℞ *For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.*

Nalbuphine Hydrochloride Injection 10 mg/ml

VARPHIN 10

Each ml contains:
Nalbuphine Hydrochloride Dihydrate
eq. to Anhydrous Nalbuphine Hydrochloride 10 mg
Water for Injections IP q.s.

DESCRIPTION
Nalbuphine hydrochloride is a synthetic opioid agonist-antagonist analgesic of the phenanthrene series. It is chemically related to both the widely used opioid antagonist, naloxone, and the potent opioid analgesic, oxymorphone. Chemically nalbuphine hydrochloride is 17-(cyclobutylmethyl)4,5α-epoxymorphinan-3,6α,14-triol hydrochloride. Nalbuphine Hydrochloride molecular formula is $C_{21}H_{27}NO_4.HCl$ and its molecular weight is 393.91g/mol.

THERAPEUTIC INDICATIONS
Nalbuphine hydrochloride can also be used as a supplement to surgical anaesthesia, an adjunct to preoperative and postoperative analgesia, and obstetrical analgesia during labour and delivery.
Geriatrics (> 65 years of age): In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, concomitant disease or other drug therapy (see, Pharmacological properties Special Populations and Conditions, Geriatrics).
Paediatrics (< 18 years of age): The safety and efficacy of nalbuphine hydrochloride has not been studied in the paediatric population. Therefore, the use of Nalbuphine Hydrochloride is not recommended in patients under 18 years of age.

POSOLOGY AND METHOD OF ADMINISTRATION
Posology: Nalbuphine Hydrochloride Injection should be used with caution within 12 hours pre-operatively and within the first 12-24 hours post-operatively (see Special Warnings and Precautions, Considerations).
Rapid intravenous injection of opioid analgesics increases the possibility of hypotension and respiratory depression.
For acute pain, it is recommended that nalbuphine hydro chloride be used for a maximum of 7 days at the lowest dose that provides adequate pain relief.
All doses of opioids carry an inherent risk of fatal or non-fatal adverse events. This risk is increased with higher doses. If nalbuphine hydrochloride is used for more than 7 days for the management of chronic non-cancer, non-palliative pain, it is recommended that 90 mg (90 morphine milligram equivalent) of nalbuphine hydrochloride not be exceeded. Each patient should be assessed for their risk prior to prescribing nalbuphine hydrochloride as the likelihood of experiencing serious adverse events can depend upon the type of opioid, duration of treatment, level of pain as well as the patient's own level of tolerance. In addition, the level of pain should be assessed routinely to confirm the most appropriate dose and the need for further use of Nalbuphine Hydrochloride.
Analgesia: The usual recommended adult dose of 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.

Recommended Dose and Dosage Adjustment
Opioid Rotation: Conversion ratios for opioids are subject to variations in kinetics governed by genetics and other factors. When switching from one opioid to another, consider reducing the calculated dose by 25-50% to minimize the risk of overdose. Subsequently, up-titrate the dose, as required, to reach the appropriate maintenance dose.
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
Oxycodone	15	30	2-4
Hydromorphone	1.5	7.5	2-4
Anileridine	25	75	2-4
Levorphanol	2	4	4-8
Meperidine	75	300	1-3
Oxymorphone	1.5	5(rectal)	3-4
Methadone	-	-	-
Heroine	5-8	10-15	3-4
Weak Opioid Agonists			
Codeine	120	200	3-4
Propoxyphene	150	100	2-4
Mixed Agonist- Antagonists			
Pentazocine	60	180	3-4
Nalbuphine	10	-	3-6
Butorphanol	2	-	3-4

Patients with Hepatic Impairment: Patients with liver dysfunction may show an exaggerated response to customary doses. In these individuals, nalbuphine hydrochloride should be used with caution and administered in reduced amounts
Patients with Renal Impairment: Patients with renal dysfunction may show an exaggerated response to customary doses. In these individuals, nalbuphine hydrochloride should be used with caution and administered in reduced amounts.
Geriatrics: Respiratory depression has occurred in the elderly following administration of large initial doses of opioids to patients who were not opioid-tolerant or when opioids were co-administered with other agents that can depress respiration. nalbuphine hydrochloride should be initiated at a low dose and slowly titrated to effect (see Special warnings and precautions and action pharmacological properties).
Use with Non-Opioid Medications: If a non-opioid analgesic is being provided, it may be continued. If the non-opioid is discontinued, consideration should be given to increasing the opioid dose to compensate for the non-opioid analgesic. nalbuphine hydrochloride can be safely used concomitantly with usual doses of other non-opioid analgesics.

