SAFETY DATA SHEET

Nalbuphine Hydrochloride Injection

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Name:	Nalbuphine Hydrochloride Injection
Synonyms	17-(cyclobutylmethyl)-4,5 α-epoxymorphinan-3,6 α,14-triol hydrochloride
Manufacturer for	Somerset Therapeutics, LLC. Somerset, NJ 08873
Customer Care	1-800-417-9175

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Nalbuphine Hydrochloride Injection is a solution containing nalbuphine hydrochloride, a narcotic analgesic indicated for the relief of moderate to severe pain. In the workplace, this material should be considered potentially irritating to the eyes and respiratory tract and a potent drug. Based on clinical use, possible target organs include the central nervous system, gastrointestinal system, respiratory system, eyes, and cardiovascular system.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Not Classified	Not Classified
Health Hazards	**Hazard Class**	**Hazard Category**
	STOT – RE	2

Label Element(s)

Pictogram



Signal Word

Warning

Hazard Statement(s)

May cause damage to organs through prolonged or repeated exposure

Precautionary Statement(s)

Prevention

Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medicalattention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Nalbuphine Hydrochloride
Chemical Formula $C_{21}H_{27}NO_4 \bullet HCl$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Nalbuphine Hydrochloride	≤ 2	23277-43-2	QD3181000

Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% may include sodium citrate, USP dihydrate and anhydrous citric acid (Buffering agent); Sodium chloride, USP (Tonicity agent) ; Hydrochloric acid (Acidifying agent) is added for pH adjustment.

4. FIRST AID MEASURES

Eye Contact Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Skin Contact Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Inhalation Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Ingestion Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. In diagnosed overdosage, intravenous administration of an opiate antagonist such as naloxone or nalmefene is antidotal. Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated.

5. FIRE FIGHTING MEASURES

Flammability None anticipated for this aqueous product.

Fire & Explosion Hazard None anticipated for this aqueous product.

Extinguishing Media As with any fire, use extinguishing media appropriate for primary cause of fire such as carbon dioxide, dry chemical extinguishing powder or foam.

Special Fire Fighting Procedures No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling No special handling required for hazard control under conditions of normal product use.

Storage No special storage required for hazard control. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions No special precautions required for hazard control.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Nalbuphine Hydrochloride	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8-hour Time Weighted Average.

Respiratory Protection Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N95 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Skin Protection If skin contact with the product formulation is likely, the use of latex or nitrile gloves is recommended.

Eye Protection Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.

Engineering Controls Engineering controls are normally not needed during the normal use of this product.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A clear solution
Odor	NA
Odor Threshold	NA
pH	3.7 (3.0 to 4.5)
Melting point/Freezing Point	NA
Initial Boiling Point/Boiling Point Range	NA
Flash Point	NA
Evaporation Rate	NA
Flammability (solid, gas)	NA
Upper/Lower Flammability or Explosive Limits	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Relative Density	NA
Solubility	Nalbuphine hydrochloride is soluble in water, ethanol, and insoluble in chloroform and ether
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined
Chemical Stability	Stable under standard use and storage conditions.
Hazardous Reactions	Not determined
Conditions to Avoid	Not determined
Incompatibilities	Not determined
Hazardous Decomposition Products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and hydrogen chloride vapor.
Hazardous Polymerization	Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity: Not determined for the product formulation. Information for the active ingredient is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Nalbuphine Hydrochloride	100	LD50	Oral Intravenous	1100 140	mg/kg mg/kg	Dog Dog

LD 50: Dosage that produces 50% mortality.

