PRODUCT MONOGRAPH

©NUBAIN

(Nalbuphine Hydrochloride)

Injection, 10 and 20 mg/mL

Opioid Analgesic
Adjunct Anesthetic

Sandoz Canada Inc.
145 Jules-Léger
Boucherville, Quebec, J4B 7K8

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(nalbuphine hydrochloride)
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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Subcutaneously, intramuscularly or intravenously	Solution for injection	Sodium chloride (only for 10 mg/mL), sodium citrate dihydrate, citric acid and water for injection. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

NUBAIN (nalbuphine hydrochloride) is indicated for the relief of moderate to severe pain.

NUBAIN can also be used as a supplement to surgical anesthesia, an adjunct to preoperative and postoperative analgesia, and obstetrical analgesia during labor and delivery.

Pediatrics (< 18 years of age): Because clinical experience in children is limited, the administration of NUBAIN in this age group is not recommended.

CONTRAINDICATIONS

NUBAIN (nalbuphine hydrochloride) should not be administered to patients who are hypersensitive to the drug or to its inactive ingredients (see DOSAGE FORMS, COMPOSITION AND PACKAGING).

WARNINGS AND PRECAUTIONS

NUBAIN should be administered as a supplement to surgical anesthesia only by persons specifically trained in the use of intravenous anesthetics and management of the respiratory effects of potent opioids.

Naloxone, resuscitative and intubation equipment and oxygen should be readily available.

Myocardial Infarction: As with all potent analgesics, NUBAIN should be used with caution in patients with myocardial infarction who have nausea or vomiting. Hemodynamic studies in patients with severe arteriosclerotic heart changes reveal that NUBAIN has circulatory effects similar to those of morphine, i.e., a minimal decrease in oxygen consumption, cardiac index, left ventricular end-diastolic pressure and cardiac work.

Dependence/Tolerance
Drug Dependence: In patients physically dependent on opiate drugs, NUBAIN (nalbuphine hydrochloride) should not be given prior to detoxification since withdrawal symptoms are likely to be produced.

On the basis of behavioral, substitution and direct addiction studies in humans NUBAIN has been shown to have low abuse potential. When compared with drugs which are not mixed agonist-antagonists, it has been reported that nalbuphine's potential for abuse would be less than that of codeine and propoxyphene. Psychological and physical dependence and tolerance may follow the abuse or misuse of nalbuphine. Therefore, caution should be observed in prescribing it for emotionally unstable patients, or for individuals with history of narcotic abuse. Such patients should be closely supervised when long-term therapy is contemplated.

Care should be taken to avoid increases in dosage which might result in physical dependence in susceptible individuals.

Abrupt discontinuation of NUBAIN following prolonged use has been followed by symptoms of narcotic withdrawal, i.e., abdominal cramps, nausea and vomiting, rhinirrhea, lacrimation, restlessness, anxiety, elevated temperature and piloerection.

Patients Dependent on Opioids: Patients who have been taking narcotics chronically may experience withdrawal symptoms upon the administration of NUBAIN. If necessary, narcotic withdrawal symptoms can be controlled by the slow intravenous administration of small increments of morphine, until symptomatic relief.

Hepatic/Biliary/Pancreatic
Biliary Tract Surgery: NUBAIN may cause spasm of the sphincter of Oddi. It is not recommended to be used for analgesia in patients with acute abdominal conditions. It should only be used for anesthesia in these patients when its benefits outweigh its potential risks.

Neurologic
Head Injury and Increased Intracranial Pressure: The possible respiratory depressant effects and the potential of potent analgesics to elevate cerebrospinal fluid pressure

(resulting from vasodilation following CO_2 retention) may be markedly exaggerated in the presence of head injury, intracranial lesions, or a pre-existing increase in intracranial pressure. Furthermore, potent analgesics can produce effects which may obscure the clinical course of patients with head injuries. Therefore, NUBAIN should be administered in these circumstances only when essential, and then should be administered with extreme caution.

Peri-Operative Considerations
Outpatients: NUBAIN may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Outpatients must be maintained under observation until adequately recovered from the NUBAIN effects.