Dose Titration: Dose titration is the key to success with opioid analgesic therapy. Proper optimization of doses scaled to the relief of the individual's pain should aim at administration of the lowest dose which will achieve the overall treatment goal of satisfactory pain relief with acceptable side effects.
Dosage adjustments should be based on the patient's clinical response.
Incompatibility with Other Therapeutic Agents: Nalbuphine Hydrochloride Injection is physically incompatible with nafcillin and ketorolac. Solutions of these drugs should not be mixed.

CONTRAINDICATIONS
Nalbuphine hydrochloride should not be administered to

- Patients who are hypersensitive to the active substance nalbuphine or other opioid analgesics or to any ingredients in the formulation.
- In patients with known or suspected mechanical gastrointestinal obstruction (e.g., bowel obstruction or strictures) or any diseases/conditions that affect bowel transit (e.g., ileus of any type).
- Patients with suspected surgical abdomen (e.g., acute appendicitis or pancreatitis).
- Patients with mild pain that can be managed with other pain medications.
- Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus.
- Patients with acute respiratory depression, elevated carbon dioxide levels in the blood and cor pulmonale.
- Patients with acute alcoholism, delirium tremens, and convulsive disorders.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure, and head injury.
- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).
- Women who are breast-feeding or pregnant (see Special Warnings and Precautions).

SPECIAL WARNINGS AND PRECAUTIONS
Limitations of Use: Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the risks of overdose and death with parenteral opioid formulations, nalbuphine hydrochloride should only be used in patients for whom alternative treatment options (e.g., non-opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate management of pain (see dosage and administration).
As with other CNS depressants, patients who have received nalbuphine hydrochloride should have appropriate surveillance. Resuscitative equipment and a narcotic antagonist such as naloxone should be readily available to manage apnea.
Addiction, Abuse, and Misuse: Nalbuphine hydrochloride poses risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Each patient's risk should be assessed prior to prescribing Nalbuphine hydrochloride, and all patients should be monitored regularly for the development of these behaviours or conditions (see warnings and precautions). Nalbuphine hydrochloride should be stored securely to avoid theft or misuse.
Cardiovascular: nalbuphine hydrochloride administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of drugs such as phenothiazines and other tranquilizers, sedative/hypnotics, tricyclic antidepressants or general anaesthetics. These patients should be monitored for signs of hypotension after initiating or titrating the dose of nalbuphine hydrochloride. The use of nalbuphine hydrochloride in patients with circulatory shock should be avoided as it may cause vasodilation that can further reduce cardiac output and blood pressure. Rapid intravenous injection of opioid analgesics increases the possibility of hypotension and respiratory depression and should be avoided (see dosage and administration).
Myocardial Infarction: As with all potent analgesics, nalbuphine hydrochloride 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 nalbuphine hydrochloride 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: As with other opioids, tolerance and physical dependence may develop upon repeated administration of nalbuphine hydrochloride and there is a potential for development of psychological dependence.
Physical dependence and tolerance reflect the neuroadaptation of the opioid receptors to chronic exposure to an opioid, and are separate and distinct from abuse and addiction. Tolerance, as well as physical dependence, may develop upon repeated administration of opioids, and are not by themselves evidence of an addictive disorder or abuse.
Use in Drug and Alcohol Addiction: nalbuphine hydrochloride is an opioid with no approved use in the management of addictive disorders. Its proper usage in individuals with drug or alcohol dependence, either active or in remission, is for the management of pain requiring opioid analgesia. Patients with a history of addiction to drugs or alcohol may be at higher risk of becoming addicted to nalbuphine hydrochloride; extreme caution and awareness is warranted to mitigate the risk.
Endocrine: Adrenal Insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.
Gastrointestinal Effects: Nalbuphine Hydrochloride and other morphine-like opioids have been shown to decrease bowel motility. Nalbuphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions (see Contraindications).
Hepatic/Biliary/Pancreatic
Biliary Tract Surgery: Nalbuphine Hydrochloride 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 anaesthesia in these patients when its benefits outweigh its potential risks.
Neonatal Opioid Withdrawal Syndrome (NOWS): Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening.
Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhoea and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the new born. Use of nalbuphine hydrochloride is contraindicated in pregnant women (see Contraindications).
Head Injury: The respiratory depressant effects of nalbuphine, and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of an already elevated intracranial pressure produced by trauma. Also, nalbuphine may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, nalbuphine must be used with extreme caution and only if it is judged essential (see contraindications).
Use in Patients with Convulsive or Seizure Disorders: The nalbuphine hydrochloride in nalbuphine hydrochloride may aggravate convulsions in patients with convulsive disorders, and may induce or aggravate seizures in some clinical settings. Therefore, nalbuphine hydrochloride should not be used in these patients (see contraindications).
Serotonin syndrome: nalbuphine hydrochloride could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. antidepressants, migraine medications). Treatment with the serotonergic drug should be discontinued if such events (characterized by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. nalbuphine hydrochloride should not be used in combination with MAO inhibitors or serotonin precursors (such as L-tryptophan, oxitriptan) and should be used with caution in combination with other serotonergic drugs (triptans, certain tricyclic antidepressants, lithium, tramadol, St. John's Wort) due to the risk of serotonergic syndrome (see drug interactions).

