INTELLIGENCE BULLETIN

Buprenorphine: Potential for Abuse

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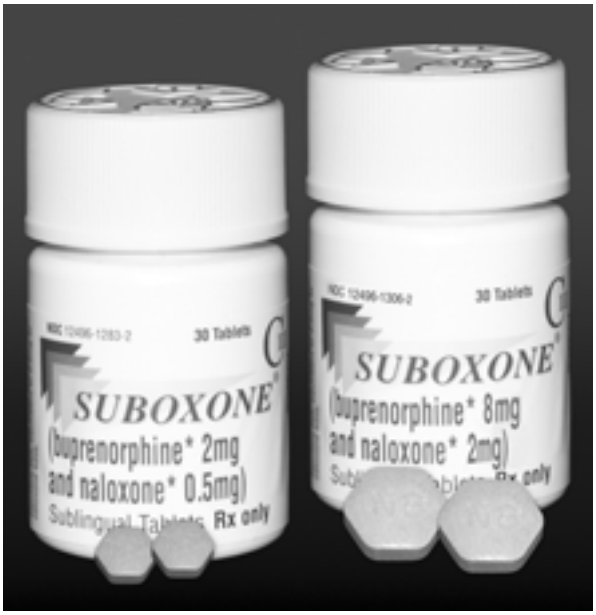
U. S. DEPARTMENT OF JUSTICE



NDIC

Within the past 2 years buprenorphine—a Schedule III drug—has been made available for use in opiate addiction therapy. Two formulations of the drug are used in such therapy. Subutex, which is pure buprenorphine, is designed to be used in the initial stages of addiction treatment. Suboxone, which contains an antiabuse component, is designed to be used in the maintenance stage of treatment. Both block the effects of opiates while reducing opiate cravings and easing withdrawal symptoms. Buprenorphine is the only opiate addiction therapy drug that can be prescribed in a physician's office; others must be dispensed in a clinic. This method of distribution is advantageous to many opiate addiction therapy patients because it is more convenient and less stigmatizing than clinic-based therapy, which typically involves methadone. Like methadone, however, buprenorphine is susceptible to abuse. Despite safety measures in place to guard against diversion of the drug, illegal distribution and abuse of buprenorphine have been reported in the United States, primarily in the Northeast region.

Background

Currently, the drug most commonly used in opiate addiction therapy in the United States is methadone, a Schedule II synthetic opiate. Methadone helps addicted individuals to stop abusing opiates by reducing opiate cravings and symptoms of withdrawal; however, there are several disadvantages to methadone-based opiate addiction therapy. Methadone can be prescribed only in licensed methadone treatment clinics, and patients must deal with the stigma attached to making daily trips to a methadone clinic. Also, these clinics commonly are located in or near urban centers, so patients in rural areas must drive long distances each day to obtain methadone. Finally, methadone abuse is increasing throughout the Northeast region, where abuse of heroin and other opiates is common, and increasingly is a factor in overdose deaths.

In a move away from clinic-based therapy, the Drug Addiction Treatment Act of 2000 (DATA) passed by Congress in 2000 allows physicians who receive specialized training to treat opiate addiction in their offices with Schedule III, IV, and V medications approved by the Food and Drug Administration (FDA) specifically to treat opiate addiction. However, at the time DATA 2000 was passed, no medications had yet been approved by FDA for that purpose.

On October 8, 2002, FDA approved buprenorphine in two formulations, Subutex and Suboxone, for use in opiate addiction therapy. Subutex (buprenorphine hydrochloride) is used in the initial stages of therapy while Suboxone (buprenorphine hydrochloride and naloxone hydrochloride) is used in the maintenance stage. Today, only these two formulations of buprenorphine meet DATA 2000 specifications; therefore, buprenorphine is the only drug that can be prescribed in a physician's office to treat opiate addiction. (A third, Buprenex, is marketed as a pain relief medication that cannot be used to treat opiate addiction.) While most commonly used to treat addiction to heroin, buprenorphine can be used to treat addiction to any type of opiate, including oxycodones such as OxyContin and Percocet.

