MATERIAL SAFETY DATA SHEET

Product Name: Bleomycin for Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

<table>
<thead>
<tr>
<th>Manufacturer Name And Address</th>
<th>Hospira, Inc.</th>
<th>Hospira Australia Pty Ltd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address</td>
<td>275 North Field Drive, Lake Forest, Illinois 60045, USA</td>
<td>1 Lexia Place, Mulgrave VIC 3170, AUSTRALIA</td>
</tr>
</tbody>
</table>

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

| Hospira, Inc., Non-Emergency | 224 212-2055 |

| Material Name | Bleomycin for Injection, USP |

| Synonyms | Blenoxane; Bleomycin A2, N1-[3-(dimethylsulfonio)propyl]-bleomycinamide; Bleomycin B2, N1-[4-(aminomimethyl)amino]butyl]-bleomycinamide. |

2. HAZARD INFORMATION / CLASSIFICATION

**Emergency Overview**

Bleomycin for Injection, USP is a lyophilized powder that contains bleomycin sulfate, a mixture of cytotoxic glycopeptide antibiotics produced by *Streptomyces verticillus*. Clinically, bleomycin sulfate is an antineoplastic antibiotic to treat certain types of cancers. It is a cytotoxic agent, and should be considered 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 lungs, liver, kidney, skin, cardiovascular system, 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 agents if workplace exposures are not properly controlled. The actual risk in the workplace is not known.

**Signs and Symptoms**

In the workplace, this product should be considered irritating to the skin, eyes, and respiratory tract. In clinical use, the most serious adverse effect is a delayed pulmonary toxicity. Interstitial pneumonitis occurs in about 10% of patients, and progresses to fibrosis and death in about 1% of patients. Other adverse effects may include rash, erythema, pruritus, vesiculation, hyperkeratosis, nail changes, alopecia, and hyperpigmentation. Fever is also a common occurrence. Acute anaphylactoid-like reactions with hyperpyrexia and cardiorespiratory distress/collapse have occurred in about 1% of patients.

**Medical Conditions Aggravated by Exposure**

Pre-existing hypersensitivity to bleomycin-like antibiotics. Pre-existing pulmonary, kidney, liver, skin, or cardiovascular ailments, or pregnancy.

**Carcinogen Lists:**

- IARC: Category 2B
- NTP: Not listed
- OSHA: Not listed

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Bleomycin Sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Formula</td>
<td>Mixture of A2 (C_{55}H_{84}N_{17}O_{21}S_{3}), B2 (C_{55}H_{84}N_{20}O_{21}S_{2})</td>
</tr>
</tbody>
</table>

<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>Bleomycin Sulfate</td>
<td>100</td>
<td>9041-93-4</td>
<td>EC5991990</td>
</tr>
</tbody>
</table>
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**
Not applicable.

**Fire & Explosion Hazard**
None anticipated for this material.

**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**
For spilled powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Collect the spilled powder using techniques that minimize powder migration. Clean affected area with soap and water. 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. Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

**Handling**
Bleomycin sulfate 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. 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.
Product Name: Bleomycin for Injection, USP

7. HANDLING AND STORAGE: continued

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

Persons with known allergies to bleomycin-like compounds, 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

<table>
<thead>
<tr>
<th>Component</th>
<th>OSHA-PEL</th>
<th>ACGIH-TLV</th>
<th>Hospira EEL</th>
<th>Other Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin Sulfate</td>
<td>8-hr TWA:</td>
<td>8-hr TWA:</td>
<td>8-hr TWA: 0.05</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Not Established</td>
<td>Not Established</td>
<td>mcg/m3</td>
<td></td>
</tr>
</tbody>
</table>

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
EEL: Employee Exposure Limit.
TWA: 8 hour Time Weighted Average.
STEL: 15-minute Short Term Exposure Limit.

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 material, 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 material.

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.
9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>A cream-colored, lyophilized powder in a vial.</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH</td>
<td>A 0.5% solution in water has a pH of 4.5 to 6.0.</td>
</tr>
<tr>
<td>Melting Point</td>
<td>158-160°F</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 Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Density (Air =1)</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate</td>
<td>NA</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in water or saline; slightly soluble in dehydrated alcohol;</td>
</tr>
<tr>
<td></td>
<td>practically insoluble in acetone.</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>NA</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>NA</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under standard use and storage conditions.</td>
</tr>
<tr>
<td>Hazardous Reactions</td>
<td>Not determined</td>
</tr>
<tr>
<td>Conditions to avoid</td>
<td>Not determined</td>
</tr>
<tr>
<td>Incompatibilities</td>
<td>Not determined</td>
</tr>
<tr>
<td>Hazardous Decomposition Products</td>
<td>Not determined. During thermal decomposition, it may be possible to</td>
</tr>
<tr>
<td></td>
<td>generate irritating vapors and/or toxic fumes of carbon oxides (COx),</td>
</tr>
<tr>
<td></td>
<td>nitrogen oxides (NOx), and sulfur oxides (SOx).</td>
</tr>
<tr>
<td>Hazardous Polymerization</td>
<td>Not anticipated to occur with this product.</td>
</tr>
</tbody>
</table>

11. TOXICOLOGICAL INFORMATION

<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>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt; 2000</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Bleomycin Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>210</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>53</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

LD50 is the dosage producing 50% mortality.
Product Name: Bleomycin for Injection, USP

11. TOXICOLOGICAL INFORMATION: continued

Acute Toxicity – continued

<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>Bleomycin Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>240</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Bleomycin Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>210</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>168</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>35</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Bleomycin Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Subcutaneous</td>
<td>86</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Bleomycin Sulfate</td>
<td>100</td>
<td>LD50</td>
<td>Subcutaneous</td>
<td>103</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Subcutaneous</td>
<td>168</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>100</td>
<td>LD50</td>
<td>Subcutaneous</td>
<td>188</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

LD50 is the dosage producing 50% mortality.