Peri-Operative Considerations: The administration of analgesics in the peri-operative period should be managed by healthcare providers with adequate training and experience (e.g., by an anaesthesiologist). In the case of planned chordotomy or other pain-relieving operations, patients should not be treated with nalbuphine hydrochloride for at least 24 hours before the operation and nalbuphine hydrochloride should not be used in the immediate post-operative period. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. The risk of withdrawal in opioid-tolerant patients should be addressed as clinically indicated.
Nalbuphine and other morphine-like opioids have been shown to decrease bowel motility. Ileus is a common post-operative complication, especially after intra-abdominal surgery with opioid analgesia. Caution should be taken to monitor for decreased bowel motility in post-operative patients receiving opioids. Standard supportive therapy should be implemented.
Psychomotor Impairment: nalbuphine hydrochloride may impair the mental and/or physical abilities needed for certain potentially hazardous activities such as driving a car or operating machinery. Patients should be cautioned accordingly. Patients should also be cautioned about the combined effects of nalbuphine with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.
Renal: Impaired Renal or Hepatic Function: Because nalbuphine hydrochloride 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, nalbuphine hydrochloride should be used with caution and administered in reduced amounts.
Respiratory: Respiratory Depression: Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression from opioid use, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status. Nalbuphine should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia (see Contraindications).
While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of nalbuphine hydrochloride the risk is greatest during the initiation of therapy or following a dose increase. Patients should be closely monitored for respiratory depression when initiating therapy with nalbuphine hydrochloride and following dose increases.

Use in Patients with Chronic Pulmonary Disease: Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression for respiratory depression, particularly when initiating therapy and titrating with nalbuphine hydrochloride , as in these patients, even usual therapeutic doses of nalbuphine hydrochloride may decrease respiratory drive to the point of apnea. In these patients, use of alternative non-opioid analgesics should be considered, if possible. The use of nalbuphine hydrochloride is contraindicated in patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see Contraindications).
Sexual Function/Reproduction: Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as low libido, erectile dysfunction, or infertility.
Special Populations
Special Risk Groups: Nalbuphine should be administered with caution to patients with a history of alcohol and drug abuse and in a reduced dosage to debilitated patients, and in patients with severely impaired pulmonary function, Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture
Pregnant Women: Studies in humans have not been conducted. nalbuphine hydrochloride crosses the placental barrier and is contraindicated in pregnant women. Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal Opioid Withdrawal Syndrome (NOWS), unlike opioid withdrawal syndrome in adults, may be life-threatening (see warnings and precautions, Neonatal Opioid Withdrawal Syndrome, adverse reactions, Post Marketing Experience). Pregnant women using opioids should not discontinue their medication abruptly as this can cause pregnancy complication such as miscarriage or still-birth. Tapering should be slow and under medical supervision to avoid serious adverse events to the foetus.
Labour, Delivery and Nursing Women: Since opioids can cross the placental barrier and are excreted in breast milk, nalbuphine hydrochloride is contraindicated in nursing women and is not recommended to be used during labour and delivery unless, in the judgement of the physician, the potential benefits outweigh the risks. Life-threatening respiratory depression can occur in the infant if opioids are administered to the mother. Naloxone, a drug that counters the effects of opiates, should be readily available if nalbuphine hydrochloride is used in this population.
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.
Paediatrics (< 18 years of age): The safety and efficacy of nalbuphine hydrochloride have not been studied in the paediatric population. Therefore, use of nalbuphine hydrochloride is not recommended in patients under 18 years of age.
Geriatrics (> 65 years of age): In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and titrate slowly, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

INTERACTION WITH OTHER MEDICINAL PRODUCTS
Interaction with Benzodiazepines and Other Central Nervous System (CNS) Depressants (including alcohol): Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants (e.g. other opioids, sedatives/hypnotics, antidepressants, anxiolytics, tranquilizers, muscle relaxants, general anaesthetics, antipsychotics, phenothiazines, neuroleptics, antihistamines, antiemetic, and alcohol) and beta-blockers, increases the risk of respiratory depression, profound sedation, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation (see Special Warnings and Precautions) and Psychomotor Impairment). nalbuphine hydrochloride should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.
Drug-Drug Interactions
Central Nervous System (CNS) Depressants: Both magnitude and duration of CNS and cardiovascular effects may be enhanced when nalbuphine hydrochloride is administered to patients receiving barbiturates, benzodiazepines, neuroleptics, halogenic gases and other nonselective CNS depressants (e.g. alcohol). When patients have received such drugs, the dose of nalbuphine hydrochloride required will be less than usual. Likewise, following the administration of nalbuphine hydrochloride the dose of other CNS-depressant drugs should be reduced.
MAO Inhibitors: It is usually recommended to discontinue MAO inhibitors 2 weeks prior to any surgical or anaesthetic procedure.