Safeguards were put in place before buprenorphine was made available to the public because of widespread pharmaceutical diversion and increased prescription drug abuse in the nation. In fact, Suboxone was designed specifically to meet FDA requirements for a more diversion-proof drug for use in opiate addiction therapy and is available only in the United States. The naloxone contained in Suboxone guards against abuse—if an abuser crushes and injects or snorts the Suboxone tablet, the naloxone in it precipitates withdrawal symptoms. Naloxone (Narcan) reverses the effects of opiates. Further, in 2002 the Drug Enforcement Administration (DEA) reassessed the potential for abuse of, diversion of, and addiction to buprenorphine and rescheduled it from a Schedule V drug to a Schedule III drug, thus increasing the penalties for illegally obtaining, possessing, or abusing buprenorphine.

To further safeguard buprenorphine from diversion, physicians prescribing the drug in either of the formulations approved for treating opiate addiction must become certified by attending a special training course and submitting their qualifications to the Substance Abuse and Mental Health Services Administration (SAMHSA). Physicians also must agree to refer patients for drug addiction counseling. After registering with SAMHSA, physicians receive a special identification number from DEA that appears on all buprenorphine prescriptions they administer. The DEA-issued identification number assigned to each certified physician aids law enforcement and antidiversion officials in tracking any diversion of the drugs.

Physicians prescribing buprenorphine therapy must maintain a log of all patients using Subutex and Suboxone and record the medication that has been prescribed to them. The medical records of these patients are subject to periodic DEA and FDA review. FDA also has stipulated that the manufacturer of Subutex and Suboxone, Reckitt Benckiser Pharmaceuticals, must investigate any reports of diversion.

More than 1,700 physicians or group practices in the United States—over 700 located in the Northeast—are certified to prescribe buprenorphine. Physicians currently are prohibited from prescribing Subutex and Suboxone to more than 30 patients at any given time. The 30-patient limit also applies to group practices. For example, a group practice of three certified physicians may prescribe Subutex and Suboxone to only 30 patients, not 90. However, Congress is considering the Drug Addiction Treatment Expansion Act of 2003. This legislation, if passed, will amend DATA 2000 by lifting the 30-patient limit imposed on group practices and allowing each physician in a group practice to prescribe buprenorphine to 30 patients.

Effects

Buprenorphine is a derivative of thebaine, an extract of opium. The drug is an opioid (synthetic opiate) partial agonist and thus can produce the euphoria, analgesia, and sedation associated with opiates; however, while it stimulates the same brain receptors as full opiate agonists such as heroin and morphine, buprenorphine produces a lesser degree of sedation and respiratory depression than those drugs and causes no significant impairment of cognitive or motor skills. Like methadone, buprenorphine reduces cravings for heroin and other opiates and reduces withdrawal symptoms, thus helping

addicted individuals to stop abusing opiates. Also like methadone, buprenorphine blocks the effects of heroin by binding to the same opiate receptors as heroin; consequently, opiate addicts who use buprenorphine are not able to get a high from heroin.

Buprenorphine also has a "ceiling effect" whereby increased doses of the drug do not produce increased effects after a certain point, or ceiling. In fact, high doses of the drug can actually precipitate withdrawal symptoms in opiate addicted individuals. Because of this ceiling effect, buprenorphine is less susceptible to abuse than other opiates; however, because high doses of the drug can cause withdrawal symptoms, buprenorphine is not as effective as methadone in treating severely opiate-addicted individuals who require larger doses of opiates in order to maintain treatment therapy. SAMHSA advises that the best candidates for buprenorphine therapy are those patients receiving 30 milligrams or less of methadone. Buprenorphine is estimated to be effective for approximately one-half to two-thirds of the opiate abuser population.

A New Form of Buprenorphine Administration

A new, extended-release formulation of buprenorphine, called a depot formulation, currently is being developed. This depot formulation is an injectable solution that contains tiny biodegradable capsules of buprenorphine. As the capsules disintegrate, they slowly release the drug over several weeks. This new formulation of buprenorphine is designed for administration in a physician's office once every 4 to 6 weeks and could further safeguard against diversion by eliminating the need for patients to possess buprenorphine in tablet form.

Advantages

The use of Subutex and Suboxone in opiate addiction therapy is likely to become more common because of several advantages. Buprenorphine can be prescribed by a local doctor and obtained from a local pharmacy, providing patients with convenient access to treatment. Further, if DATA 2003 is passed, the number of patients that can be treated by group practices will increase. Because patients can visit their local doctors, buprenorphine therapy is far more discreet, making it preferable for many patients who must deal with the stigma attached to making daily trips to a methadone clinic. This treatment option also is more convenient than methadone therapy for many abusers who would otherwise have to drive long distances each day to obtain methadone. Further, buprenorphine therapy can provide treatment in rural areas with inadequate access to treatment and in areas where methadone clinics have reached full capacity.

