Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section

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DEA/DC/DOE

BUPRENORPHINE

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

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. 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. In June 2010, FDA approved an extended-release transdermal film containing buprenorphine (Butrans®) for the management of moderate to severe chronic pain in patients who required a continuous, extended period, around-the-clock opioid analgesic.

In 2002, after reviewing the available data and receiving a schedule III recommendation from the Department of Health and Human Services (HHS), the Drug Enforcement Administration (DEA) placed buprenorphine and all products containing buprenorphine into schedule III. Since 2003, diversion, trafficking, and abuse of buprenorphine have become more common in the United States. Diversion, trafficking, and abuse of buprenorphine products have occurred in Europe and other areas of the world.

Licit Uses:

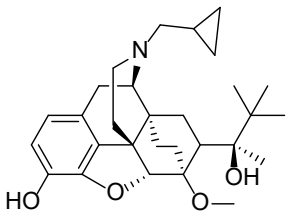
Buprenorphine is intended for the treatment of pain (Buprenex) and opioid addiction (Suboxone and Subutex). In 2001, 2005, and 2006, the Narcotic Addict Treatment Act was amended to allow qualified physicians, under certification of HHS, to prescribe schedule III–V narcotic drugs for narcotic addiction, 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. The Substance Abuse and Mental Health Services Administration (SAMHSA) and DEA have approved nearly 15,700 physicians for office-based narcotic buprenorphine treatment. Of those physicians, approximately 13,150 were approved to treat up to 30 patients per provider, and approximately 2,500 were approved to treat up to 100 patients. Currently, more than 3,000 physicians have submitted their intention to treat up to 100 patients per provider.

According to the IQVIA National Prescription Audit™, total prescriptions dispensed for buprenorphine-containing products in the United States was approximately 9.1 million in 2012. This number has steadily increased since then, with approximately 15.9 million prescriptions dispensed in 2018 and 18.3 million prescriptions in 2024.

Chemistry:

Buprenorphine has the molecular formula $C_{29}H_{41}NO_4$ and a molecular weight of 467.64 g/mol. The structure of buprenorphine is shown below:



Pharmacology:

Buprenorphine has a unique pharmacological profile and produces effects that are typical of both pure mu-opioid receptor agonists (e.g., morphine) and partial agonists (e.g., pentazocine), depending on the dose, pattern of use, and population taking the drug. As an analgesic, buprenorphine is about 20–30 times more potent than morphine. Like morphine, buprenorphine 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 agonist activity.

Buprenorphine is a long-acting (24–72 hours) opioid that produces less respiratory depression at high doses compared to other narcotic drugs; however, severe respiratory depression can occur when buprenorphine is combined with other central nervous system depressants, especially benzodiazepines. This combination has resulted in deaths.

Suboxone includes the addition of naloxone, which is intended to block the euphoric high resulting from the injection of this drug by non-buprenorphine maintained narcotic abusers.

Illicit Uses:

Like other commonly abused opioids, buprenorphine can produce significant euphoria. Data from other countries indicate that buprenorphine has been abused through various routes of administration (e.g., sublingual, intranasal, injection) and has gained popularity as a heroin substitute and 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.

DEA's National Forensic Laboratory Information System (NFLIS) Drug database is a system that collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug received the following number of reports related to buprenorphine: 21,320 in 2019; 17,614 in 2020; 14,502 in 2021; 13,378 in 2022; and 11,326 in 2023.

The American Association of Poison Control Centers Annual Report indicated that U.S. poison centers recorded 4,040 case mentions; 2,368 single substance exposure cases; and 1 death involving toxic exposure from buprenorphine in 2022.

USER POPULATION:

In countries where buprenorphine has gained popularity as a drug of abuse, this substance 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.