# SAFETY DATA SHEET

## Nalbuphine Hydrochloride Injection

## 1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

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|---|---|
| **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** $C_{21}H_{27}NO_4 \cdot HCl$

| 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

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|---|---|
| **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

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|---|---|
| **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<br>Intravenous | 1100<br>140 | mg/kg<br>mg/kg | Dog<br>Dog |

LD 50: Dosage that produces 50% mortality.

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| **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. |

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| **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

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|---|---|
| **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

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|---|---|
| **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

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|---|---|
| **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 Regulatio**ns**

## 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<br>S24: Avoid contact with the skin<br>S25: Avoid contact with eyes<br>S37/39 Wear suitable gloves and eye/face protection. |

## 16. OTHER INFORMATION

Notes:

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|---|---|
| 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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