

Mitoxantrone for Injection Concentrate

1. PRODUCT IDENTIFICATION

Product Name Mitoxantrone for Injection Concentrate
Product Use Medical Treatment; Antineoplastic
Manufacturer SICOR Pharmaceuticals, Inc.
Address 19 Hughes
Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
1-202-483-7617 (International Collect)

Business Phone 1-800-729-9991
Website Address <http://www.sicorinc.com>

Common Names Novantrone®
Chemical Name 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]-9,10-anthracenedione dihydrochloride
Chemical Formula C₂₂H₂₈N₄O₆ · 2HCl
Chemical Family Synthetic antineoplastic anthracenedione
How Supplied 10mL solution in a 10mL clear glass vial
12.5mL solution in a 20mL clear glass vial
15mL solution in a 20mL clear glass vial
(1.165 mg/mL Mitoxantrone Hydrochloride is equivalent to 1 mg/mL Mitoxantrone free base)

Date of Preparation: December 12, 2003

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	Wt%	EXPOSURE LIMITS IN AIR				
			ACGIH		OSHA		Other
			TLV	STEL	PEL	STEL	
Mitoxantrone Hydrochloride	65271-80-9	0.2 free base	NE	NE	NE	NE	NE
Sodium Acetate	127-09-3	0.005	NE	NE	NE	NE	NE
Acetic Acid	64-19-7	0.046	10 ppm	15 ppm	10 ppm	NE	NE
Sodium Chloride	7647-14-5	0.8	NE	NE	NE	NE	NE
Water (for injection)	7732-18-5	Balance	NE	NE	NE	NE	NE

NE - Not Established

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 – 1998 format
 CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is a clear, dark blue, odorless liquid. Harmful if swallowed or absorbed through the skin. Overexposure may be harmful to the blood, bone marrow and cardiovascular system. Reproductive and developmental toxicant. Avoid exposure during pregnancy. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling.

Mitoxantrone for Injection Concentrate

3. HAZARD IDENTIFICATION cont.

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness and swelling of the eyes and redness and a burning sensation on the skin. Extravasation at the infusion site has been reported, which may result in erythema, swelling, pain, burning and/or blue discoloration of the skin. This can result in tissue necrosis. Phlebitis has also been reported at the site of the infusion.

Ingestion: Ingestion is not an anticipated route of occupational exposure. However, the active ingredient, Mitoxantrone Hydrochloride is moderately toxic if ingested. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, therapeutic effects including changes in the heart, blood and bone marrow, nausea, vomiting, and diarrhea, may occur. See package insert for other adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as diarrhea, nausea, vomiting, decreases in white blood cell count, increased susceptibility to infection, and occasionally hypersensitivity reactions (anaphylaxis) may occur.

Cancer: Mitoxantrone Hydrochloride has demonstrated carcinogenic effects in laboratory animals (see Section 11). It has also been reported to cause secondary leukemias in cancer and multiple sclerosis patients treated at clinical doses.

Chronic: Based on animal data, Mitoxantrone Hydrochloride, the active ingredient, is considered a potential reproductive and developmental toxicant (see Section 11).

Pre-Existing Medical Conditions: Pre-existing cardiovascular and immune system disorders may be aggravated by exposure to this material.

Mitoxantrone for Injection Concentrate

4. FIRST-AID MEASURES

Skin Exposure: Remove contaminated shoes and clothing and cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: If irritation or redness develops, move victim away from exposure and into fresh air. Flush eyes with clean water and seek medical attention.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Victims of chemical exposure must be taken for medical attention. Take a copy of the MSDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians Desk Reference for additional treatment information.

5. FIRE-FIGHTING MEASURES

Flash Point: Non-flammable Autoignition Temperature: Not applicable

Flammable Limits (in air by volume, %): Lower: Not applicable Upper: Not applicable

Fire Extinguishing Equipment: Use extinguishing agent suitable for type of surrounding fire.

Water Spray: OK Carbon Dioxide: OK Halon: OK
Foam: OK Dry Chemical: OK Other: Any "ABC" Class

Unusual Fire and Explosion Hazards: No unusual fire or explosion hazards are expected.

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

Special Fire Fighting Procedures: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.

NFPA HAZARD CLASS: Health: 2 (Moderate)
 Flammability: 0 (Least)
 Reactivity: 0 (Least)

Mitoxantrone for Injection Concentrate

6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

7. HANDLING and STORAGE

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from sources of ignition and any incompatible materials or conditions (see Section 10). Store at room temperature 15-25°C (59-77°F). Do not freeze.

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.

Mitoxantrone for Injection Concentrate

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances 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 warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	ND	Evaporation Rate (n-BuAc=1):	ND
Specific Gravity (water = 1):	0.996	Melting/Freezing Point:	0°C (32°F)
Solubility in Water:	~5-10mg/mL	Boiling Point:	100°C
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	3.0-4.5
Odor Threshold: ND			
Appearance and Color: Clear, dark blue liquid			

ND = No Data

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Oxides of carbon and nitrogen and hydrogen chloride.