Aspiration Hazard
None anticipated from normal handling of this material.

Dermal Irritation/Corrosion
None anticipated from normal handling of this material. This material is anticipated to be irritating to the skin.

Ocular Irritation/Corrosion
None anticipated from normal handling of this material. This material is anticipated to be irritating to the eyes.

Dermal or Respiratory Sensitization
None anticipated from normal handling of this material. In clinical use, acute anaphylactoid-like reactions with hyperpyrexia and cardiorespiratory distress/collapse have occurred in about 1% of patients at clinical doses.

Reproductive Effects
The effects of bleomycin on fertility have not been fully evaluated. Bleomycin has been shown to be teratogenic in rats. Intraperitoneal administration to rats at a dosage of 1.5 mg/kg/day on days 6-15 of gestation caused skeletal malformations, and shortened innominate artery and hydronephrosis. Bleomycin is an abortifacient, but not teratogenic, in rabbits at an intravenous dosage of 1.2 mg/kg/day when given on gestation days 6-18.

Mutagenicity
Bleomycin has been shown to be mutagenic in a battery of in vitro and in vivo assays.

Carcinogenicity
In a study where bleomycin was administered to rats by subcutaneous injection at a dosage of 0.35 mg/kg weekly, a dose-related increase in injection site fibrosarcomas, as well as various renal tumors, was noted.

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

12. ECOLOGICAL INFORMATION

Aquatic Toxicity
Not available for product.

Persistence/ Biodegradability
Not determined

Bioaccumulation
Not determined

Mobility in Soil
Not determined

Notes:
13. DISPOSAL CONSIDERATIONS

**Waste Disposal**
Disposal should be performed in accordance with the federal, state or local regulatory requirements.

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

14. TRANSPORTATION INFORMATION

**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 Regulations

15. REGULATORY INFORMATION

**TSCA Status**
- Exempt

**CERCLA Status**
- Not listed

**SARA 302 Status**
- Not listed

**SARA 313 Status**
- Not listed

**RCRA Status**
- Not listed

**PROP 65 (Calif.)**
- Not listed


**U.S. OSHA Classification**
- Possible Skin Irritant
- Possible Eye Irritant
- Reproductive Toxin
- Target Organ Toxin
**Product Name:** Bleomycin for Injection, USP

### 15. REGULATORY INFORMATION: continued

<table>
<thead>
<tr>
<th>GHS Classification*</th>
<th>Acute Oral Toxicity</th>
<th>Eye Irritation</th>
<th>Skin Irritation</th>
<th>Toxic to Reproduction</th>
<th>Mutagenicity</th>
<th>Target Organ Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard Class</td>
<td>5</td>
<td>2B</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hazard Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Where medicinal products are not exempt, the recommended GHS workplace classification for this product is as follows:

<table>
<thead>
<tr>
<th>Symbol</th>
<th>NA</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal Word</td>
<td>Warning</td>
<td>Warning</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard Statement</th>
<th>May be harmful if swallowed</th>
<th>Causes eye irritation</th>
<th>Causes skin irritation</th>
<th>Suspected of damaging fertility or the unborn child</th>
<th>Suspected of causing genetic defects if ingested</th>
<th>May cause damage to the lungs, liver, kidney, skin, and the cardiovascular system through prolonged or repeated exposure.</th>
</tr>
</thead>
</table>

**GHS Precautionary Statements:**

**Prevention:**
- Do not eat, drink or smoke when using this product.
- Obtain special instructions before use.
- Do not handle until all safety precautions have been read and understood.
- Use personal protective equipment as required.
- Avoid breathing dust or vapors.
- In case of inadequate ventilation wear respiratory protection.
- Wear protective gloves.
- Wash hands thoroughly after handling.
- Contaminated work clothing should not be allowed out of the workplace.

**Response:**
- IF SWALLOWED: Call a POISON CENTER or doctor if you feel unwell.
- IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms call a POISON CENTER or a doctor.
- IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs, seek medical attention. Take off contaminated clothing and wash before reuse.
- 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.

If exposed or concerned, get medical attention.
EU Classification
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance bleomycin sulfate.

Classification(s):

<table>
<thead>
<tr>
<th>Type</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritant</td>
<td>Category 2</td>
</tr>
<tr>
<td>Mutagen</td>
<td>Category 2</td>
</tr>
<tr>
<td>Toxic for Reproduction</td>
<td>Category 2</td>
</tr>
<tr>
<td>Carcinogen</td>
<td>Category 3</td>
</tr>
</tbody>
</table>

Symbol:

Indication of Danger:

Xi  T  T  Xn

Risk Phrases:
- R36/37/38 - Irritating to eyes, respiratory system and skin
- R40 - Limited evidence of a carcinogenic effect
- R46 - May cause heritable genetic damage
- R48/25 - Danger of serious damage to health by prolonged exposure if swallowed
- R60 - May impair fertility
- R61 - May cause harm to the unborn child
- R64 - May cause harm to breastfed babies

Safety Phrases:
- S22: Do not breathe dust
- S24: Avoid contact with the skin;
- S36/37/39 Wear suitable protective clothing, 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
16. OTHER INFORMATION: continued

MSDS Coordinator: Global Occupational Toxicology
Date Prepared: August 14, 2008
Revision Date: November 9, 2009

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