine for some other reason.

In patients who are opioid addicted and who have severe chronic pain, methadone several times per day or other “round the clock” (rather than as required) long-acting, fullagonist medications may be the best alternative for treatment. This form of treatment is often best undertaken in conjunction with an Opioid Treatment Program (OTP). However, if the physician is (1) otherwise qualified to treat the condition causing the pain and (2) careful to document that the primary purpose of the opioid pharmacotherapy is the management of that pain condition, then it may be acceptable to treat that patient in the office setting without further referral. As long as this type of patient remains compliant and is not abusing the pain medication or other drugs, there is no legal need for the patient to be treated in an OTP or with buprenorphine for the preexisting or concurrent addictive disorder. However, the Drug Enforcement Administration (DEA) frowns on the use of this as a rationale to treat the “pain of withdrawal” or spurious and ill-defined pain conditions to justify unsanctioned opioid maintenance. Patients who are on chronic opioids for pain management and who have a history of drug abuse or addiction can be referred to a 12-Step program or other self-help group to help them maintain their level of recovery. Random drug screening also can reassure the physician that both physician and patient are staying within lawful bounds.

Because all pharmacological treatment with opioids is highly regulated, physicians who desire to use opioids to treat chronic pain in patients who are at risk for opioid addiction or relapse are advised to consult with a colleague knowledgeable in opioid maintenance pharmacology.
Patients Recently Discharged From Controlled Environments

This section focuses on the assessment and treatment of patients with opioid addiction who are recently released from controlled environments (e.g., prison) and who would be presumed to have involuntarily detoxified from opioids while incarcerated. Other situations that may warrant special consideration include (1) patients discharged from extended hospital or rehabilitation center stays, (2) patients returning from extended overseas travel/expatriate duty in countries without easy access to licit or illicit opioids, and (3) other conceivable situations that may have caused an involuntary break in active use of and addiction to opioids.

The findings on patient assessment will help to clarify the diagnosis of opioid dependence/addiction and whether a patient is at serious risk for resumption of an addiction lifestyle if not treated with a buprenorphine maintenance regimen. Other considerations for providers include possible psychosocial needs and issues, as well as collateral contacts that may be required when treating patients who may have continuing involvement with the criminal justice system.

Opioid Addiction in Patients Under the Jurisdictions of Criminal Justice Systems

It is well documented that the crimes committed by most of the more than 1 million individuals incarcerated in the United States are related to the abuse of or addiction to drugs. Opioids are the preferred contraband drugs of choice in prisons and can be relatively easy to obtain in some institutions. Prison environments and inmate culture reinforce the addiction cycle and addiction lifestyle. Recidivism rates are higher in patients with a history of opioid addiction because they are typically reincarcerated after failing parole or drug-testing requirements.

Assessment of Patients Who Are Opioid Addicted and Who Are Recently Released From Controlled Environments

Physicians should consider the following factors when assessing for addiction in patients recently released from controlled environments: length of incarceration; postrelease addiction patterns and cycles; addiction treatment history (drug-free, outpatient, recovery, or therapeutic community); self-help involvement (before, during, and since incarceration); and reported triggers of illegal drug use and addiction upon release. Physicians should evaluate for the presence of comorbid mental health issues or history of other drug or alcohol use that could complicate buprenorphine treatment. (See chapter 3 for further information.) If office-based buprenorphine treatment is being considered, physicians should carefully assess the patient’s level of commitment to treatment and the likelihood of self control.

Assessing Psychosocial Issues

Attention to psychosocial issues is important in patients who are coming out of controlled environments. Issues that often affect the success of addiction treatment include

- Number and/or length of incarcerations
- Types of crimes committed (e.g., violent offenses, drug-related)
- Gang affiliations
- Type and length of parole or probation (e.g., whether the patient will be given regular or random drug testing)
- The patient’s collateral contacts and reporting requirements
• Prior and current involvement of the patient’s social support system (e.g., the presence of opioid addiction problems or current use in family members)
• Recent changes in familial or marital relationships
• Whether permission from the criminal justice system is required for treatment with buprenorphine

Physicians should ask the patient whether he or she has a reasonable plan for a stable lifestyle (e.g., involvement in job, school, family) and whether the plan includes total abstinence from drug and alcohol use. If there is no plan, the physician should ask why not and offer to help the patient create one.

Final determination of a patient’s appropriateness for buprenorphine treatment will involve analysis of the subjective assessment and disclosed information, as well as a review of medical records to determine treatment compliance and cooperation. Physicians should assess a patient’s psychosocial needs and the compatibility of the patient with the potential limitations of an outpatient, office-based environment.