Renal
Impaired Renal or Hepatic Function: Because NUBAIN is metabolized in the liver and excreted by the kidneys, patients with renal or liver dysfunction may show an exaggerated response to customary doses. In these individuals, NUBAIN should be used with caution and administered in reduced amounts.

Respiratory
Impaired Respiration: At the usual adult dose of dose 10 mg/70 kg, NUBAIN causes respiratory depression approximately equal to that produced by equal doses of morphine. In contrast to morphine, respiratory depression is not appreciably increased with higher doses of NUBAIN. Respiratory depression induced by NUBAIN can be reversed by naloxone hydrochloride when indicated. NUBAIN should be administered with caution at low doses to patients with impaired respiration (e.g., from other medication, uremia, bronchial asthma, severe infection, cyanosis or respiratory obstructions).

Special Populations
Pregnant Women There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, nalbuphine should be used during pregnancy only if, in the judgment of the physician, the potential benefits outweigh the possible risks (see **TOXICOLOGY**, **Reproduction and Teratology**).

Women Giving Birth
NUBAIN should be used in women during labour and delivery only when benefits outweigh the potential risks, and newborns should be monitored for respiratory depression, apnea, bradycardia, and arrhythmias. NUBAIN can produce respiratory depression in the neonate. It should be administered with extreme caution to women delivering premature infants.

The placental transfer of nalbuphine is high, relatively rapid and variable with a maternal to fetal ratio ranging from 1:0.37 to 1:6.03. Fetal and neonatal adverse effects that have been reported following the administration of nalbuphine to the mother during labour include fetal bradycardia, respiratory depression at birth, apnea, cyanosis, and hypotonia.

Severe and prolonged fetal bradycardia has been reported. Permanent neurological damage attributed to fetal bradycardia has occurred. A sinusoidal fetal heart rate pattern associated with the use of nalbuphine has also been reported.

Nursing Women: Limited data suggest that NUBAIN is excreted in maternal milk in small amounts (less than 1% of the administered dose) considered clinically insignificant. Caution should be exercised when NUBAIN is administered to a nursing mother.

Pediatrics (< 18 years of age): Because clinical experience in children under the age of 18 years is limited, the administration of NUBAIN in this age group is not recommended.

Monitoring and Laboratory Tests
NUBAIN may interfere with enzymatic methods for the detection of opioids depending on the specificity and sensitivity of the tests. Please consult the test manufacturer for specific details.

ADVERSE REACTIONS

In clinical trials with NUBAIN (nalbuphine hydrochloride) the most frequently reported side effects were: sedation (36% of 1066), sweating or clammy (9%), nausea or vomiting (6%), dizziness or vertigo (5%), dry mouth (4%) and headache (3%).

Less Common Clinical Trial Adverse Drug Reactions:

Central Nervous System: nervousness, crying, depression, restlessness, euphoria, hostility, confusion, faintness, floating, unusual dreams, numbness, feeling of heaviness, and psychotomimetic effects such as hallucinations, feeling of unreality and dysphoria. The incidence of psychotomimetic effects, such as unreality, depersonalization, delusions, dysphoria and hallucinations has been shown to be less than that which occurs with pentazocine.

Cardiovascular: Hypertension, hypotension, bradycardia, tachycardia.

Gastrointestinal: Cramps, dyspepsia, bitter taste.

Respiration: Depression, dyspnea, asthma.

Dermatological: Itching, burning, urticaria.

Miscellaneous: Speech difficulty, urinary urgency, blurred vision, flushing and warmth.

Allergic Reactions: Anaphylactic/anaphylactoid and other serious hypersensitivity reactions have been reported following the use of nalbuphine and may require immediate, supportive medical treatment. These reactions may include shock, respiratory distress, respiratory arrest, bradycardia, cardiac arrest, hypotension, or laryngeal edema. Other

allergic-type reactions reported with patients using NUBAIN include stridor, bronchospasm, wheezing, edema, rash, pruritis, nausea, vomiting, diaphoresis, weakness, and shakiness.

Post-marketing: Other reports include pulmonary edema, agitation and injection site reactions such as pain, swelling, redness, burning and hot sensations.

