



NALBUPHINE HYDROCHLORIDE (Trade Name: Nubain®)

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DEA/OD/ODE

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. In 2011, there were 32,000 nalbuphine prescriptions dispensed in the U.S., 24,000 dispensed in 2012, and 2,000 prescriptions dispensed in the first quarter of 2013 (IMS Health™).

Chemistry/Pharmacology:

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.

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.

User Population:

The American Association of Poison Control Centers (AAPCC) 2011 Annual Report indicates that there were 32 exposures related to nalbuphine (15 single substance exposures) in that year. No deaths were associated with nalbuphine in 2011.

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).

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 the National Forensic Laboratory Information System (NFLIS) and the System to Retrieve Information from Drug Evidence (STRIDE), federal, state and local forensic laboratories two drug exhibits were identified as nalbuphine in 2011 and four in 2012. As of the first quarter of 2013, there have been no reports of nalbuphine in NFLIS or STRIDE.

Control Status:

When the Controlled Substances Act (CSA) was enacted in 1970, nalbuphine was placed in schedule II. Endo Laboratories, Inc. subsequently petitioned the DEA to exclude nalbuphine from all schedules of the CSA in 1973. After receiving a medical and scientific review and a scheduling recommendation from the Department of Health, Education and Welfare, forerunner to the Department of Health and Human Services, nalbuphine was removed from schedule II of the CSA in 1976. Presently, nalbuphine is not a controlled substance under the CSA.

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