Mitoxantrone for Injection Concentrate

11. TOXICOLOGICAL INFORMATION

Toxicity Data: The following information is for Mitoxantrone Hydrochloride, the active ingredient

IV LD50(rat) = 4800 ug/kg	Oral LD50(rat) = 682 mg/kg	IP LD50(rat) = 8mg/kg
IV LD50(mouse) = 9700 ug/kg	Oral LD50(mouse) = 502 mg/kg	IP LD50(mouse) = 15560 ug/kg
IV LD50(dog) = 375 ug/kg	SubQ LD50(rat) = 5500 ug/kg	IP LD50(dog) = >1200 ug/kg
IV LD50 (monkey) >1 mg/kg	SubQ LD50 (mouse) = 19700 ug/kg	Skin LD50(rat) = 1640 mg/kg
		Skin LD50(rabbit) = 125 mg/kg

Carcinogenicity: Positive in laboratory animals. Intravenous treatment of rats and mice, once every 21 days for 24 months, resulted in an increased incidence of fibroma and external auditory canal tumors in rats at a dose of 0.03 mg/kg and hepatocellular adenoma in male mice at a dose of 0.1 mg/kg. Intravenous treatment of rats, once every 21 days in rats

Mitoxantrone Hydrochloride has also reported to cause secondary leukemia's in cancer and multiple sclerosis patients treated at clinical doses. It is listed as carcinogenic by IARC.

Irritancy of Product: This product is expected to be irritating to contaminated skin, eyes and other tissues. The active ingredient is irritating to the eyes and the skin.

Sensitization to the Product: Rare cases of hypersensitivity reactions have been reported.

Reproductive Toxicity Information: Listed below is information concerning the effects of Mitoxantrone Hydrochloride on human and animal reproductive systems.

Mutagenicity: Mutagenic in a battery of assay, including Ames gene mutation and a mammalian gene mutation assay, in vitro and in vivo system assays for clastogenic effects and induction of DNA damage in rat hepatocytes.

Embryotoxicity/Teratogenicity: Treatment of pregnant rats during organogenesis was associated with fetal growth retardation at dose ≥ 0.1 mg/kg/day. When pregnant rats were treated during organogenesis, an increased incidence of premature delivery was observed at doses ≥ 0.1 mg/kg/day. No teratogenic effects were observed in rabbits at these doses.

Mitoxantrone for Injection Concentrate

11. TOXICOLOGICAL INFORMATION cont..

Reproductive Toxicity: No studies on fertility were reported but Mitoxantrone Hydrochloride should be considered a reproductive toxicant based on clinical effects on female menstrual cycle

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: This product will be relatively stable under ambient environmental conditions.

Effect of Materials on Plants or Animals: No specific information is available on the effect of Mitoxantrone Hydrochloride on plants or animals in the environment. Due to the small product size and dilute concentration of the components, this product is not anticipated to cause adverse effects.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect of Mitoxantrone Hydrochloride on plants or animals in the aquatic environment. Due to the small product size and dilute concentration of the components, this product is not anticipated to cause adverse effects.

13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" or "characteristic" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

14. TRANSPORTATION INFORMATION

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable

Mitoxantrone for Injection Concentrate

15. REGULATORY INFORMATION

U.S. REGULATIONS:

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. TSCA Inventory Status: Mitoxantrone Hydrochloride is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product contains a chemical, Mitoxantrone Hydrochloride, which is known to the State of California to cause developmental and reproductive effects.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS:

Canadian DSL/NDSL Status: Mitoxantrone Hydrochloride is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): Mitoxantrone Hydrochloride should be administered under the supervision of a qualified physician. Avoid over-exposure. Harmful if swallowed or absorbed through the skin. Overexposure may be harmful to the blood, bone marrow and cardiovascular system. Reproductive and developmental toxicant. Avoid exposure during pregnancy. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Avoid contact with eyes, skin and clothing. Do not eat, drink or smoke when handling Mitoxantrone Hydrochloride. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

16. OTHER INFORMATION

Issue Date: 12/12/03

Previous Issue Date: None

The information in this document is believed to be correct as of the date issued. **HOWEVER, NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR ANY OTHER WARRANTY IS EXPRESSED OR IS TO BE IMPLIED REGARDING THE ACCURACY OR COMPLETENESS OF THIS INFORMATION, THE RESULTS TO BE OBTAINED FROM THE USE OF THIS INFORMATION OR THE PRODUCT, THE SAFETY OF THIS PRODUCT, OR THE HAZARDS RELATED TO ITS USE.** This information and product are furnished on the condition that the person receiving them shall make his own determination as to the suitability of the product for his particular purpose and on the condition that he assume the risk of his use thereof.