

Daunorubicin Hydrochloride Injection

**1. PRODUCT IDENTIFICATION**

**Product Name** Daunorubicin Hydrochloride Injection  
**Product Use** Medical Treatment; Antineoplastic Agent  
**Manufacturer** Teva Parenteral Medicines, Inc.  
**Address** 11 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.tevausea.com>

**Common Chemical Name** Cerubidine®  
 (1*S*,3*S*)-3-Acetyl-1,2,3,4,6,11-hexahydro-3,5,12-trihydroxy-10-methoxy-6,11 dioxo-1-naphthaceny 3-amino-2,3,6-trideoxy-(alpha)-L- *lyxo* -hexopyranoside hydrochloride

**Chemical Formula** C<sub>27</sub>H<sub>29</sub>NO<sub>10</sub>·HCl  
**Chemical Family** Anthracycline cytotoxic agent  
**How Supplied** 5 mg/mL, in a 4 mL polymer vial

**Date of Preparation:** December 4, 2005

**2. COMPOSITION AND INGREDIENTS**

CHEMICAL NAME	CAS#	Wt%	EXPOSURE LIMITS IN AIR				
			ACGIH		OSHA		Other
			TLV	CEIL	PEL	CEIL	
Daunorubicin, USP	23541-50-6	0.5	NE	NE	NE	NE	*0.5 µg/m <sup>3</sup>
Sodium Chloride	7647-14-5	0.9	NE	NE	NE	NE	NE
Water for Injection	7732-18-5	98.6	NE	NE	NE	NE	NE

NE - Not Established      C - Ceiling Limit      \* Identified for a closely related antineoplastic compound, doxorubicin

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 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 red liquid. It is a cytotoxic agent. Irritant. May cause damage to the bone marrow, reproductive system and heart. Harmful to the fetus. May cause allergic skin reactions. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Do not taste or swallow. Wash thoroughly after handling.

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### 3. HAZARD IDENTIFICATION cont...

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous injection under the supervision of physicians. It must NOT be given by the intramuscular or subcutaneous route.

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, itching, burning and skin damage. Extravasation during infusion may cause local pain, severe tissue lesions and necrosis. May cause an allergic skin reaction.

Ingestion: Ingestion is not an anticipated route of occupational exposure. The active ingredient, Daunorubicin Hydrochloride, is toxic if swallowed. 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, effects including bone marrow suppression with decreased blood cells, nausea, vomiting, severe gastrointestinal distress, fever, rash, loss of blood pressure, cardiac irregularities and hair loss 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 nausea, vomiting, diarrhea, fever, rash, hair loss and loss of blood pressure may occur.

Cancer: Daunorubicin Hydrochloride is considered possibly carcinogenic (see Section 11).

Chronic: Daunorubicin Hydrochloride, is considered a potential developmental and reproductive toxicant (see Section 11).

Target Organs: Potential hazard to the bone marrow and heart (see Section 11).

Pre-Existing Medical Conditions: Pre-existing bone marrow, reproductive and heart disorders may be aggravated by exposure to this material.



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### 4. FIRST-AID MEASURES

Skin Exposure: Remove contaminated shoes and clothing, and flush affected area(s) with large amounts of water. If skin surface is damaged, apply a clean dressing and seek medical attention. If skin surface is not damaged, cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops, seek medical attention.

Eye Exposure: Move victim away from exposure and into fresh air. If irritation or redness develops, flush eyes with clean water and seek medical attention. For direct contact, hold eyelids apart and flush the affected eye(s) with clean water for at least 15 minutes. 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.

Note to physicians: Daunorubicin is a potent cytotoxic antineoplastic drug. It should only be administered under the supervision of physicians experienced in cancer chemotherapy.

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: The size and nature of this product is such that it will not contribute to the intensity of a fire. Use extinguishing agent suitable for type of surrounding fire.

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.



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### 5. FIRE-FIGHTING MEASURES cont...

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

### 6. ACCIDENTAL RELEASE MEASURES

#### Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled solution with proper sorbents.

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

**DAUNORUBICIN IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.**

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 unopened vials in refrigerator at 2° to 8°C (36° to 46°F). Prepared solution for infusion store at room temperatures between 15° to 30°C (59° to 86°F) for up to 24 hours. Protect from light.

