MATERIAL SAFETY DATA SHEET

Product Name: LEVOPHED (norepinephrine bitartrate) Injection, USP

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
LEVOPHED (norepinephrine bitartrate) Injection, USP

Synonyms
Levarterenol bitartrate; (-)-α-(aminomethyl)-3,4-dihydroxybenzyl alcohol tartrate (1:1) (salt) monohydrate; (-)-Norepinephrine bitartrate salt monohydrate; L-Noradrenaline bitartrate monohydrate.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
L-Norepinephrine Bitartrate Monohydrate

Chemical Formula
C₈H₁₁NO₃ • C₄H₆O₆ • H₂O

Preparation
Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium chloride and sodium metabisulfite.

<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>L-Norepinephrine Bitartrate Monohydrate</td>
<td>0.1</td>
<td>108341-18-0</td>
<td>NA</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>L-Norepinephrine Bitartrate Monohydrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview
LEVOPHED (norepinephrine bitartrate) Injection, USP is a solution containing norepinephrine bitartrate, a vasoconstrictor agent, and sodium metabisulfite, a preservative. In the workplace, this material should be considered possibly irritating to the skin, eyes and respiratory tract. The metabisulfite preservative may induce allergic reactions in people sensitive to sulfites. Possible target organs include the nervous system, cardiovascular system, respiratory system, and skin.

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 known from occupational exposure. This product contains sodium metabisulfite which may cause allergic-type reactions, including anaphylactic symptoms and/or life-threatening asthmatic episodes in susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown, but occurs more frequently in asthmatics than in non-asthmatics. In clinical use, adverse effects may include hypertension, bradycardia, restlessness,
palpitations, tremor, weakness, headache and elevated blood pressure. Overdosage can result in severe hypertension, bradycardia, increased peripheral resistance, decreased cardiac output and potentially fatal arrhythmias including ventricular tachycardia and fibrillation. Prolonged administration can result in depletion of plasma volume and electrolyte imbalance. Administration to pregnant women can cause fetal anoxia by provoking uterine contractions; therefore, the drug should not be used during pregnancy.

Medical Conditions Aggravated by Exposure
Pre-existing hypersensitivity to sulfites or related materials; concurrent therapy with monoamine oxidase inhibitors or related drugs. Pre-existing nervous system, cardiovascular system, respiratory system, or skin ailments.

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.

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.
Product Name: LEVOPHED (norepinephrine bitartrate) Injection, USP

Special Precautions

No special precautions required for hazard control.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>Exposure limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-Norepinephrine Bitartrate Monohydrate</td>
<td>Hospira EEL</td>
<td>mg/m3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>L-Norepinephrine Bitartrate Monohydrate</td>
<td>Hospira STEL</td>
<td>N/A</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, Colorless</td>
</tr>
<tr>
<td>Odor</td>
<td>None</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>3 - 4.5</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point</td>
<td>NA</td>
</tr>
<tr>
<td>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 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>
<tr>
<td>Specific Gravity:</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility:</td>
<td>Norepinephrine is sparingly soluble in water, very slightly soluble in alcohol and ether, and readily soluble in acids.</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature:</td>
<td>NA</td>
</tr>
</tbody>
</table>
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) and nitrogen oxides (NOx).

Hazardous Polymerization
Not anticipated to occur with this product.

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>
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</thead>
<tbody>
<tr>
<td>l-Norepinephrine bitartrate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>210</td>
<td>mcg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>l-Norepinephrine bitartrate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>1.03</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>l-Norepinephrine bitartrate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>26.8</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>l-Norepinephrine</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>20</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>l-Norepinephrine</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>550</td>
<td>mcg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>250</td>
<td>mcg/kg</td>
<td>Rabbit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td>mcg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>l-Norepinephrine</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>6</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>l-Norepinephrine</td>
<td>100</td>
<td>LD50</td>
<td>Subcutaneous</td>
<td>5</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
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</table>

Aspiration Hazard
None anticipated from normal handling of this product.

Dermal Irritation/Corrosion
None anticipated from normal handling of this product. However, inadvertent contact with this product may be irritating to mucous membranes.

Ocular Irritation/Corrosion
None anticipated from normal handling of this product. However, inadvertent contact of this product with eyes may produce irritation.

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product. However, this product contains sodium metabisulfite and may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes, in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown, but sulfite sensitivity occurs more frequently in asthmatic than in non-asthmatic people.

Reproductive Effects
No studies have been conducted in animals with norepinephrine bitartrate. However, administration to pregnant women can cause fetal anoxia by
Product Name: LEVOPHED (norepinephrine bitartrate) Injection, USP

provoking uterine contractions; therefore, the drug should not be used during pregnancy.

Mutagenicity Studies to evaluate the genotoxic potential of norepinephrine bitartrate have not been conducted.

Carcinogenicity Long-term studies in animals to evaluate the carcinogenic potential of norepinephrine bitartrate have not been conducted.

Target Organ Effects Based on clinical use, possible target organs include the nervous system, cardiovascular system, respiratory system, or skin.

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

ADR/ADG/DOT STATUS: Not regulated

IMDG STATUS: Not regulated

ICAO/IATA STATUS: Not regulated

Transport Comments: None

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>L-Norepinephrine Bitartrate Monohydrate</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 Target Organ Toxin

Classification Possible Irritant
Product Name: LEVOPHED (norepinephrine bitartrate) Injection, USP

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 L-Norepinephrine Bitartrate Monohydrate.

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases:
S23 - Do not breathe vapors.
S24 - Avoid contact with skin.
S25 - Avoid contact with eyes.
S37/39 - Wear suitable gloves and eye/face protection.
### 16. OTHER INFORMATION:

**Notes:**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</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>LD&lt;sub&gt;50&lt;/sub&gt;</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:** 10/13/2011  
**Obsolete Date:** 01/07/2008

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