

NALBUPHINE HYDROCHLORIDE (Trade Name: Nubain®)

Introduction:

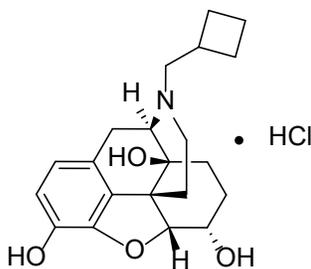
Nalbuphine (Nubain®), which was approved for marketing in the United States in 1979 is a synthetic opioid with mixed agonist-antagonist property. Chemically, it is related to the opioid antagonist, naloxone, and the potent opioid agonist, oxymorphone. Nalbuphine remains the only narcotic analgesic of this type not controlled under the Controlled Substances Act (CSA).

Licit Uses:

Nalbuphine is approved for use in the United States as the hydrochloride salt in an injectable formulation (10 or 20 mg/mL). It is available by brand name (Nubain®) and generic formulations. Nalbuphine is indicated for the treatment of moderate to severe acute pain. As an injectable formulation, nalbuphine is primarily used in hospitals and rarely prescribed by physicians compared to other opioid analgesics. According to IQVIA National Prescription Audit™, total prescriptions dispensed in the United States for nalbuphine were 12,315 in 2018, 951 in 2020, 3,343 in 2022, and 2,711 in 2024.

Chemistry:

Nalbuphine is chemically known as 17-(cyclobutylmethyl)-4,5 α -epoxymorphinan-3,6 α ,14-triol. The CAS number for nalbuphine is 20594-83-6. Nalbuphine hydrochloride (Nubian®) is the hydrochloride salt form of nalbuphine which has a CAS number of 23277-43-2. It is soluble in water and ethanol and is available only as an injectable solution. The chemical structure for nalbuphine hydrochloride is shown below.



Pharmacology:

Nalbuphine is a potent analgesic of the phenanthrene drug class. Its analgesic potency is equivalent to morphine. Nalbuphine acts as a kappa opioid receptor agonist and an antagonist at mu-opioid receptors. The onset of action of nalbuphine occurs within 2 to 3 minutes after intravenous administration and in less than 15 minutes following subcutaneous or intramuscular injection. Its duration of

analgesic activity has been reported to range from 3 to 6 hours.

Nalbuphine produces respiratory depression and considerable sedation that may impair mental and physical abilities in the performance of tasks such as driving automobiles or operating machinery. Nalbuphine may also cause psychological or physical dependence and tolerance. Abrupt discontinuation after prolonged use can cause signs and symptoms of opioid withdrawal.

Illicit Uses:

As a drug of abuse, nalbuphine is less attractive as a substitute for heroin addicts or highly tolerant opioid abusers due to its potent antagonist effects. Nalbuphine is 10 times more potent than pentazocine as an antagonist and will precipitate withdrawal in an opiate-tolerant individual. A limited number of anecdotal reports suggest that nalbuphine is abused by health care professionals and body builders (anabolic steroid users).

User Population:

America's Poison Centers' reports indicate that there were two case mentions of nalbuphine use in 2023, one substance exposure related to nalbuphine in 2022, and four exposures in 2021. No deaths were associated with nalbuphine in 2021, 2022, or 2023.

Illicit Distribution:

Nalbuphine is rarely encountered by law enforcement personnel or submitted to forensic laboratories for analysis. This may be, in part, due to its non-controlled status. DEA's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug has received over 200 reports of nalbuphine since it was first reported in 1998; however, there has been no more than 1 report per year since 2015.

Control Status:

Nalbuphine is not a controlled substance under the CSA.

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.