DRUG INTERACTIONS

Interaction With Other Central Nervous System Depressants

Although NUBAIN possesses narcotic antagonist activity, there is evidence that in non-dependent patients it will not antagonize a narcotic analgesic administered just before, concurrently, or just after an injection of NUBAIN. Therefore, patients receiving a narcotic analgesic, general anesthetics, phenothiazines or other tranquilizers, sedatives, hypnotics, or other CNS depressants (including alcohol) with NUBAIN may exhibit an additive effect. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

DOSAGE AND ADMINISTRATION

Analgesia

The usual recommended adult dose of NUBAIN (nalbuphine hydrochloride) is 10 mg for a 70 kg individual, administered subcutaneously, intramuscularly or intravenously. This dose may be repeated every 3 to 6 hours as required. In non-tolerant individuals, the recommended dosage range is 10 mg to 20 mg, with a maximum single dose of 20 mg and a maximum total daily dose of 160 mg. Dosage should be adjusted according to the severity of the pain, physical status of the patient, and other medications which the patient may be receiving (see Interaction with Other Central Nervous System Depressants under WARNING).

Recommended Dose and Dosage Adjustment

Opioid Analgesics - Approximate Analgesic Equivalences

Drug	Equivalent Dose (mg) [compared to morphine 10 mg IM]		Duration of Action (hours)
	Parenteral	Oral	
Strong Opioid Agonists			
Morphine (single dose)	10	60	3 - 4
(chronic dose)	10	20 – 30	3 - 4
Hydromorphone	1.5 - 2	6 – 7.5	2 - 4
Anileridine	25	75	2 - 3
Levorphanol	2	4	4 - 8
Meperidine	75	300	1 - 3
Oxymorphone	1.5	5 (rectal)	3 – 4
Heroine	5 – 8	10 – 15	3 – 4

Drug	Equivalent Dose (mg) [compared to morphine 10 mg IM]		Duration of Action (hours)
	Parenteral	Oral	
Weak Opioid Agonists			
Codeine	120	200	3 – 4
Oxycodone	5 – 10	10 – 15	2 – 4
Propoxyphene	50	100	2 – 4
Mixed Agonist- Antagonists			
Pentazocine	60	180	3 – 4
Nalbuphine	10		3 – 6
Butorphanol	2		3 – 4

Patients who have been taking narcotics chronically for pain under medical supervision may experience withdrawal symptoms upon the administration of NUBAIN. If NUBAIN is administered to these patients as an analgesic, it should be introduced gradually. NUBAIN should not be used as a substitute for other narcotics or for tapering individuals dependent on these drugs.

Patients Dependent on Narcotics: If the previous analgesic was morphine, meperidine, codeine, or other narcotic with similar duration of activity, one fourth of the anticipated dose of NUBAIN can be administered initially and the patient observed for signs of withdrawal, i.e., abdominal cramps, nausea and vomiting, lacrimation, rhinorrhea, anxiety, restlessness, elevation of temperature or piloerection. If untoward symptoms do not occur, progressively larger doses may be tried at appropriate intervals until the desired level of analgesia is obtained with NUBAIN.

Balanced Anesthesia
Balanced anesthesia with NUBAIN requires larger doses than for the multiple doses recommended above for analgesia. Induction schedules with NUBAIN range from 0.3 mg/kg to 5 mg/kg intravenously over a 10 to 15 minute period.

After induction with NUBAIN is completed, maintenance doses of 0.25 mg/kg to 0.5 mg/kg can be used as required in single doses. Significant respiratory depression at the end of anesthesia rarely occurs with proper use of NUBAIN. Naloxone remains the specific antidote for any respiratory depression.

As a component to regional anesthesia, NUBAIN can be used in doses of 0.2 mg/kg to 0.5 mg/kg of body weight. NUBAIN produces sedation and additional analgesia to such regional techniques as alveolar nerve block and can be an adjunct to spinal anesthesia, regional nerve blocks, block of extremities, etc.

Incompatibility With Other Therapeutic Agents
NUBAIN is physically incompatible with nafcillin and ketorolac. Solutions of these drugs should not be mixed.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre for the most current information.

