



BUPRENORPHINE

(Trade Names: Buprenex®, Suboxone®, Subutex®)

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DEA/OD/ODE

Introduction:

Buprenorphine was first marketed in the United States in 1985 as a schedule V narcotic analgesic. Initially, the only available buprenorphine product in the United States had been a low-dose (0.3 mg/ml) injectable formulation under the brand name, Buprenex®. Diversion, trafficking and abuse of other buprenorphine products have occurred in Europe and other areas of the world.

In October 2002, the Food and Drug Administration (FDA) approved two buprenorphine products (Suboxone® and Subutex®) for the treatment of narcotic addiction. Both products are high dose (2 mg and 8 mg) sublingual (under the tongue) tablets: Subutex® is a single entity buprenorphine product and Suboxone® is a combination product with buprenorphine and naloxone in a 4:1 ratio, respectively. After reviewing the available data and receiving a schedule III recommendation from the Department of Health and Human Services (DHHS), the DEA placed buprenorphine and all products containing buprenorphine into schedule III in 2002. Since 2003, diversion, trafficking and abuse of buprenorphine have become more common in the United States. In June 2010, FDA approved an extended release transdermal film containing buprenorphine (Butrans®) for the management of moderate to severe chronic pain in patients requiring a continuous, extended period, around-the-clock opioid analgesic.

Licit Uses:

Buprenorphine is intended for the treatment of pain (Buprenex®) and opioid addiction (Suboxone® and Subutex®). In 2001, 2005, and 2006, the Narcotic Addict Treatment Act was amended to allow qualified physicians, under certification of the DHHS, to prescribe schedule III-V narcotic drugs (FDA approved for the indication of narcotic treatment) for narcotic addiction, up to 30 patients per physician at any time, outside the context of clinic-based narcotic treatment programs (Pub. L. 106-310). This limit was increased to 100 patients per physician, who meet the specified criteria, under the Office of National Drug Control Policy Reauthorization Act (P.L. 69-469, ONDCPRA), which became effective on December 29, 2006.

Suboxone® and Subutex® are the only treatment drugs that meet the requirement of this exemption. Currently, there are nearly 15,700 physicians who have been approved by the Substance Abuse and Mental Health Services Administration (SAMHSA) and the DEA for office-based narcotic buprenorphine treatment. Of those physicians, approximately 13,150 were approved to treat up to 30 patients per provider and about 2,500 were approved to treat up to 100 patients. More than 3,000 physicians have submitted their intention to treat up to 100 patients per provider.

IMS Health™ National Prescription Audit Plus indicates that 9.3 million buprenorphine prescriptions were dispensed in the U.S. in 2012. From January to March 2013, 2.5 million buprenorphine prescriptions were dispensed.

Chemistry/Pharmacology:

Buprenorphine has a unique pharmacological profile. It produces the effects typical of both pure mu agonists (e.g., morphine) and partial agonists (e.g., pentazocine) depending on dose, pattern of use and population taking the drug. It is

about 20-30 times more potent than morphine as an analgesic; and like morphine it produces dose-related euphoria, drug liking, papillary constriction, respiratory depression and sedation. However, acute, high doses of buprenorphine have been shown to have a blunting effect on both physiological and psychological effects due to its partial opioid activity.

Buprenorphine is a long-acting (24-72 hours) opioid that produces less respiratory depression at high doses than other narcotic treatment drugs. However, severe respiratory depression can occur when buprenorphine is combined with other central nervous system depressants, especially benzodiazepines. Deaths have resulted from this combination.

The addition of naloxone in the Suboxone® product is intended to block the euphoric high resulting from the injection of this drug by non-buprenorphine maintained narcotic abusers.

User Population:

In countries where buprenorphine has gained popularity as a drug of abuse, it is sought by a wide variety of narcotic abusers: young naïve individuals, non-addicted opioid abusers, heroin addicts and buprenorphine treatment clients.

Illicit Uses:

Like other opioids commonly abused, buprenorphine is capable of producing significant euphoria. Data from other countries indicate that buprenorphine has been abused by various routes of administration (sublingual, intranasal and injection) and has gained popularity as a heroin substitute and as a primary drug of abuse. Large percentages of the drug abusing populations in some areas of France, Ireland, Scotland, India, Nepal, Bangladesh, Pakistan, and New Zealand have reported abusing buprenorphine by injection and in combination with a benzodiazepine.

The National Forensic Laboratory Information System (NFLIS) is a DEA database that collects scientifically verified data on drug items and cases submitted to and analyzed by state and local forensic laboratories. The System to Retrieve Information from Drug Evidence (STRIDE) provides information on drug seizures reported to and analyzed by DEA laboratories. In 2012, federal, state and local forensic laboratories identified 10,804. In the first quarter of 2013, 1,905 buprenorphine exhibits were identified.

According to the Drug Abuse Warning Network (DAWN ED), an estimated 21,483 emergency department visits were associated with nonmedical use of buprenorphine in 2011, nearly five times the 4,440 estimated number of buprenorphine ED visits in 2006. The American Association of Poison Control Centers Annual Report indicates that U.S. poison centers recorded 3,625 case mentions and three deaths involving toxic exposure from buprenorphine in 2011.

Control Status:

Buprenorphine and all products containing buprenorphine are controlled in Schedule III of the Controlled Substances Act.

Comments and additional information are welcomed by the Office of Diversion Control, Drug and Chemical Evaluation Section. Fax 202-353-1263, Telephone 202-307-7183, or Email ODE@usdoj.gov.