Determining Appropriateness for Buprenorphine Treatment

A number of issues should be considered in determining the most appropriate treatment modality for patients with addiction who are recently released from controlled environments. If a methadone clinic alternative is available, the physician should determine the factors that may preclude referral. The existing doctor/patient relationship should be assessed, as well as eligibility for other assistance, and the presence of a solid support system. A physician’s limitations with regard to potentially intensive buprenorphine monitoring activities should be considered, as a treating physician may be called on to determine, verify, and explain a treatment regimen (e.g., to parole and probation officers); to document the patient’s compliance; and to interact with the legal system, employers, and others. Physicians should consider potential issues associated with detoxification in jail if a patient is reincarcerated. The cost of treatment needs to be considered, as well as whether the costs are covered by a patient’s health insurance. Additionally, potential risk issues need to be considered (e.g., diversion, overdose, criminal activity while in a limited, professional care setting, mixing with other patients).

Healthcare Professionals Who Are Addicted to Opioids

A substantial problem of addiction to prescription opioids exists among physicians and other health professionals, especially within certain specialties (e.g., anesthesiology) (Talbott et al. 1987). Prescription opioid addiction in health professionals should be viewed as an occupational hazard of the practice of medicine. Health professionals who have substance abuse disorders often require specialized, extended care.

If the addictive drug of choice is present in the workplace, reentry planning after initial treatment should consider relapse by the health professional who is in early recovery. The opioid antagonist naltrexone and other adjunctive medications are often required. Naltrexone has been a routine adjunct for the treatment of anesthesiologists who are addicted to opioids. The key to successful naltrexone use by a highly motivated patient is a strong social support system that includes a significant other, coworker, or health professional who directly observes the naltrexone use on a regular basis.

Buprenorphine may be an appropriate treatment option for some health professionals who are opioid dependent, but the use of a partial agonist would need to be part of a comprehensive, monitored recovery plan. If the professional has already come under regulatory scrutiny, such a plan might require approval by the State authority to which the professional reports.
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Overview
This chapter discusses policies and procedures relating to the Drug Addiction Treatment Act of 2000 (DATA 2000), to preparations for providing opioid addiction treatment in practices that are new to this form of care, to State and Federal laws and regulations that protect the privacy and confidentiality of addiction treatment information, and to the use of buprenorphine in federally regulated Opioid Treatment Programs (OTPs). Physicians should become thoroughly familiar with these issues before engaging in the practice of opioid addiction treatment (Brooks 1997). In addition, readers are referred to appendix F, which contains additional information about many of these topics.

The DATA 2000 Waiver
DATA 2000 enables qualifying physicians to receive a waiver from the special registration requirements in the Narcotic Addict Treatment Act (NATA) of 1974 (and its enabling regulations, including Title 42, Part 8 of the Code of Federal Regulations, that govern OTPs) for the provision of opioid addiction treatment. This waiver allows qualifying physicians (see “Physician Waiver Qualifications”) to prescribe or dispense Schedule III, IV, and V “narcotic” medications for the treatment of opioid addiction in the office and other clinical settings if (and only if) those medications have been approved by the Food and Drug Administration (FDA) for use in addiction treatment. As of this writing, Subutex® (buprenorphine) and Suboxone® (buprenorphine/naloxone) sublingual tablets are the only Schedule III, IV, or V pharmaceuticals to have received such FDA approval. NATA makes it illegal for narcotics to be used “off label” to treat opioid addiction. This prohibition extends even to other forms of buprenorphine (e.g., Buprenex®) that have not been specifically approved for the treatment of opioid addiction.
Notification of Intent
To receive a DATA 2000 waiver to practice opioid addiction treatment with approved Schedule III, IV, and V opioid medications, a physician must notify the Substance Abuse and Mental Health Services Administration (SAMHSA) of his or her intent to begin dispensing or prescribing this treatment. This Notification of Intent must be submitted to SAMHSA before the initial dispensing or prescribing of opioid treatment. Notification of Intent forms can be obtained on the SAMHSA Buprenorphine Web site at http://www.buprenorphine.samhsa.gov. Forms can be submitted to SAMHSA online or printed out and then submitted via ground mail or fax.

The Notification of Intent must contain information on the physician’s qualifying credentials (as defined below) and additional certifications, including that the physician has the capacity to refer addiction patients for appropriate counseling and other nonpharmacological therapies, and that the physician will not have more than 30 patients on such addiction treatment at any one time. (Note that the 30-patient limit applies both to physicians in solo practice and to entire group practices, and the limit is not affected by the number of locations of practice of the physicians or groups.)

Physicians who meet the qualifications defined in DATA 2000 are issued a waiver by SAMHSA and a special identification number by the Drug Enforcement Administration (DEA). DEA has issued regulations that require physicians to include this identification number on all records when dispensing and on all prescriptions when prescribing approved opioid medications (currently only Subutex® and Suboxone®) for opioid addiction.

