NALBUPHINE HYDROCHLORIDE
(Trade Name: Nubain®)

December 2019

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 2016, there were 14,803 nalbuphine prescriptions dispensed in the U.S., and 14,633 dispensed in 2017; out of which, 14,330 prescriptions were picked-up and/or sold to prescribing patients. For 2018, there were a total of 12,315 prescriptions sold for nalbuphine and an estimated 6,244 prescriptions for the first six months of 2019 (IQVIA™ formerly 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)-4,5α-epoxymorphinan-3,6α, 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.

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).

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 the National Forensic Laboratory Information System (NFLIS) and the System to Retrieve Information from Drug Evidence (STRIDE)/STARLiMS federal, state and local forensic laboratories, two drug exhibits were identified as nalbuphine in 2015 and one in 2016 and 2017, as well as, 2018.

User Population:
The American Association of Poison Control Centers (AAPCC) 2016 Annual Report indicates that there were 11 exposures related to nalbuphine (5 single substance exposures) in that year. For 2017, there were a total of 17 exposures in which 11 were single substance exposures. No deaths were associated with nalbuphine in 2016 or 2017.

Control Status:
Nalbuphine is not a controlled substance under the CSA.