Symptoms

These are expected to be similar to those of other drugs of this class. The administration of single I.M. doses of 72 mg of NUBAIN to eight normal subjects has been reported to have resulted primarily in symptoms of sleepiness and mild dysphoria.

Treatment

Naloxone hydrochloride administered intravenously is a specific antidote for NUBAIN. Since the duration of action of NUBAIN may exceed that of NARCAN, the patient should be kept under continued surveillance and repeated doses of NARCAN should be administered as necessary. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

ACTION AND CLINICAL PHARMACOLOGY

NUBAIN (nalbuphine hydrochloride) is a synthetic opioid agonist-antagonist analgesic for parenteral use, related chemically to the opioid oxymorphone, and to the opioid antagonist naloxone. Nalbuphine has an analgesic (agonist action) potency equivalent to that of morphine on a milligram for milligram basis. Receptor studies show that nalbuphine binds to mu, kappa, and delta receptors, but not to sigma receptors. Nalbuphine is primarily a kappa agonist/ mu antagonist analgesic. 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 of nalbuphine is five hours and in clinical studies the duration of analgesic activity has been reported to range from three to six hours. The narcotic antagonist activity of NUBAIN is one-fourth as potent as that of nalorphine and ten times that of pentazocine.

At the usual adult dose of 10 mg / 70 kg, nalbuphine may produce respiratory depression equivalent to that of equianalgesic doses of morphine. However, NUBAIN exhibits a ceiling effect such that increases in dose greater than 30 mg do not produce further respiratory depression.

Nalbuphine by itself has potent opioid antagonist activity at doses equal to or lower than its analgesic dose. When administered following or concurrent with mu agonist opioid analgesics (e.g., morphine, oxymorphone, fentanyl), nalbuphine may partially reverse or block opioid-induced respiratory depression from the mu agonist analgesic. Nalbuphine may precipitate withdrawal in patients dependent on opioid drugs. Nalbuphine should be used with caution in patients who have been receiving mu opioid analgesics on a regular basis.

STORAGE AND STABILITY

Store at controlled room temperature (15°c to 30°c). Protect from excessive light. Store in carton until contents have been used.

SPECIAL HANDLING INSTRUCTIONS

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

DOSAGE FORMS, COMPOSITION AND PACKAGING

NUBAIN (10.0 mg/mL) 1 mL Ampoule: Each mL contains 10.0 mg nalbuphine hydrochloride, 2.0 mg sodium chloride, 9.41 mg sodium citrate dihydrate, 12.62 mg citric acid and water for injection; pH adjusted with hydrochloric acid.

NUBAIN (20.0 mg/mL) 1 mL Ampoule: Each mL contains 20.0 mg nalbuphine hydrochloride, 9.41 mg sodium citrate dihydrate, 12.62 mg citric acid and water for injection; pH adjusted with hydrochloric acid.

NUBAIN is available in 1 mL ampoules, boxes of 2 x 5 ampoules.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

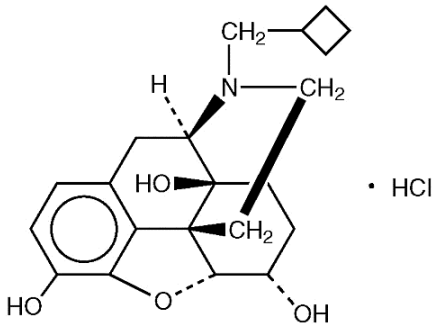
Proper name: nalbuphine hydrochloride

Chemical name: 17- (cyclobutylmethyl)-4,5-epoxy-, morphinan - 3,6,14-triol, hydrochloride

Molecular formula $C_{21}H_{27}NO_4 \bullet HCl$

Molecular mass: 393.91 g/mol

Structural formula:



Physicochemical properties: NUBAIN (nalbuphine hydrochloride) is a synthetic narcotic agonist-antagonist analgesic of the phenanthrene series. It is chemically related to both the widely used narcotic antagonist, naloxone, and the potent narcotic analgesic, oxymorphone, The pH is adjusted with hydrochloric acid. Nalbuphine hydrochloride is soluble in H2O (35.5 mg/mL at 25°C) and ethanol (0.8%); insoluble in CHCl3 and ether. Nalbuphine hydrochloride has pKa values of 8.71 and 9.96

NUBAIN (nalbuphine hydrochloride) is a Schedule G (Controlled) drug.