Immediate-Type Notifications
Under DATA 2000, a physician may initiate opioid addiction treatment for “an individual patient” after submitting a Notification of Intent to SAMHSA but before receipt of a waiver and identification number. To provide this “immediate-type” treatment, a physician must not only submit the usual Notification of Intent to SAMHSA but also must include notification of intent to begin immediately treating an individual patient. SAMHSA’s Notification of Intent form includes a checkbox for indicating this immediate-type intent.

Physician Waiver Qualifications
To qualify for a waiver under DATA 2000, a licensed physician (M.D. or D.O.) must meet any one or more of the following criteria:

- The physician holds a subspecialty board certification in addiction psychiatry from the American Board of Medical Specialties.
- The physician holds an addiction certification from the American Society of Addiction Medicine (ASAM).
- The physician holds a subspecialty board certification in addiction medicine from the American Osteopathic Association (AOA).
- The physician has, with respect to the treatment and management of patients who are opioid addicted, completed not less than 8 hours of training (through classroom situations, seminars at professional society meetings, electronic communications, or otherwise) that is provided by ASAM, the American Academy of Addiction Psychiatry, the American Medical Association, AOA, the American Psychiatric Association, or any other organization that the Secretary of the U.S. Department of Health and Human Services (DHHS) determines is appropriate for purposes of this subclause.
- The physician has participated as an investigator in one or more clinical trials leading to the approval of a narcotic drug in Schedule III, IV, or V for maintenance or detoxification treatment, as demonstrated by a statement submitted to the DHHS Secretary by the sponsor of such approved drug.
- The physician has such other training or experience as the State medical licensing
Proper training on the use of buprenorphine will be key to the successful introduction of this new treatment paradigm, regardless of the clinical setting of buprenorphine treatment. Thus, SAMHSA and the consensus panel strongly encourage all physicians who plan to practice opioid addiction treatment with buprenorphine to participate in a DATA 2000-qualifying 8-hour training program on buprenorphine. SAMHSA maintains a list of upcoming DATA 2000-qualifying buprenorphine training sessions on the SAMHSA Buprenorphine Web site at http://www.buprenorphine.samhsa.gov. These sessions include Web-based courses accessible from the physician’s own computer. Detailed information about the DATA 2000 paradigm and the physician waiver process also can be found on the SAMHSA Buprenorphine Web site. Additionally, information can be obtained by contacting the SAMHSA Buprenorphine Information Center by phone at 866-BUP-CSAT (866-287-2728) or by e-mail at info@buprenorphine.samhsa.gov.

For More Information

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Preparation for Office-Based Opioid Treatment

Prior to embarking on the provision of office-based addiction treatment services, medical practices that will be new to this type of care should undertake certain preparations to ensure the highest quality experience for patients, providers, and staff. Providers and practice staff should have an appropriate level of training, experience, and comfort with this new form of treatment. Linkages with other medical and mental health professionals should be established to ensure the availability of comprehensive community-based treatment services.

Physician Training, Experience, and Comfort Level

Physicians who intend to treat opioid addiction should seek to establish a level of comfort and expertise with this form of care. A physician’s comfort level in providing treatment for addiction will vary according to the physician and his or her practice situation. For example, a physician might choose to refer a patient with addiction and depression, depending on the severity of depression, whether a psychologist or psychiatrist is available in the area, and whether the patient can afford specialized mental health care, among other factors. Expertise in treating opioid addiction includes knowledge of applicable practice standards or guidelines, familiarity with the evidence supporting the recommended treatments, protocols for primary treatment or referral of patients with certain complicating conditions (e.g., severe depression), and knowledge of any applicable regulations or laws. Physicians must become knowledgeable about the most up-to-date treatments for opioid addiction,
including pharmacotherapy, psychosocial interventions, self-help and mutual-help groups, and other appropriate treatments. Physicians who treat opioid-addicted patients with buprenorphine should participate in addiction medicine training and professional activities and should learn from other professionals in addiction treatment. Basic and ongoing training in addiction treatment will greatly enhance a physician’s effectiveness in treating opioid addiction.

Each patient presents with different and usually complex needs. Physicians who treat patients with opioid addiction in the office-based setting must consider and plan for the full range of their patients’ needs before initiating treatment. Candidates for buprenorphine treatment of opioid addiction should be assessed for a broad array of biopsychosocial needs in addition to opioid use and addiction, and should be treated and/or referred for help in meeting those needs.

Establishing Office Procedures

Before undertaking the provision of office-based buprenorphine treatment, physicians should make arrangements to provide comprehensive care and contingency plans for patients who may not be appropriate candidates for this treatment. In addition, physicians should arrange for other physicians with DATA 2000 waivers to be available to provide care to the treating physician’s opioid addiction patients in the treating physician’s absence (e.g., while on vacation).

