MATERIAL SAFETY DATA SHEET

Product Name: Nalbuphine Hydrochloride Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

Emergency Telephone
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (02) 8014 4880

Hospira, Inc., Non-Emergency
224-212-2000

Product Name
Nalbuphine Hydrochloride Injection

Synonyms
17-(cyclobutylmethyl)-4,5α-epoxymorphinan-3,6α,14-triol hydrochloride

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Nalbuphine Hydrochloride

Chemical Formula
C_{21}H_{27}NO_4 \cdot HCl

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% may include sodium citrate dihydrate and citric acid, anhydrous; sodium hydroxide and/or hydrochloric acid are added for pH adjustment. Multiple-dose vials contain methylparaben and propylparaben as preservatives.

<table>
<thead>
<tr>
<th>Component</th>
<th>Approximate Percent by Weight</th>
<th>CAS Number</th>
<th>RTECS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nalbuphine Hydrochloride</td>
<td>\leq 2</td>
<td>23277-43-2</td>
<td>QD3181000</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

Carcinogen List

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nalbuphine Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

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.

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
In the workplace, 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 adverse reactions which occur less frequently may include nervousness, depression, restlessness, crying, euphoria, floating, hostility, unusual dreams, confusion, faintness; cardiovascular effects like
Product Name: Nalbuphine Hydrochloride Injection

hypertension, hypotension, bradycardia, and tachycardia; gastrointestinal cramps, respiratory depression, shortness of breath, itching of skin, urticaria, urinary urgency, and flushing and warmth have also been reported. Anaphylactic/ anaphylactoid and other serious hypersensitivity reactions have been reported following the use of nalbuphine and may include reactions such as shock, respiratory distress, respiratory arrest, bradycardia, cardiac arrest, hypotension, or laryngeal edema. Some of these allergic reactions may be life threatening. Other allergic-type reactions reported include stridor, bronchospasm, wheezing, edema, rash, pruritus, nausea, vomiting, diaphoresis, weakness, and shakiness.

Medical Conditions Aggravated by Exposure

Pre-existing hypersensitivity to this material; pre-existing central nervous system, respiratory system, gastrointestinal system, and cardiovascular system ailments; pre-existing issues with chemical dependency.

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 overdose, 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. |
| 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 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

<table>
<thead>
<tr>
<th>Exposure limits</th>
<th>Component</th>
<th>Type</th>
<th>mg/m3</th>
<th>ppm</th>
<th>µg/m3</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nalbuphine Hydrochloride</td>
<td>Not Applicable</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>None Established</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Liquid</td>
</tr>
<tr>
<td>Color</td>
<td>Clear</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>3.7 (3.0 to 4.5)</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
<tr>
<td>Upper/Lower Flammability or</td>
<td>NA</td>
</tr>
<tr>
<td>Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Density:</td>
<td>NA</td>
</tr>
</tbody>
</table>
Product Name: Nalbuphine Hydrochloride Injection

Specific Gravity: NA
Solubility: Soluble in water ethanol. Insoluble in chloroform & ether
Partition coefficient: n-octanol/water: NA
Auto-ignition temperature: NA
Decomposition temperature: 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.

11. TOXICOLOGICAL INFORMATION

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

<table>
<thead>
<tr>
<th>Ingredient(s)</th>
<th>Percent</th>
<th>Test Type</th>
<th>Route of Administration</th>
<th>Value</th>
<th>Units</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nalbuphine Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>1100</td>
<td>mg/kg</td>
<td>Dog</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intravenous</td>
<td>140</td>
<td>mg/kg</td>
<td>Dog</td>
</tr>
</tbody>
</table>

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. 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
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.

Mutagenicity
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 rats. Reproduction studies have been
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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.

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.

Target Organ Effects
Based on clinical use, possible target organs include the central 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.

13. DISPOSAL CONSIDERATIONS

Waste Disposal
All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal
Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

DOT STATUS
Not regulated

IMDG STATUS:
Not regulated

ICAO/IATA STATUS:
Not regulated
15. REGULATORY INFORMATION

USA Regulations

<table>
<thead>
<tr>
<th>Substance</th>
<th>TSCA Status</th>
<th>CERCLA Status</th>
<th>SARA 302 Status</th>
<th>SARA 313 Status</th>
<th>PROP 65 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nalbuphine Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

RCRA Status: Not Listed

U.S. OSHA Classification

- Target Organ Toxin
- Possible Irritant

GHS 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: Not Applicable

Hazard Category: Not Applicable

Signal Word: Not Applicable

Symbol: Not Applicable

Prevention

P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

Hazard Statement: Not Applicable

Response:

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. Wash hands after handling.

Get medical attention if you feel unwell.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance Nalbuphine Hydrochloride.

Classification(s): Not Applicable

Symbol: Not Applicable

Indication of Danger: Not Applicable

Risk Phrases: Not Applicable

Safety Phrases:

- S23 - Do not breathe vapor.
- S24 - Avoid contact with skin.
- S25 - Avoid contact with eyes.
- S37/39 - Wear suitable gloves and eye/face protection.
**16. OTHER INFORMATION:**

<table>
<thead>
<tr>
<th>Notes:</th>
<th>Definition:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH TLV</td>
<td>American Conference of Governmental Industrial Hygienists – Threshold Limit Value</td>
</tr>
<tr>
<td>CAS</td>
<td>Chemical Abstracts Service Number</td>
</tr>
<tr>
<td>CERCLA</td>
<td>US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act</td>
</tr>
<tr>
<td>DOT</td>
<td>US Department of Transportation Regulations</td>
</tr>
<tr>
<td>EEL</td>
<td>Employee Exposure Limit</td>
</tr>
<tr>
<td>IATA</td>
<td>International Air Transport Association</td>
</tr>
<tr>
<td>LD50</td>
<td>Dosage producing 50% mortality</td>
</tr>
<tr>
<td>NA</td>
<td>Not applicable/Not available</td>
</tr>
<tr>
<td>NE</td>
<td>Not established</td>
</tr>
<tr>
<td>NIOSH</td>
<td>National Institute for Occupational Safety and Health</td>
</tr>
<tr>
<td>OSHA PEL</td>
<td>US Occupational Safety and Health Administration – Permissible Exposure Limit</td>
</tr>
<tr>
<td>Prop 65</td>
<td>California Proposition 65</td>
</tr>
<tr>
<td>RCRA</td>
<td>US EPA, Resource Conservation and Recovery Act</td>
</tr>
<tr>
<td>RTECS</td>
<td>Registry of Toxic Effects of Chemical Substances</td>
</tr>
<tr>
<td>SARA</td>
<td>Superfund Amendments and Reauthorization Act</td>
</tr>
<tr>
<td>STEL</td>
<td>15-minute Short Term Exposure Limit</td>
</tr>
<tr>
<td>TSCA</td>
<td>Toxic Substance Control Act</td>
</tr>
<tr>
<td>TWA</td>
<td>8-hour Time Weighted Average</td>
</tr>
</tbody>
</table>

**MSDS Coordinator:** Hospira GEHS  
**Date Prepared:** 10/27/2011  
**Obsolete Date:** 10/21/2008

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