CLINICAL TRIALS

Animal tests show that parenterally administered nalbuphine HCI is an analgesic of the agonist-antagonist type. When administered subcutaneously in the mouse antiphenylquinone writhing tests nalbuphine hydrochloride, at the time of peak activity, was 2.3 times as potent as morphine sulfate 8.3 times as potent as codeine phosphate and 3.5 times as potent as pentazocine hydrochloride. In the same tests, orally administered nalbuphine, at peak activity time, was 0.27 times as potent as morphine, about equipotent with codeine, and 2.4 times as potent as pentazocine.

The onset of the analgesic effect of nalbuphine, codeine, and morphine by the subcutaneous route in mice was prompt; the peak time of the effect was similar for the three drugs. The duration of the effect of nalbuphine was the same as that of codeine~~;~~, but morphine lasted longer. Orally, the onset of the analgesic effect of nalbuphine, codeine and morphine in mice was prompt. The peak times of effect for both nalbuphine and codeine were 5 minutes after administration, and the morphine peak time was after 20 minutes. The duration of the effect of all three drugs was similar.

Nalbuphine resembled known narcotic antagonists in several other tests. Administered subcutaneously, it blocked the oxymorphone, etonitazine and morphine-induced Straub tail response in mice, and oxymorphone-induced loss of righting reflex in rats. Oral nalbuphine also blocked the induction of oxymorphone-induces Straub tail response in mice. When administered subcutaneously to mice, nalbuphine was about three times as potent as an agonist than as an antagonist, based upon the results of the antiphenylquinone test for antagonist activity and upon the blockage of morphine-induced Straub tail response for antagonist activity.

Nalbuphine's predominant component, the alpha epimer, was 9.4 times as active as the beta epimer as an analgesic (in the mouse antiphenylquinone writhing test), 1.9 times as active as a narcotic antagonist (in blocking morphine-induced Straub tail response in mice), when tested subcutaneously. The beta epimer appeared to be qualitatively similar to the alpha epimer in its analgesic and narcotic antagonist actions but was quantitatively less potent.

TOXICOLOGY

Acute Toxicology: The animals which died within 14 days of dosing: mouse 1240 mg/kg (S.C.), 775 mg/kg (I.M.), 490 mg/kg (I.V.); rat: >1000 mg/kg (S.C.), 1200-1240 mg/kg (I.M.), 182-218 mg/kg (I.V.); dog: 200 mg/kg (S.C.), ~140 mg/kg (I.V.).

Depending on species and route of administration, the animals died either during clonic-tonic convulsions, in respiratory failure following clonic-tonic convulsions, or in respiratory failure without prior convulsions. Deaths generally occurred rapidly, and always within 72 hours of dosing. Other signs included cyanosis, depression, emesis, piloerection, ptosis, rapid or laboured respiration, salivation and tremor. Surviving

animals generally appeared normal within 24 hours of dosing and most signs had disappeared within 2 to 4 hours. There were no obvious sex differences in response to the drug. Other than skin sores at subcutaneous and intramuscular injection sites, there were no drug-induced abnormalities at autopsy.

Subacute Toxicology: Nalbuphine HCI was administered subcutaneously to groups of 20 male and 20 female young rats for two weeks (14 daily injections in 16 days) at dosage levels of 0, 6.6, 20 and 100 mg/kg/day. The only evidence of toxicity was decreased body weight at high dosage level. Some local irritation was observed at the injection site, but this was apparently due to repeated injections in the same area. Nalbuphine HCI was administered subcutaneously to groups of male and two female young adult beagles for two weeks (14 daily injections in 15 days) at dosage levels of 0, 2, 4, and 50 mg/kg/day. At the high dosage level, the signs of toxicity were slight weight loss, slight tremoring and hind-limb weakness, slight salivation and a few occurrences of emesis. Except for some mild local irritation at the injection sites in the 50 mg/kg/day group, due to large volumes of a 20 mg/ml drug solution, there were no other signs of toxicity. When nalbuphine HCI was administered intravenously to groups of three male and three female young adult beagle dogs once a day, 7 days a week for at least 2 weeks at dosage levels of 4, 8, and 32 mg/kg/day, there were no significant signs of toxicity.