Occupational Exposure Potential	Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact.
Signs and Symptoms	None anticipated from normal handling of this product. This material should be considered potentially irritating to the eyes. In clinical use, adverse effects may include sedation, sweaty/clammy, nausea/vomiting, dizziness/vertigo, dry mouth, pinpoint pupils, and headache. Nalbuphine hydrochloride causes respiratory depression approximately equal to that produced by equal doses of morphine. Other reactions may include nervousness, depression, restlessness, confusion, faintness; and cardiovascular effects like hypertension, hypotension, bradycardia, and tachycardia. Anaphylactic/ anaphylactoid and other serious hypersensitivity reactions have been reported may include shock, respiratory distress, respiratory arrest, or laryngeal edema. Other allergic-type reactions reported include stridor, bronchospasm, wheezing, edema, rash, pruritus, nausea, vomiting, diaphoresis, weakness, and shakiness.
Aspiration Hazard	None anticipated from normal handling of this product.
Dermal Irritation/ Corrosion	None anticipated from normal handling of this product.
Ocular Irritation/ Corrosion	None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation with redness and tearing.
Dermal or Respiratory Sensitization	None anticipated from normal handling of this product. However, anaphylactic/ anaphylactoid and other serious hypersensitivity reactions have been reported following the clinical use of nalbuphine in patients.

Reproductive Effects	None anticipated from normal handling of this product. A reproduction study was performed in male and female rats at subcutaneous dosages up to 56 mg/kg/day or 330 mg/m2/day. Nalbuphine hydrochloride did not affect either male or female fertility in rats. Reproduction studies have been performed in rats by subcutaneous administration of nalbuphine up to 100 mg/kg/day (590 mg/m2/day), and in rabbits by intravenous administration of nalbuphine up to 32 mg/kg/day (378 mg/m2/day). The results did not reveal evidence of developmental toxicity, including teratogenicity, or harm to the fetus. However, neonatal body weight and survival rates were reduced at birth and during lactation when nalbuphine was subcutaneously administered to female and male 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 4 times the maximum recommended human dose.
Mutagenicity	Nalbuphine hydrochloride did not have mutagenic activity in the AMES test with four bacterial strains, in the Chinese Hamster Ovary HGPRT assays or in the Sister Chromatids Exchange Assay. However, nalbuphine hydrochloride induced an increased frequency of mutation in the mouse lymphoma assay. Clastogenic activity was not observed in the mouse micronucleus test of the cytogenicity bone marrow assay in rats.
Carcinogenicity	Long term carcinogenicity studies were performed in rats (24 months) and mice (19 months) by oral administration at doses up to 200 mg/kg (1180 mg/m2) and 200 mg/kg (600 mg/m2) per day, respectively. There was no evidence of an increase in tumors in either species related to nalbuphine hydrochloride administration. The maximum recommend human dose (MRHD) in a day is 160 mg subcutaneously, intramuscularly or intravenously, or approximately 100 mg/m2/day for a 60 kg subject.
Carcinogen Lists	**IARC:** Not listed **NTP:** Not listed **OSHA:** Not listed
Specific Target Organ Toxicity – Single Exposure	NA
Specific Target Organ Toxicity – Repeat Exposure	Based on clinical use, possible target organs include the nervous system, gastrointestinal system, respiratory system, eyes, and cardiovascular system.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined for product.
Persistence/Biodegradability	Not determined for product.
Bioaccumulation	Not determined for product.
Mobility in Soil	Not determined for product.

Notes:

13. DISPOSAL CONSIDERATIONS

Waste Disposal	All waste materials must be properly characterized. Further, disposal should beperformed in accordance with the federal, state or local regulatory requirements.
Container Handling andDisposal	Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA
ICAO/IATA STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA
IMDG STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA

Notes: DOT - US Department of Transportation Regulation**s**

15. REGULATORY INFORMATION

US TSCA Status	Exempt
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US PROP 65 (Calif.)	Not listed

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

GHS/CLP Classification*

*In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.

Classification(s)	NA
Symbol	NA
Indication of Danger	NA
Risk Phrases	NA
Safety Phrases	S23: Do not breathe vapor/spray S24: Avoid contact with the skin S25: Avoid contact with eyes S37/39 Wear suitable gloves and eye/face protection.

16. OTHER INFORMATION

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD_{50}	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

Prepared by: Somerset Therapeutics Limited

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