Serotonergic Agents: Co administration of nalbuphine with a serotonergic agent, such as a Selective Serotonin Re-Uptake Inhibitor or a Serotonin Norepinephrine Re-Uptake Inhibitor, may increase the risk of serotonin syndrome, a potentially life-threatening condition (see Special Warnings and Precautions).

PREGNANCY LACTATION AND FERTILITY
Pregnancy: Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome. Available data with nalbuphine hydrochloride in pregnant women are insufficient to inform a drug-associated risk for major birth defects and miscarriage.
Lactation: Limited data suggest that nalbuphine hydrochloride (nalbuphine hydrochloride) is excreted in maternal milk but only in a small amount (less than 1% of the administered dose) and with a clinically insignificant effect. Infants exposed to nalbuphine hydrochloride through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.
Fertility: Not Known

UNDESIRABLE EFFECTS

Adverse effects of nalbuphine hydrochloride (nalbuphine hydrochloride) injection are similar to those of other opioid analgesics, and represent an extension of pharmacological effects of the drug class. The major hazards of opioids include respiratory and central nervous system depression and to a lesser degree, circulatory depression, respiratory arrest, shock and cardiac arrest.

Sedation: Sedation is a common side effect of opioid analgesics, especially in opioid naïve individuals. Sedation may also occur partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Most patients develop tolerance to the sedative effects of opioids within three to five days and, if the sedation is not severe, will not require any treatment except reassurance. If excessive sedation persists beyond a few days, the dose of the opioid should be reduced and alternate causes investigated.

Nausea and Vomiting: Nausea is a common side effect on initiation of therapy with opioid analgesics and is thought to occur by activation of the chemoreceptor trigger zone, stimulation of the vestibular apparatus and through delayed gastric emptying. The prevalence of nausea declines following continued treatment with opioid analgesics. When instituting therapy with an opioid for chronic pain, the routine prescription of an antiemetic should be considered. In the cancer patient, investigation of nausea should include such causes as constipation, bowel obstruction, uremia, hypercalcemia, hepatomegaly, tumor invasion of celiac plexus and concurrent use of drugs with emetogenic properties. Persistent nausea which does not respond to dosage reduction may be caused by opioid-induced gastric stasis and may be accompanied by other symptoms including anorexia, early satiety, vomiting and abdominal fullness. These symptoms respond to chronic treatment with gastrointestinal prokinetic agents.

Constipation: Practically all patients become constipated while taking opioids on a persistent basis. In some patients, particularly the elderly or bedridden, fecal impaction may result. It is essential to caution the patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid therapy. Stimulant laxatives, stool softeners, and other appropriate measures should be used as required. As fecal impaction may present as overflow diarrhoea, the presence of constipation should be excluded in patients on opioid therapy prior to initiating treatment for diarrhoea.

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.

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 and etc.

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

Androgen deficiency: Chronic use of opioids may influence the hypothalamic-pituitary- gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility.

OVERDOSE

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 nalbuphine hydrochloride 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 nalbuphine hydrochloride. Since the duration of action of nalbuphine hydrochloride may exceed that of naloxone, the patient should be kept under continued surveillance and repeated doses of naloxone should be administered as necessary. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Opioid Agonist/Antagonist

ATC Code: N02AF02

Mechanism of Action: Nalbuphine is a phenanthrene derivative with mixed opioid agonist and antagonist activity (agonist at kappa opiate receptors and partial antagonist at μ receptors in the CNS). It inhibits the ascending pain pathways and alters the perception of and response to pain.

Pharmacodynamic Properties

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 nalbuphine hydrochloride 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, nalbuphine hydrochloride 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 patient dependent on opioid drugs. Nalbuphine should be used with caution in patients who have been receiving mu opioid analgesics on a regular basis.

Pharmacokinetics: The onset of action of nalbuphine hydrochloride 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 5 hours, and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours. The metabolic pathway for nalbuphine has not been defined, but is likely hepatic.

STORAGE: Store below 30°C. Protect from light. Do not freeze.
Don't use Nalbuphine Hydrochloride Injection after the expiry date printed on label and carton.
Keep out of reach of children
Don't use Nalbuphine Hydrochloride Injection in case any foreign particulate, leakage or breakage found

PRESENTATION:

Primary Pack: 1ml USP Type-I glass ampoule.

Secondary Pack: Such five ampoules are placed in blister and packed in printed carton along with packing insert.

Marketed By:

VARENYAM®

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