SAFETY DATA SHEET

Product Name: Mitoxantrone Injection, USP (Concentrate)

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Names And Addresses	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA	Hospira Australia Pty Ltd 1 Lexia Place Mulgrave VIC 3170 AUSTRALIA
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	Mitoxantrone Injection, USP (Concentrate)	
Synonyms	1, 4-dihydroxy-5, 8-bis[[2-[(2-hydroxyethyl) amino]ethyl]amino]-9,10-anthracenedione dihydrochloride.	

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Mitoxantrone Injection, USP (Concentrate) is a solution containing mitoxantrone hydrochloride, an anthracenedione antibiotic structurally and pharmacologically related to doxorubicin. Mechanistically, it intercalates into and crosslinks DNA, disrupting DNA and RNA replication. It also binds to topoisomerase II, resulting in DNA strand breaks and inhibition of DNA repair. Clinically, it is used to treat multiple sclerosis and adult acute myeloid leukemias, hormone-refractory prostate cancer, liver cancer, and ovarian cancer. It is a cytotoxic agent, and in the workplace should be considered a potential occupational reproductive hazard and a potential carcinogen. Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, cardiovascular system, lungs, liver, and skin.

U.S. OSHA GHS Classification

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

Health Hazards	**Hazard Class**	**Hazard Category**
	Toxic to Reproduction	2
	Carcinogenicity	2

Label Element(s)

Pictogram

Signal Word Warning

Hazard Statement(s)

Suspected of damaging fertility or the unborn child
Suspected of causing cancer

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
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

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. If eye irritation persists, get medical attention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Mitoxantrone Hydrochloride
Chemical Formula $C_{22}H_{28}N_4O_6 \bullet 2\ HCl$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Mitoxantrone Hydrochloride	0.2	70476-82-3	CB0386900

Non-hazardous ingredients include Water for Injection. Hazardous ingredients present at less than 1% include sodium chloride and sodium acetate; acetic acid may be added to adjust the pH.

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 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

Isolate area around the spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the spilled liquid with a suitable material, and clean the affected area with soap and water. Additionally, application of a 50% solution of household bleach (in water) for 10 minutes can be used to further decontaminate the affected spill area. Use care to avoid splashing when applying the bleach solution. Absorb the bleach using a suitable material, and clean again with soap and water. Dispose of all spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Mitoxantrone hydrochloride is a cytotoxic anti-neoplastic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic anti-neoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic anti-neoplastic 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. 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 product.

Storage

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

Special Precautions

Persons with known hypersensitivities to mitoxantrone 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 this product.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Mitoxantrone Hydrochloride	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.

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 (N99 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.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION: continued

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	Local exhaust ventilation may be used 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

Appearance/Physical State	A sterile, non-pyrogenic, dark blue aqueous solution
Odor	NA
Odor Threshold	NA
pH	3.0 to 4.5
Melting point/Freezing Point	NA
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	Sparingly soluble in water; practically insoluble in acetone, in acetonitrile, and in chloroform; slightly soluble in methyl alcohol
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	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), nitrogen oxides (NOx), and hydrogen chloride.
Hazardous Polymerization	Not anticipated to occur with this product.

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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
Mitoxantrone Hydrochloride	100	LD50	Oral	682 502	mg/kg mg/kg	Rat Mouse
Mitoxantrone Hydrochloride	100	LD50	Intravenous	4.8 9.7 0.38	mg/kg mg/kg mg/kg	Rat Mouse Dog
Mitoxantrone Hydrochloride	100	LD50	Dermal	125 1640	mg/kg mg/kg	Rabbit Rat

LD50 is the dosage producing 50% mortality.

Occupational Exposure Potential

Information on the absorption of this product via inhalation or skin contact is not available. 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. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms

None anticipated from normal handling of this product. This product should be considered irritating to the skin, eyes and respiratory tract. In clinical use, mitoxantrone may produce bone marrow suppression, hepatotoxicity, nausea, vomiting and diarrhea; headaches and seizures, alopecia, menstrual disorders including amenorrhea, upper respiratory tract infections, urinary tract infections, stomatitis, arrhythmias, diarrhea, and abnormal urines. Use of mitoxantrone has also been associated with interstitial pneumonitis and cardiotoxicity. Congestive heart failure (potentially fatal) can occur either during therapy, or months to years after therapy; the risk of cardiotoxicity increases with cumulative dose/prolonged administration. Extravasation can result in tissue necrosis with resultant need for debridement and skin grafting. Phlebitis has also been reported at the site of the infusion. Secondary acute myelogenous leukemia (AML) has been reported in patients treated with mitoxantrone.

Aspiration Hazard

None anticipated from normal handling of this product.

Dermal Irritation/ Corrosion

None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with redness and discomfort.

Ocular Irritation/ Corrosion

None anticipated from normal handling of this product. However, inadvertent eye contact of this product with eyes may produce irritation with stinging, redness, tearing and discomfort.

Dermal or Respiratory Sensitization

None anticipated from normal handling of this product. In clinical use, hypotension, urticaria, dyspnea, and rashes have been reported occasionally. Anaphylaxis/ anaphylactoid reactions have been reported rarely.

Reproductive Effects

None anticipated from normal handling of this product. Administration of mitoxantrone to pregnant rats during organogenesis was associated with fetal growth retardation at dosages >= 0.1 mg/kg/day. When pregnant rabbits were treated during organogenesis, an increased incidence of premature delivery was observed at dosages >= 0.1 mg/kg/day. No teratogenic effects were noted in these studies, but the maximum dosages tested were well below the recommended human dose.

Mutagenicity

Mitoxantrone was clastogenic in the *in vivo* rat bone marrow assay, and also in two *in vitro* assays; it induced DNA damage in primary rat hepatocytes and sister chromatid exchanges in Chinese hamster ovary cells. Mitoxantrone was mutagenic in bacterial and mammalian test systems (Ames/Salmonella and E. coli and L5178Y TK+/-mouse lymphoma).

11. TOXICOLOGICAL INFORMATION: continued

Carcinogenicity

Treatment of rats and mice with mitoxantrone intravenously once every 21 days for 24 months produced an increased incidence of fibroma and external auditory canal tumors in rats at a dosage of 0.03 mg/kg, and hepatocellular adenoma in male mice at a dosage of 0.1 mg/kg. Intravenous treatment of rats, once every 21 days for 12 months with mitoxantrone resulted in an increased incidence of external auditory canal tumors in rats at a dosage of 0.3 mg/kg.

Clinically, secondary acute myelogenous leukemia (AML) has been reported in multiple sclerosis and cancer patients treated with mitoxantrone. In general, one study suggests that the cumulative probability of developing secondary leukemia is about 2.2% at 4 years.

Carcinogen Lists

IARC: Group 2B – possibly carcinogenic to humans

NTP: Not listed

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, gastro-intestinal system, nervous system, cardiovascular system, lungs, liver, and skin.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product. For the active ingredient:

IC_{100} = 10 mg/ml in a growth inhibition assay in P. putida.

Persistence/Biodegradability

Not determined for product. Mitoxantrone was not biodegradable in a 28-day Ready biodegradation assay.

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 containers 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 chemical(s) known to the State of California 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
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

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. If eye irritation persists, get medical 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 vapor/spray S24: Avoid contact with the skin S25: Avoid contact with eyes S37/39 Wear suitable gloves and eye/face protection.

16. OTHER INFORMATION

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
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