While it is possible to overdose on buprenorphine, it is safer than methadone because of its ceiling effect and decreased degree of respiratory depression. Also, because of the various safeguards in place, buprenorphine is more difficult to divert than methadone. The abuse of methadone poses a growing threat as evidenced by increasing mortality rates associated with it, whether diverted or legally prescribed. (See text box.)

Methadone Overdose Deaths

The abuse of methadone has contributed to an increase in overdose deaths, particularly in the Northeast region. For example, medical examiner data indicate that methadone is increasingly involved in overdose deaths in Maine. The number of overdose deaths in Maine where methadone was listed as the cause of death fluctuated, but increased overall from 4 in 1997 to 14 in 2001. In the first 6 months of 2002, methadone was listed as the cause of death in 18 deaths. Furthermore, methadone appeared as a factor in 33 percent of all accidental overdose deaths in Maine from 1997 through 2003, one of the two highest percentages of all drugs during that period.

Diversion

Buprenorphine is a synthetic opiate and produces the euphoric effects sought by opiate abusers; therefore, it is susceptible to abuse in both of the forms approved for treating opiate addiction. Subutex, the form that does not contain naloxone, is more vulnerable to abuse because it can be crushed and injected or snorted without causing withdrawal symptoms in the abuser. The FDA recommends that physicians limit the use of Subutex to supervised administration sessions; however, physicians are not required to do so, creating opportunities for Subutex diversion. Subutex has been prescribed legally for years in some foreign countries, where its diversion for illicit use is common. There are lucrative black markets for diverted Subutex in Germany, New Zealand, and the United Kingdom. In France, India, and Scotland, where buprenorphine is far more common in opiate addiction therapy than methadone, many individuals are addicted to Subutex. Suboxone is not available in these countries.

Suboxone also can be diverted and abused; however, it is more likely to be abused by individuals who are addicted to low doses of opiates since it can precipitate withdrawal symptoms in high doses. The naloxone in Suboxone guards against abuse by causing withdrawal symptoms in abusers who crush and either inject or snort the drug; however, law enforcement and pharmacist reporting indicates that Suboxone is being abused successfully when snorted.

Using buprenorphine and heroin in combination does not produce increased effects, but if buprenorphine and methadone are abused together, the effects of both drugs are enhanced. Consequently, diverted buprenorphine may be attractive to patients currently using methadone for opiate addiction therapy.

Despite controls designed to make buprenorphine diversion-proof, there have been reports of buprenorphine diversion throughout the United States, primarily in the Northeast region.

- **Chittenden County, Vermont**. A pharmacist in this area reports that Suboxone is being diverted and sold for $25 per 8-milligram tablet. Abusers are grinding the tablets and snorting them.
- **Washington County, Maine**. The Washington County Sheriff's Office reports that buprenorphine is being diverted in that area and sold for $50 per tablet. The size of the tablet is unknown, and it is unclear whether Subutex or Suboxone tablets are being diverted in this case.
- **Pennsylvania**. The Pennsylvania Department of Health reports that diverted Subutex and Suboxone are being illegally distributed on the street. Specific locations have not been identified.

Outlook

It is unlikely that buprenorphine will render methadone therapy obsolete because it is not as effective in patients who require large doses of opiates in maintenance therapy. However, buprenorphine can provide opiate addiction therapy to individuals addicted to lower doses of opiates, to those in rural areas with inadequate access to treatment, and to those in areas where methadone clinics have reached full capacity. With more physicians obtaining certification to prescribe buprenorphine every day, this form of therapy has the potential to become as common as methadone therapy.

Because of its ceiling effect and ability to precipitate withdrawal symptoms if taken in high doses, buprenorphine is more susceptible to abuse by individuals who are addicted to low doses of opiates or individuals in the early stages of opiate addiction. The drug also can be abused in combination with methadone, making buprenorphine diversion more problematic in areas where heroin abuse and methadone therapy are common, such as the Northeast region. As buprenorphine therapy becomes more widespread, the potential for increased diversion of Subutex and Suboxone should be closely monitored.

Sources

State

Maine

Washington County Sheriff's Office

Pennsylvania

Department of Health

Federal

U.S. Department of Health and Human Services
- Food and Drug Administration
- National Institutes of Health
  - National Institute on Drug Abuse
- Substance Abuse and Mental Health Services Administration

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