Chronic Toxicology: Nalbuphine HCI was administered subcutaneously to starting groups of 35 male and 35 female young adult rats once a day, seven days a week for up to six months at dosage levels of 0, 7, 14 and 56 mg/kg/day. There was an interim sacrifice of 15 males and 15 females after three months. The drug caused a slight reduction in body weight gain, a slight to moderate increase in food consumption and decrease in food efficiency, a slight to marked but reversible hair loss and a slight normochromic, normocytic anemia, depending on the dosage level, frequency of dosing and animal's sex. Nalbuphine HCI was administered subcutaneously to groups of four male and four female adult beagle dogs once a day, seven days a week for six months at dosage levels of 0, 4, 8, and 50 mg/kg/day. The drug caused weight loss at all dosage levels.

Carcinogenesis and Mutagenesis: No evidence of carcinogenicity was found in a 24-month carcinogenicity study in rats and an 18-month carcinogenicity study in mice at oral doses as high as the equivalent of approximately three times the maximum recommended therapeutic dose. No evidence of a mutagenic/genotoxic potential to NUBAIN was found in the Ames, Chinese Hamster Ovary HGPRT, and Sister Chromatid Exchange, mouse micronucleus, and rat bone marrow cytogenicity assays. Nalbuphine induces an increased frequency of mutation in mouse lymphoma cells.

Reproduction and Teratology: The reproductive effects of parenterally administered nalbuphine HCI were evaluated in 1) a Segment I fertility and general reproductive performance study in rats at subcutaneous dosage levels of 14, 28 and 56 mg/kg/day, 2) a Segment II teratology study in rats at subcutaneous dosage levels of 7, 14, and 100 mg/kg/day and in rabbits at intravenous dosage levels of 4, 8 and 32 mg/kg/day, and 3) a Segment III perinatal-postnatal study in rats at subcutaneous dosage levels of 14, 28 and 56 mg/kg/day. No adverse effects of compound administration were observed during the

evaluation of fertility and general reproductive performance and there was no evidence of compound-induced embryotoxicity or teratogenesis.

Reproduction studies have been performed in rabbits and in rats at dosages as high as approximately 14 and 31 times respectively the maximum recommended daily dose and revealed no evidence of impaired fertility or harm to the fetus due to NUBAIN.

Neonatal body weight and survival was reduced when NUBAIN was subcutaneously administered to female rats prior to mating and throughout gestation and lactation or to pregnant rats during the last third of gestation and throughout lactation at doses approximately 8 to 17 times the maximum recommended therapeutic dose. The clinical significance of this effect is unknown.

Local Irritation Study: A solution of nalbuphine HCI (10 mg/ml) was tested for local irritation by high subcutaneous injection in the shaved abdomen of young mice. Both the 24- and 48- hour readings showed only slight irritation.

Special Studies – Distant Alopecia: The purpose of these studies was to determine the maximum "no-effect" dosage level for distant hair loss in rats and dogs. Nalbuphine hydrochloride was administered subcutaneously to groups of 35 male and 35 female rats at dosages of 0.1 to 56 mg/kg/day. The number of rats exhibiting alopecia increased with increases in dosage, but never exceeded 44 % (at the highest dose level of 56 mg/kg/day). The onset of alopecia was not dose-related or dose-related or dose-dependent (appearing within the first 3 weeks) and the time to peak effect was generally from 3 to 12 weeks. The degree of alopecia ranged from slight to marked and was seen on the abdomen, chest, back, neck, sides, limbs, paw, hip, shoulders and head. The threshold dose was estimated to be 0.16 mg/kg/day.

Dose of 0.1 to 50 mg/kg/day were administered subcutaneously to groups of four male and four female beagle dogs once daily for 1-1/2 to 2-1/2 months. Alopecia was seen at all dosage levels, including the controls, and its incidence increased with dose. All animals in the 4 mg/kg/day group exhibited alopecia. The onset of alopecia was dose-related and generally occurred within eight weeks. The degree of alopecia ranged from slight to marked and was seen on the abdomen, muzzle, chest, ears, limbs, neck, forehead, and tail. The threshold dose for alopecia was estimated to be 0.09 mg/kg/day.

