MATERIAL SAFETY DATA SHEET

Product Name: Doxorubicin Hydrochloride For 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
Doxorubicin Hydrochloride For Injection, USP

Synonyms
Hydroxydaunorubicin hydrochloride; Adriamycin hydrochloride; 5,12-Naphthacenedione, (8S,10S)-10-[(3-amino-2,3,6-trideoxy-α-L-lyxohexopyranosyl)oxy]-8-glycoloyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-5,12-naphthacenedione hydrochloride.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Doxorubicin Hydrochloride

Chemical Formula
C_{27}H_{29}NO_{11} \cdot HCl

Preparation
Non-hazardous ingredients include lactose (about 84%).

<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>Doxorubicin Hydrochloride</td>
<td>16</td>
<td>25316-40-9</td>
<td>QI9295900</td>
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</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>Doxorubicin Hydrochloride</td>
<td>2A</td>
<td>REASONABLY ANTICIPATED</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview
Doxorubicin Hydrochloride For Injection, USP is a powder containing doxorubicin hydrochloride, an antineoplastic anthracycline antibiotic similar to daunorubicin and epirubicin. Clinically, it is used to treat some types of cancers. It is a cytotoxic agent, and in the workplace should be considered a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Based on clinical use, possible target organs may include the bone marrow, cardiovascular system, immune system, gastrointestinal tract, 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. Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact.
**Product Name: Doxorubicin Hydrochloride For Injection, USP**

**Signs and Symptoms**

During occupational use, this material should be considered irritating to the skin, eyes, and respiratory tract. In clinical use, doxorubicin hydrochloride is very irritating, sometimes producing thrombophlebitis and streaking of the skin over the vein used for injection. Doxorubicin produces bone-marrow depression; white cell counts reach a nadir 10 to 15 days after a dose and usually recover by about 21 days. Doxorubicin also produces cardiac toxicity. Toxicity may be acute (and usually transient) and is characterized by disturbances of cardiac function, marked by ECG abnormalities and, sometimes, arrhythmias. However, more severe cardiac toxicity (e.g., irreversible congestive heart failure) may also be delayed, and sometimes fatal. Gastrointestinal toxicity may include moderate to severe nausea and vomiting, stomatitis, and esophagitis (which may progress to ulceration). More rarely, facial flushing, conjunctivitis, and lachrymation may occur. Alopecia occurs in the majority of patients. Urine may be colored red as well. Occasional hypersensitivity reactions may also occur. Hyperuricemia may occur and is thought to be due to tumor lysis syndrome. Oligospermia or azoospermia have occurred in men treated with doxorubicin, mainly in combination therapies. This effect may be permanent. However, sperm counts have been reported to return to normal levels in some instances.

**Medical Conditions Aggravated by Exposure**

Pre-existing hypersensitivity to doxorubicin hydrochloride. Pre-existing bone marrow, blood, gastrointestinal, cardiovascular, or skin 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. However, many organic powders will combust at high temperatures.

**Fire & Explosion Hazard**

None anticipated for this product. Avoid the creation of dusty environments.

**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
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soap and water. Additionally, a 5% 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. Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Doxorubicin Hydrochloride 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. 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. Persons with known hypersensitivities to doxorubicin hydrochloride, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling open containers of this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

<table>
<thead>
<tr>
<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>Doxorubicin Hydrochloride</td>
<td>Not Applicable</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 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 concentrations are not expected to be excessive. Since protection provided by air purifying respirators is limited, a powered air purifying respirator or supplied air should be considered during an uncontrolled release event if exposure levels are not known, or during events where air-purifying respirators may not provide adequate protection. 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 also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Solid</td>
</tr>
<tr>
<td>Color</td>
<td>Lyophilized red powder or plug</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>(4.0 - 5.5) for 5 mg/mL solution</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>204-205°C</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point</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>
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<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>
<tr>
<td>Specific Gravity:</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility:</td>
<td>Soluble in water and dilute alcohols</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

Reactivity Not determined.

Chemical Stability Doxorubicin hydrochloride is sensitive to light and heat.

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.