Office policies and procedures for opioid addiction treatment should be established, written, and clearly communicated to staff members and patients. Staff members should be trained and educated about opioid addiction, addiction treatment, patient confidentiality (see “Confidentiality and Privacy” section below), medication treatments, nonpharmacological treatments, behavioral characteristics of addiction, and the medical approach to addiction treatment.

Common behaviors and defense mechanisms of addicted patients should be anticipated. Medication must be stored in a secure location, and the possibility of diversion must be minimized. Office items (e.g., prescription pads, syringes, needles) and staff possessions should be secured to minimize theft.

Establishing Treatment Linkages

Establishing linkages with other medical professionals is essential. Because patients addicted to opioids commonly have coexisting medical and psychiatric conditions, most physicians will need to establish linkages with other medical and mental health specialists, particularly those specializing in the evaluation and treatment of common comorbid conditions (e.g., hepatitis B and C, HIV, tuberculosis, mood disorders, anxiety disorders, personality disorders, risk of suicide and homicide). Physical examinations and laboratory evaluations will need to be completed either onsite or offsite from the office of the physician who provides office-based buprenorphine treatment.

An up-to-date listing of community referral resources (e.g., therapy groups, support groups, residential therapeutic communities, sober-living options) should be given to patients. Referral resource lists are available from the substance abuse agencies of some local and State governments. To maximize followthrough with referrals, it is most helpful if the physician has firsthand knowledge of these groups and programs. When referrals are made, compliance will increase if staff call to make appointments in the presence of patients. When making referrals to support groups, it is helpful to have an individual in the group who is willing to accompany the patient to his or her first meeting. Referrals to social workers and case managers are often beneficial in helping patients address legal, employment, and family issues.
Summary

Figure 6–1 summarizes the policies, procedures, and items that should be established or arranged for in a medical practice prior to initiating office-based opioid addiction treatment.

Confidentiality and Privacy

Prior to initiating office-based opioid addiction treatment, practice policies and procedures should be established that will guarantee the privacy and confidentiality of addiction treatment patients. Providers must comply with all applicable laws and regulations regarding the privacy and confidentiality of medical records in general, and of information pertaining to addiction treatment services in particular.

The privacy and confidentiality of individually identifiable information relating to patients receiving drug or alcohol treatment is protected by SAMHSA confidentiality regulation Title 42, Part 2 of the Code of Federal Regulations (42 C.F.R. Part 2). This regulation mandates that addiction treatment information in the possession of substance abuse treatment providers be handled with a greater degree of confidentiality than general medical information.

Occasionally, physicians will need to communicate with pharmacists and other healthcare providers about the addiction treatment of a particular patient (e.g., to verify a Suboxone® or Subutex® prescription). Regulation 42 C.F.R. Part 2 requires physicians providing opioid addiction treatment to obtain signed patient consent before disclosing individually identifiable addiction treatment information to any third party. A sample consent form with all the elements required by 42 C.F.R. Part 2 is included as appendix D. It is recommended that physicians have each new buprenorphine patient sign a copy of this form to prevent confidentiality problems at
Figure 6–2

Privacy and Confidentiality Issues in Addiction Treatment

- Information covered by the doctor/patient privilege
- Circumstances in which confidential information is protected from disclosure
- Exceptions to State laws protecting medical information
- Duty to report
- Communications with third parties (e.g., families, employers, allied healthcare providers, third-party payers, law-enforcement officers, responses to subpoenas)
buprenorphine treatment along with methadone and levo-alpha-acetyl-methadol (LAAM). The rule enables OTPs that are certified by SAMHSA to provide Subutex® and Suboxone® for opioid maintenance or detoxification treatment.

The provision of opioid addiction treatment with Subutex® and Suboxone® in SAMHSA-certified OTPs does not require a DATA 2000 waiver. Additionally, such treatment is not subject to the 30-patient limit that applies to individual physicians and group practices providing opioid addiction treatment outside the OTP system under the authority of a DATA 2000 waiver. The provision of opioid addiction treatment with Subutex® or Suboxone® in treatment settings other than OTPs, even by physicians who are licensed to work in OTPs, does require a DATA 2000 waiver and is subject to the 30-patient limit for individual physicians and group practices.

OTPs providing Subutex® and Suboxone® for opioid maintenance or detoxification treatment must conform to the Federal opioid treatment standards set forth under 42 C.F.R. § 8.12. These regulations require that OTPs provide medical, counseling, drug abuse testing, and other services to patients admitted to treatment. To offer Subutex® and Suboxone®, OTPs need to modify their registration with the DEA to add Schedule III narcotics to their registration certificates. OTPs can initiate this streamlined process by fax or letter. The letter should include the OTP’s DEA registration number and request that the registration be amended to list Schedule III narcotic drugs. The letter must be signed by the program sponsor (program director) or medical director. Further information about this process can be found on the DEA Drug Registration Web site at http://www.deadiversion.usdoj.gov/drugreg/change_requests/sched_change.htm.