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PART III: CONSUMER INFORMATION

© **NUBAIN**
(nalbuphine hydrochloride)
Injection, 10 and 20 mg/mL

This leaflet is part III of a three-part "Product Monograph" published when NUBAIN was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about NUBAIN. Contact your doctor if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
NUBAIN is indicated in adults:
- for the relief of moderate to severe pain.
- to aid anesthesia for surgery.
- to help manage pain before and after surgery.
- to help manage pain during child birth.

What it does:
NUBAIN is a pain medication belonging to the class of medicines known as opioids. It relieves pain by acting on specific nerve cells of the spinal cord and brain

When it should not be used:
- If you have a known history of allergic reactions or sensitivity to this drug or other agents in the same drug family

What the medicinal ingredient is:
Nalbuphine hydrochloride

What the nonmedicinal ingredients are:
Sodium chloride (only for 10 mg/mL), sodium citrate dihydrate, citric acid and water for injection. pH adjusted with hydrochloric acid.

What dosage forms it comes in:
Solution for injection: 10 mg/mL, 20 mg/mL

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions
NUBAIN should only be administered by persons with the appropriate training and experience with this kind of drug. Complete resuscitation (life-saving) equipment and an antidote to rapidly counteract the effects of the drug should always be available.

BEFORE being given NUBAIN, talk to your doctor if you:
- plan on operating a car or heavy machinery after receiving NUBAIN.
- have a condition with any part of your body, such as your heart, kidney, lung, or liver.
- have heavy alcohol use.
- use any drugs not given to you by a doctor.
- are pregnant or breast feeding.
- have a known allergic reaction to this drug or any other pain medications or any other general anesthetics.
- have had a head injury, or if you experience difficulties breathing.
- have a history of drug abuse or dependence.
- are less than 18 years of age.

Other warnings you should know about:
There are important differences between physical dependence and addiction, and each is a reason for close medical supervision and honest discussions with your doctor. If you have questions or concerns about abuse, addiction or physical dependence, please tell your doctor.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with NUBAIN include: sleeping pills (barbiturates), phenothiazines or other tranquilizers, pain medication (opioids), general anesthetics, or other depressants of the central nervous system.

Alcohol may also change the effect of NUBAIN.

PROPER USE OF THIS MEDICATION

Usual adult dose:
NUBAIN will be given to you as an injection either under the skin, into a muscle or into your vein.
Your doctor will determine your dose based on how much you weigh.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

During or after the use of NUBAIN, talk to your doctor or nurse if you feel anything unusual or bothering (see the following table).

These are not all the possible side affects you may feel when taking NUBAIN. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom/effect	Talk with your doctor or pharmacist		Stop taking drug and seek immediate medical help
	Only if severe	In all cases	
Common			
Dizziness, light-headedness, sensation of spinning	✓		
Drowsiness	✓		
Nausea and/or vomiting	✓		
Sweating, clammy skin	✓		
sleepiness	✓		
Les common			
Dry mouth	✓		
Headache	✓		
Rare			
Skin: reactions at the injection site such as pain, swelling, redness, burning and hot sensations, itching, rash.	✓		
Difficulty breathing, shortness of breath, wheezing		✓	
Slow or fast, pounding irregular heartbeat or pulse, fainting		✓	
Confusing, restlessness, euphoria, hostility, floating, unusual dreams, numbness, changes in speech	✓		
Allergic reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing.			✓

This is not a complete list of side effects. For any unexpected effects following the administration of NUBAIN, contact your doctor or pharmacist.

HOW TO STORE IT

NUBAIN should be stored between 15°C and 30°C and protected from light. Store in carton until contents have been used.

Keep out of reach and sight of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document, plus the full product monograph prepared for health professionals, can be obtained by contacting the sponsor, Sandoz Canada Inc., at: 1-800-361-3062
or
by written request at:
145, Jules-Léger
Boucherville, (QC), Canada
J4B 7K8

or by e-mail at :
medinfo@sandoz.com

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