



## MATERIAL SAFETY DATA SHEET

**Product Name: Mitoxantrone Injection, USP (Concentrate)**

### 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  
Australia

**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** Mitoxantrone Injection, USP (Concentrate)

**Synonyms** 1, 4-dihydroxy-5, 8-bis[[2-[(2-hydroxyethyl) amino]ethyl]amino]-9,10-anthracenedione dihydrochloride

### 2. COMPOSITION/INFORMATION ON INGREDIENTS

**Active Ingredient Name** Mitoxantrone Hydrochloride

**Chemical Formula**  $C_{22}H_{28}N_4O_6 \cdot 2 HCl$

**Preparation** 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.

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

### 3. HAZARD INFORMATION

#### Carcinogen List

Substance	IARC	NTP	OSHA
Mitoxantrone Hydrochloride	2B – possibly carcinogenic to humans	Not Listed	Not Listed

**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 cross links 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 leukemia's, 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, harmful to the fetus, and a potential human carcinogen. Based on clinical

## Product Name: Mitoxantrone Injection, USP (Concentrate)



use, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, cardiovascular system, lungs, liver, skin, and the fetus.

<b>Occupational Exposure Potential</b>	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.
<b>Signs and Symptoms</b>	None known from occupational exposure. 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.
<b>Medical Conditions Aggravated by Exposure</b>	Pre-existing hypersensitivity to mitoxantrone HCl. Pre-existing bone marrow, cardiovascular, gastrointestinal, central nervous system, pulmonary, liver, or skin ailments; or pregnancy.

### 4. FIRST AID MEASURES

<b>Eye contact</b>	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.
<b>Skin contact</b>	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.
<b>Inhalation</b>	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
<b>Ingestion</b>	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

### 5. FIRE FIGHTING MEASURES

<b>Flammability</b>	None anticipated for this aqueous product.
<b>Fire &amp; Explosion Hazard</b>	None anticipated for this aqueous product.
<b>Extinguishing media</b>	As with any fire, use extinguishing media appropriate for primary cause of fire.
<b>Special Fire Fighting Procedures</b>	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** Isolate area around the spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb the spilled liquid with a suitable material, then 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, then 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.

**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 this product.

## 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### Exposure Guidelines

Component	Type	Exposure limits			
		mg/m <sup>3</sup>	ppm	µg/m <sup>3</sup>	Note
Mitoxantrone Hydrochloride	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 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.

**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.

## Product Name: Mitoxantrone Injection, USP (Concentrate)



<b>Eye protection</b>	As a minimum, the use of chemical safety goggles is recommended when handling this product.
<b>Engineering Controls</b>	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

<b>Appearance/Physical State</b>	Liquid
<b>Color</b>	Sterile, non-pyrogenic, dark blue aqueous solution
<b>Odor</b>	None
<b>Odor Threshold:</b>	NA
<b>pH:</b>	3.0 to 4.5
<b>Melting point/Freezing point:</b>	NA
<b>Initial Boiling Point/Boiling Point Range:</b>	NA
<b>Evaporation Rate:</b>	NA
<b>Flammability (solid, gas):</b>	NA
<b>Upper/Lower Flammability or Explosive Limits:</b>	NA
<b>Vapor Pressure:</b>	NA
<b>Vapor Density:</b>	NA
<b>Specific Gravity:</b>	NA
<b>Solubility:</b>	Sparsely soluble in water; practically insoluble in acetone, in acetonitrile, and in chloroform; slightly soluble in methyl alcohol.
<b>Partition coefficient: n-octanol/water:</b>	NA
<b>Auto-ignition temperature:</b>	NA
<b>Decomposition temperature:</b>	NA

### 10. STABILITY AND REACTIVITY

<b>Reactivity</b>	Not determined.
<b>Chemical Stability</b>	Stable under standard use and storage conditions.
<b>Hazardous Reactions</b>	Not determined.
<b>Conditions to avoid</b>	Not determined.
<b>Incompatibilities</b>	Not determined.
<b>Hazardous decomposition products</b>	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.
<b>Hazardous Polymerization</b>	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:

<b>Ingredient(s)</b>	<b>Percent</b>	<b>Test Type</b>	<b>Route of Administration</b>	<b>Value</b>	<b>Units</b>	<b>Species</b>
Mitoxantrone Hydrochloride	100	LD50	Oral	682	mg/kg	Rat
				502	mg/kg	Mouse
Mitoxantrone Hydrochloride	100	LD50	Intravenous	4.8	mg/kg	Rat
				9.7	mg/kg	Mouse
				0.38	mg/kg	Dog
Mitoxantrone Hydrochloride	100	LD50	Dermal	125	mg/kg	Rabbit
				1640	mg/kg	Rat

**Aspiration Hazard**

None anticipated from normal handling of this material.

**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**

Administration of mitoxantrone to pregnant rats during organogenesis was associated with fetal growth retardation at dosages  $\geq 0.1$  mg/kg/day. When pregnant rabbits were treated during organogenesis, an increased incidence of premature delivery was observed at dosages  $\geq 0.1$  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).

**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.

**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 bone marrow, gastrointestinal system, central nervous system,

**Product Name: Mitoxantrone Injection, USP (Concentrate)**



cardiovascular system, lungs, liver, skin, and the fetus.

**12. ECOLOGICAL INFORMATION**

**Aquatic Toxicity** Not determined for product. For the active ingredient: IC100 = 10 mg/ml in a growth inhibition assay in *P. putida*.

**Persistence/Biodegradability** Mitoxantrone was not biodegradable in a 28-day Ready biodegradation assay.

**Bioaccumulation** Not determined for product

**Mobility in Soil** Not determined.

**13. DISPOSAL CONSIDERATIONS**

**Waste Disposal** All waste materials must be properly characterized. 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

**IMDG STATUS:** Not regulated

**ICAO/IATA STATUS:** Not regulated

**15. REGULATORY INFORMATION**

**USA Regulations**

Substance	TSCA Status	CERCLA Status	SARA 302 Status	SARA 313 Status	PROP 65 Status
Mitoxantrone Hydrochloride	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

## Product Name: Mitoxantrone Injection, USP (Concentrate)



**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 Mitoxantrone 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 - 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
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
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: 10/19/2012

Obsolete Date: 10/26/2011

**Product Name: Mitoxantrone Injection, USP (Concentrate)**

**Disclaimer:**

The information and recommendations contained herein are based upon tests believed to be reliable. However, Hospira does not guarantee their accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage may be required. Hospira assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.