



NALBUPHINE HYDROCHLORIDE (Brand Name: Nubain®)

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Introduction:

In the search for narcotic analgesics with less abuse potential, a number of synthetic opiates were developed. These substances are referred to as mixed agonist-antagonists analgesics. Nalbuphine (Nubain®) belongs to this group of substances. It was approved for marketing in the United States in 1979 and remains as the only narcotic analgesic of this type (that is marketed in the U.S.) not controlled under the Controlled Substances Act (CSA).

Licit Uses:

Nalbuphine is approved for use in the U.S. as the hydrochloride salt in an injectable formulation containing 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. According to IQVIA National Prescription Audit™, total prescriptions dispensed for nalbuphine were 14,803 in 2016, 14,329 in 2017, 12,315 in 2018, 10,592 in 2019, 951 in 2020, and 4,389 in 2021. Annual nalbuphine prescriptions decreased to 10,592 in 2019, 951 in 2020, and then increased to 4,389 in 2021.

Chemistry:

Nalbuphine hydrochloride (Nubain®) is classified as a synthetic opioid agonist-antagonist. Chemically, it is related to the opioid antagonist, naloxone and the potent opioid agonist oxymorphone. The chemical name for nalbuphine is 17-(cyclobutylmethyl)-4,5 α -epoxymorphinan-3,6 α , 14-triol hydrochloride. It is soluble in water and ethanol and available only as an injectable solution.

Pharmacology:

Nalbuphine is a potent analgesic. Its analgesic potency is essentially equivalent to morphine. It binds to mu, kappa, and delta opioid receptors. Nalbuphine is metabolized by the liver and excreted by the kidneys.

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. The plasma half-life is 5 hours and the duration of analgesic activity has been reported to range from 3 to 6 hours.

Nalbuphine, like other potent opioids, is associated with respiratory depression. Unlike morphine and other potent mu agonists, nalbuphine produces less respiratory depression as the dose is increased due to its agonist-antagonist "ceiling" effect. Nalbuphine produces considerable sedation and may impair mental and physical abilities in the performance of such tasks as driving automobile or operating machinery.

Nalbuphine may cause psychological or physical dependence and tolerance. Abrupt discontinuation after prolonged use can cause signs and symptoms of opioid withdrawal.

Illicit Uses:

As an injectable formulation, nalbuphine is primarily used in hospitals and rarely prescribed by physicians compared to other opioid analgesics. In addition, as a drug of abuse it is less attractive as a substitute by heroin addicts or highly tolerant opioid abusers due to its potent antagonist effects. Nalbuphine is ten 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 by body builders (anabolic steroid users).

User Population:

The American Association of Poison Control Centers (AAPCC) 2019 Annual Report indicates that there were a total of seven exposures in which four were single substance exposures. In 2020, they reported that there were two exposures related to nalbuphine (one single substance exposure) in that year. The 2021 Annual reports indicate there were a total of four exposures (one single substance exposure). From 2019 to 2021 there are no deaths associated with nalbuphine.

Illicit Distribution:

Nalbuphine is rarely encountered by law enforcement personnel or submitted to forensic laboratories for analysis. This may, in part, be due to its non-control status. According to DEA's National Forensic Laboratory Information System (NFLIS) Drug database, participating federal, state and local forensic drug laboratories submitted only one report of nalbuphine in 2019 and one in 2021.

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.