MATERIAL SAFETY DATA SHEET

Product Name: NIPENT® (pentostatin for injection)

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address

Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

Hospira Australia Pty Ltd
1 Lexia Place
Mulgrave, VIC 3170
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Emergency Telephone

CHEMTREC: North America: 800-424-9300;
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Hospira, Inc., Non-Emergency

224-212-2000

Product Name

NIPENT® (pentostatin for injection)

Synonyms

(R)-3-(2-deoxy-β-D-erythro-pentofuranosyl)-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name

Pentostatin

Chemical Formula

$C_{11}H_{16}N_4O_4$

Preparation

Non-hazardous ingredients include: 50 mg of mannitol (1% after reconstitution). Hazardous ingredients present at less than 1% are: sodium hydroxide and/or hydrochloric acid, which are added to adjust the pH. Pentostatin approximate percent by weight after reconstitution is 0.2%.

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Pentostatin	17	53910-25-1	NI2931000

3. HAZARD INFORMATION

Carcinogen List

Substance	IARC	NTP	OSHA
Pentostatin	Not Listed	Not Listed	Not Listed

Emergency Overview

NIPENT® (pentostatin for injection) is a lyophilized powder containing pentostatin for reconstitution in single dose vials. Pentostatin is an anti-neoplastic agent that disrupts normal purine metabolism and DNA synthesis. It is a cytotoxic agent, and in the workplace should be considered potentially irritating to the eyes and respiratory tract, a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the bone marrow, central nervous system, cardiovascular system, gastrointestinal tract, liver, kidneys, lungs, skin, and the fetus.

Occupational Exposure Potential	There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known.
Signs and Symptoms	During occupational use, this product should be considered irritating to the eyes and respiratory tract. In clinical use, adverse effects have included myelosuppression, headache, diarrhea, nausea and vomiting, hepatotoxicity, central nervous system toxicity, impaired renal function, pulmonary toxicity (cough, dyspnea, and pneumonia), rashes, conjunctivitis, hair loss, joint and muscle pain, and cardiovascular disorders including arrhythmias, angina pectoris, and heart failure. Occasionally, hypersensitivity reactions have also been reported.
Medical Conditions Aggravated by Exposure	Pre-existing hypersensitivity to pentostatin. Pre-existing bone marrow, blood, gastrointestinal, cardiovascular, liver, kidney, skin, and lung ailments; or pregnancy.

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 product.
Fire & Explosion Hazard	None anticipated for this product.
Extinguishing media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal	Put on suitable protective clothing and equipment as specified by site spill procedures. For spilled powder, isolate the area around spill. Collect the spilled powder using techniques that minimize powder migration. Clean affected area with soap and water. Alternatively, a 10% solution of household bleach in water can be used to clean the affected spill areas. Dispose of materials according to the applicable federal, state, or local regulations. If a spill occurs after reconstitution, absorb liquid with suitable material and clean affected area with soap and water. A 10% solution of household bleach can be used to further clean the affected spill areas. Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Pentostatin, the active ingredient in NIPENT® (pentostatin for injection), is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastics agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements. Avoid ingestion, inhalation, skin contact, and eye contact. When handling the powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this material.

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. To maintain product integrity, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

Persons with known hypersensitivities to pentostatin, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure limits				
Component	**Type**	**mg/m3**	**ppm**	**µg/m3**	**Note**
Pentostatin	Not Applicable	N/A	N/A	N/A	None Established

Respiratory protection

Respiratory protection is normally not needed during intended product use. However, if the generation of dusts or 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 (N99 or equivalent) is recommended under conditions where airborne dust or 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

When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

Eye protection

As a minimum, the use of chemical safety goggles is recommended when handling this product.

Engineering Controls

When handling the dry powder, local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is recommended during reconstitution.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	Solid
Color	White to off-white solid
Odor	Odorless
Odor Threshold:	NA
pH:	After reconstitution, the pH is between 7.0 and 8.5
Melting point/Freezing point:	220 - 225^{o}C
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:	Freely soluble in water.
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) 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
Pentostatin	100	LD50	Oral	227	mg/kg	Mouse
Pentostatin	100	LD50	Intravenous	122	mg/kg	Mouse
Pentostatin	100	LD50	Intraperitoneal	72	mg/kg	Mouse

Aspiration Hazard None anticipated from normal handling of this product.

Dermal Irritation/Corrosion None anticipated from normal handling of this material. However, inadvertent skin contact may produce irritation with redness.

Ocular Irritation/Corrosion None anticipated from normal handling of this material. However, inadvertent eye contact may produce irritation with redness, tearing, and discomfort.

Dermal or Respiratory Sensitization None anticipated from normal handling of this material. Occasionally, hypersensitivity reactions have been reported during clinical use of this product.

Reproductive Effects *Fertility studies have not been conducted in animals; however, in a 5-day intravenous toxicity study in dogs, mild seminiferous tubular degeneration was reported at dosages of 1 and 4 mg/kg. Pentostatin was administered intravenously to pregnant rats at dosages of 0, 0.01, 0.1, or 0.75 mg/kg/day on days 6 through 15 of gestation. Maternal toxicity occurred at dosages of 0.1 and 0.75 mg/kg/day. Teratogenic effects (primarily increased incidences of various skeletal malformations) occurred at dosages of 0.75 mg/kg/day. Pentostatin was also teratogenic in mice when given as a single 2 mg/kg intraperitoneal injection on day 7 of gestation. Pentostatin was not teratogenic in rabbits when given intravenously at dosages of 0, 0.005, 0.01, or 0.02 mg/kg/day on days 6 through 18 of gestation; however, maternal toxicity, abortions, early deliveries, and deaths occurred in all drug-treated groups. *Abstracted from the Nipent® Package Insert

Mutagenicity *Pentostatin was nonmutagenic when tested in Salmonella typhimurium strains TA-98, TA-1535, TA-1537, and TA-1538, but exhibited a positive response trend in the TA-100 strain, with and without metabolic activation. Formulated pentostatin was clastogenic in an in vivo mouse bone marrow micronucleus assay at dosages of 20 mg/kg and above. Pentostatin was not mutagenic to V79 Chinese hamster lung cells, with or without metabolic activation

Carcinogenicity *The carcinogenic potential of pentostatin has not been fully evaluated in long-term animal studies. *Abstracted from the Nipent® Package Insert

Target Organ Effects This material should be considered irritating to the eyes and respiratory tract. Following an accidental over-exposure, possible target organs may include the bone marrow, central nervous system, cardiovascular system, gastrointestinal tract, liver, kidneys, skin, lungs, and the fetus.

12. ECOLOGICAL INFORMATION

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

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
Pentostatin	Not Listed	Not Listed	Not Listed	Not Listed	Listed

RCRA Status Not Listed

U.S. OSHA Classification
Possible Carcinogen
Target Organ Toxin
Reproductive 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 Pentostatin

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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:

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
Date Prepared: 10/27/2011
Obsolete Date: 02/23/2010

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