

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 $C_8H_{11}NO_3 \bullet C_4H_6O_6 \bullet H_2O$

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

Component	Approximate Percent by Weight	CAS Number	RTECS Number
L-Norepinephrine Bitartrate Monohydrate	0.1	108341-18-0	NA

3. HAZARD INFORMATION

Carcinogen List

Substance	IARC	NTP	OSHA
L-Norepinephrine Bitartrate Monohydrate	Not Listed	Not Listed	Not Listed

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,

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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.
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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.
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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**Exposure Guidelines**

Component	Exposure limits				
	Type	mg/m3	ppm	µg/m3	Note
L-Norepinephrine Bitartrate Monohydrate	Hospira EEL	N/A	N/A	0.5	
L-Norepinephrine Bitartrate Monohydrate	Hospira STEL	N/A	N/A	5	

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	Liquid
Color	Clear, Colorless
Odor	None
Odor Threshold:	NA
pH:	3 - 4.5
Melting point/Freezing point:	NA
Initial Boiling Point/Boiling Point Range:	NA
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	NA
Vapor Pressure:	NA
Vapor Density:	NA
Specific Gravity:	NA
Solubility:	Norepinephrine is sparingly soluble in water, very slightly soluble in alcohol and ether, and readily soluble in acids.
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature:	NA

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

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
l-Norepinephrine bitartrate	100	LD50	Intravenous	210	mcg/kg	Rat
l-Norepinephrine bitartrate	100	LD50	Intravenous	1.03	mg/kg	Mouse
l-Norepinephrine bitartrate	100	LD50	Intraperitoneal	26.8	mg/kg	Mouse
l-Norepinephrine	100	LD50	Oral	20	mg/kg	Rat
l-Norepinephrine	100	LD50	Intravenous	550 250 100	mcg/kg mcg/kg mcg/kg	Mouse Rabbit Rat
l-Norepinephrine	100	LD50	Intraperitoneal	6	mg/kg	Mouse
l-Norepinephrine	100	LD50	Subcutaneous	5	mg/kg	Mouse

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

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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**

Substance	TSCA Status	CERCLA Status	SARA 302 Status	SARA 313 Status	PROP 65 Status
L-Norepinephrine Bitartrate Monohydrate	Not Listed	Not Listed	Not Listed	Not Listed	Not Listed

RCRA Status Not Listed
U.S. OSHA Classification Target Organ Toxin
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:

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
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS

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