



BUPRENORPHINE

(Trade Names: Buprenex®, Suboxone®, Subutex®,
Zubsolv®, Sublocade®, Butrans®)

May 2022

Introduction:

Buprenorphine is a schedule III narcotic analgesic. It 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®.

In October 2002, the Food and Drug Administration (FDA) approved two buprenorphine products (Suboxone® and Subutex®)¹ for the treatment of narcotic addiction. Both products are high dose (2 mg and 8 mg) sublingual (under the tongue) tablets. 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 (HHS), 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. Diversion, trafficking, and abuse of other buprenorphine products have occurred in Europe and other areas of the world. Between 2010 and 2017, FDA has approved additional buprenorphine formulations: Butrans® (extended release transdermal film containing buprenorphine), Zubsolv® (buprenorphine/naloxone sublingual tablets), and Sublocade® (buprenorphine extended-release injection).

Licit Uses:

Buprenorphine is intended for the treatment of pain (Buprenex®) and opioid addiction (Suboxone®, Zubsolv®, and Sublocade®). In 2001, 2005, and 2006, the Narcotic Addict Treatment Act was amended to allow qualified physicians, under certification of HHS, to prescribe schedule III-V narcotic drugs (FDA approved for the indication of narcotic treatment) for opioid 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.

Since then, guidelines have been updated to allow physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, and certified nurse midwives to treat up to 30 patients at any one time with opioid use disorder using buprenorphine without having to make certain training related certifications (86 FR 22439). Qualified practitioners who undertake the required training may treat up to 100 patients using buprenorphine for the treatment of opioid use disorder. After one year at the 100- patient limit, qualifying practitioners may increase their patient limit to 275.

IQVIA™ National Prescription Audit Plus indicates that since 2002, 171 million buprenorphine prescriptions have been dispensed in the United States. Of these 171 million, almost 138 million prescriptions (80.2%) were buprenorphine and naloxone combination products (data as of May 24, 2022).

Chemistry and Pharmacology:

Buprenorphine is an opioid receptor partial agonist. It produces the effects typical of both classic mu opioid receptor 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 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 combination products (Suboxone® and Zubsolv®) is intended to block the euphoric high resulting from the injection of this drug by non-buprenorphine maintained narcotic abusers.

Illicit Uses:

Like other opioids commonly abused, buprenorphine is capable of producing significant euphoria. Data from the United States and 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.

Illicit Distribution:

The National Forensic Laboratory Information System (NFLIS-Drug) is a DEA database that collects scientifically verified data on drug items and cases submitted to and analyzed by Federal, state, and local forensic laboratories. Between 1997 and 2002, there were 42 reports of buprenorphine to NFLIS-Drug. From 2002 to present, there have been 207,088 reports of buprenorphine to NFLIS-Drug, with the highest number of annual reports occurring in 2019 with 21,255 reports (queried May 24, 2022).

According to the Substance Abuse and Mental Health Services Administration's (SAMHSA) Treatment Episode Data Set (TEDS) 2019, there were an estimated 8,522 admissions of persons 12 and older to publicly funded substance use treatment centers for buprenorphine use. Of these 8,522 admissions, buprenorphine was the primary drug of abuse in 3,694 (43%) admissions.

According to the 2020 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 38th Annual report, U.S. poison centers recorded 4,958 case mentions with buprenorphine, 2,948 single substance exposure cases, and two deaths involving toxic exposure from buprenorphine in 2020.

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.

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 Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.

¹ Subutex® has been discontinued by the manufacturer.