SAFETY DATA SHEET

Product Name: Doxorubicin Hydrochloride For Injection, USP

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Name And Address	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA
Emergency Telephone	CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia - 61-290372994; UK - 44-870-8200418
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-methyoxy-5,12-naphthacenedione hydrochloride.

2. HAZARD(S) IDENTIFICATION

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 potentially corrosive/irritating to eyes and skin, a potential occupational reproductive hazard and a potential human carcinogen. Based on clinical use, possible target organs may include the bone marrow, cardiovascular system, immune system, and gastrointestinal tract.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Not Classified	Not Classified

Health Hazards	**Hazard Class**	**Hazard Category**
	Eye Damage/Irritation	1
	Skin Corrosion/Irritation	2
	Toxic to Reproduction	2
	Germ Cell Mutagenicity	2
	Carcinogenicity	2
	STOT – RE	2

Label Element(s)

Pictogram

Signal Word

Danger

Hazard Statement(s)

Causes serious eye damage
Causes skin irritation
Suspected of damaging fertility or the unborn child
Suspected of causing genetic defects
Suspected of causing cancer
May cause damage to organs through prolonged or repeated exposures

2. HAZARD(s) IDENTIFICATION: continued

Precautionary Statement(s)

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Do not breathe dust, vapor or spray
Wash hands thoroughly after handling
Wear protective gloves/eye protection/face protection

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a doctor.

IF ON SKIN (OR HAIR): Take off immediately all contaminated clothing. Rinse skin with water/shower. Wash contaminated clothing before reuse. If skin irritation occurs: Get medical advice/attention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name	Doxorubicin Hydrochloride	Lactic Acid
Chemical Formula	$C_{27}H_{29}NO_{11} \bullet HCl$	$C_3H_6O_3$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Doxorubicin Hydrochloride	16	25316-40-9	QI9295900
Lactic Acid	84	51-21-5	OD2800000

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 elevated 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 such as carbon dioxide, dry chemical extinguishing powder or foam.

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

For spilled powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Collect the spilled powder using techniques that minimize powder migration. Clean affected area with 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

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Doxorubicin Hydrochloride	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established
Lactic Acid	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8-hour Time Weighted Average.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION: continued

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 also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A sterile lyophilized red powder or plug
Odor	Odorless
Odor Threshold	NA
pH	The pH of a 5 mg/mL solution is between 4.0 and 5.5
Melting point/Freezing Point	204-205^{o}C
Initial Boiling Point/Boiling Point Range	NA
Flash Point	NA
Evaporation Rate	NA
Flammability (solid, gas)	NA
Upper/Lower Flammability or Explosive Limits	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Relative Density	NA
Solubility	Soluble in water and dilute alcohols
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	NA

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 active ingredient is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Doxorubicin Hydrochloride	100	LD50	Oral	570, 698	mg/kg	Mouse
Doxorubicin Hydrochloride	100	LD50	Intravenous	12.5 1.24, 12.5, 21.1 5.98	mg/kg mg/kg mg/kg	Rat Mouse Rabbit
Doxorubicin Hydrochloride	100	LD50	Intraperitoneal	16 4.6-11.2	mg/kg mg/kg	Rat Mouse
Lactic Acid	100	LD50	Oral	3543 4875 1810	mg/kg mg/kg mg/kg	Rat Mouse Guinea Pig
Lactic Acid	100	LD50	Dermal	>2000	mg/kg	Rabbit

LD50 is the dosage producing 50% mortality.

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 dust and aerosol generation, and skin contact.

Signs and Symptoms None anticipated from normal handling of this product. This material should be considered severely irritating to the skin and respiratory tract, and irritating/corrosive to eyes. 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.

11. TOXICOLOGICAL INFORMATION: continued

Aspiration Hazard	None anticipated from normal handling of this product.
Dermal Irritation/Corrosion	None anticipated from normal handling of this product. Lactic acid was moderately to severely irritating in a skin irritation study in animals. Inadvertent contact of this product with skin may produce irritation.
Ocular Irritation/Corrosion	None anticipated from normal handling of this product. Lactic acid was severely irritating/corrosive in an eye irritation study in animals. Inadvertent contact of this product with eyes may produce severe irritation with redness, tearing and possibly eye damage.
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	None anticipated from normal handling of this product. 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. Doxorubiciin was embryotoxic at dosages of 1 mg/kg/day in rats and is embryotoxic and abortifacient 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.
Carcinogen Lists	**IARC:** Group 2A **NTP:** Reasonably Anticipated **OSHA:** Not listed
Specific Target Organ Toxicity – Single Exposure	NA
Specific Target Organ Toxicity – Repeat Exposure	Based on clinical use, possible target organs may include the bone marrow, cardiovascular system, immune system, and gastrointestinal tract.

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.

Notes:
1. LC50: Concentration in water that produces 50% mortality in fish.
2. EC50: Concentration in water that produces 50% inhibition of growth in algae.

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
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

US TSCA Status	Exempt.
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US PROP 65 (Calif.)	This product is, or contains a chemical(s) known to the State of California to cause cancer and to cause developmental toxicity.

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

GHS/CLP 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	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Do not breathe dust, vapor or spray
Wash hands thoroughly after handling
Wear protective gloves/eye protection/face protection
Avoid release into the environment. Collect spillage

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a doctor.

IF ON SKIN (OR HAIR): Take off immediately all contaminated clothing. Rinse skin with water/shower. Wash contaminated clothing before reuse. If skin irritation occurs: Get medical advice/attention.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.

Classification(s)	NA
Symbol	NA
Indication of Danger	NA
Risk Phrases	NA
Safety Phrases	S23: Do not breathe dust/vapor/spray S24: Avoid contact with the skin S25: Avoid contact with eyes S37/39 Wear suitable gloves and eye/face protection S61: Avoid release into the environment

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
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS
Date Prepared: October 18, 2012
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