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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<tbody>
<tr>
<td>Doxorubicin Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>570-698</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Doxorubicin Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>12.5</td>
<td>mg/kg</td>
<td>Rat</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2-12.5, 21.1</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.98</td>
<td>mg/kg</td>
<td>Rabbit</td>
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<tr>
<td>Doxorubicin Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>16</td>
<td>mg/kg</td>
<td>Rat</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.6-11.2</td>
<td>mg/kg</td>
<td>Mouse</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. However, inadvertent contact of this product with skin may produce irritation.

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

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product. However, in clinical use, hypersensitivity reactions have been occasionally reported in patients.

Reproductive Effects
Doxorubicin produced mild to moderate ovarian and testicular atrophy in mice after a single dosage of 36 mg/kg. Decreased testicular weights and hypospermia were present in rats after repeat dosages ≥ 0.25 mg/kg/day. Diffuse degeneration of the seminiferous tubules and a marked decrease in spermatogenesis were noted in dogs after repeat dosages of 1 mg/kg/day. Doxorubicin decreased fertility in female rats at the dosages of 0.05 and 0.2 mg/kg/day when administered from 14 days before mating through late gestation period. A single intravenous dosage of doxorubicin at 0.1 mg/kg was toxic to male reproductive organs producing testicular atrophy and oligospermia in rats. Doxorubicin was embryotoxic at dosages of 1 mg/kg/day in rats and is embryotoxic and abortifacent at a dosage of 0.5 mg/kg/day in rabbits. Embryotoxicity was characterized by increased embryo-fetal deaths and reduced live litter sizes. Oligospermia or azoospermia have occurred in men treated with doxorubicin, mainly in combination therapies. This effect may be permanent. However, in some cases, sperm counts have been reported to return to normal levels, sometimes several years after the end of the therapy.

Mutagenicity
Doxorubicin was mutagenic as it induced DNA damage in rabbit spermatozoa and dominant lethal mutations in mice. Doxorubicin was mutagenic in the in vitro Ames assay, and clastogenic in multiple in vitro assays (CHO cell, V79 hamster cell, human lymphoblast, and SCE assays) and the in vivo mouse micronucleus assay.

Carcinogenicity
Doxorubicin has been shown to be carcinogenic in the rat. The drug caused the appearance of breast fibroadenomas after a single IV dose of 8.0 mg/kg at an average of 33 weeks in 6 of 25 animals. Another animal developed a breast adenocarcinoma. Secondary leukemia, with or without a preleukemic phase, has been reported in patients treated with topoisomerase-II inhibitors including the anthracyclines such as doxorubicin. Secondary leukemia is more common when anthracyclines are given in combination with DNA-damaging
antineoplastic agents (0.5%) and/or in combination with radiotherapy (2.5 %) with a risk estimated at 1.5% at 10 years. Secondary leukemia can have a 1-3 year latency period, and can occur as late as 10 years following treatment.

Target Organ Effects

This material should be considered irritating to the skin, eyes, and respiratory tract. Based on clinical use, possible target organs may include the bone marrow, cardiovascular system, immune system, gastrointestinal tract, skin, and the fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product. EC50(16 hr) > 1000 mg/L in Pseudomonas putida for doxorubicin EC50(96 hr) = 13 mg/L in Pseudokirchneriella subcapitata for doxorubicin

EC50(48hr) = 2 mg/L in Daphnia magna for doxorubicin

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>
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<tbody>
<tr>
<td>Doxorubicin Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Listed</td>
</tr>
</tbody>
</table>

RCRA Status

Not Listed

U.S. OSHA Classification

Possible Carcinogen

Target Organ Toxin

Reproductive Toxin

Possible Irritant
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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 Doxorubicin Hydrochloride.

Classification(s):
Not Applicable

Symbol:
Not Applicable

Indication of Danger:
Not Applicable

Risk Phrases:
Not Applicable

Safety Phrases:
S23 - Do not breathe vapor.
S24/25 - Avoid contact with skin and 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
LD50 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
Product Name: Doxorubicin Hydrochloride For Injection, USP

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: 09/16/2011
Obsolete Date: 06/30/2009

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