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.



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### 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 100 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: A full body gown which is closed at the front and has long sleeves is recommended.

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):	NA	Evaporation Rate (n-BuAc=1):	NA
Specific Gravity (water = 1):	2.6 Approx.	Melting/Freezing Point:	40-400°C
Solubility in Water:	Completely	Boiling Point:	NA
Vapor Pressure, mm Hg @ 25°C.	NA	pH:	3-4
Odor Threshold: Odorless			
Appearance and Color: Red liquid			

ND = Not Determined NA = Not Applicable

### 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. It would not be compatible with acids and caustics.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Heat may cause product to decompose, destroying the product or producing toxic fumes.



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### 11. TOXICOLOGICAL INFORMATION

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

Oral LD50(rat) = 290 mg/kg	IV LD50(rat) = 14300 ug/kg	IP LD50(rat) = 14300 ug/kg
Oral LD50(Mouse) = 205 g/kg	IV LD50(mouse) = 50 mg/kg	IP LD50(mouse) = 3050 ug/kg
SubQ(mouse) = 28800 ug/kg	IM LD50(rat) = 2790 ug/kg	IM LD50(mouse) = 23300 ug/kg
SubQ(rat) = 33200 ug/kg		

Suspected Cancer Agent: One study identified a significant increase in tumor formation in the kidneys of female rats given single intravenous injections of 5, 10, or 20 mg/kg an observed for one year. Another study found that a single intravenous dose of 12.5 mg/kg daunorubicin given to female rats induced tumor formation in all 25 animals within 12 months, with a high incidence of mammary tumors. Daunomycin, a material with a similar metabolite, has been identified as a carcinogen (2B) by IARC. It is not listed as carcinogenic by NTP or OSHA.

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

Sensitization to the Product: Rare instances of allergic reactions have occurred from clinical use. No data on allergic sensitization potential from repeated skin contact.

Target Organ(s): Causes bone marrow suppression (decreased white blood cell count and platelets, neutropenia and thrombocytopenia) and cardiac toxicity, typically characterized by tachycardia, arrhythmias, dyspnea, hypotension, pericardial effusion and a peculiar form of congestive heart failure.

Reproductive Toxicity Information: Listed below is information concerning the effects of Daunorubicin Hydrochloride on human and animal reproductive systems. This material is classified as a Pregnancy Category D (Positive evidence of risk). Currently, there have been no studies in pregnant women.

Mutagenicity: Daunorubicin Hydrochloride is reportedly mutagenic in a battery of bacteria and cultured rodent cells (Ames bacterial cell test, mouse leukocyte, Chinese hamster lung cells), and is mutagenic in *in-vivo* bone marrow studies. An increased frequency of micronuclei was induced in pregnant rats treated with ten times the human therapeutic dose.

Embryotoxicity/Teratogenicity/Reproductive Toxicity: Increased frequencies of fetal death and of malformations of the heart, eye and digestive and genitourinary tracts were observed in offspring of rats treated during pregnancy with one to ten times the human therapeutic dose of daunorubicin. There have been several reports of pregnant women who have been treated with daunorubicin. In one study, among nine cases exposed during the first trimester of pregnancy, there were no teratogenic effects, but two women delivered prematurely, and another two had still births (one of which showed significant myocardial necrosis). Another study involving first trimester exposure reported that two of four women exposed had spontaneous abortions within three weeks of treatment. Additional studies of exposure to daunorubicin during the last two trimesters of pregnancy have reported transient neonatal bone marrow suppression and 'fetal distress', along with premature delivery.

Reproductive Toxicity: Daunorubicin reportedly impairs fertility in mice. It has not been conclusively demonstrated that daunorubicin impairs fertility in humans.

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## 11. TOXICOLOGICAL INFORMATION cont...

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 on plants or animals in the environment.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect on plants or animals in the aquatic environment.

## 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



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### 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: Daunorubicin 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 known to the State of California to cause cancer or reproductive effects:

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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/NDL Status: Daunorubicin 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): Irritant. Harmful to the Fetus. May Cause Damage to the Bone Marrow, Heart and Reproductive System. May cause allergic skin reactions. Daunorubicin Hydrochloride should be administered under the supervision of a qualified physician. Avoid over-exposure. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy. Avoid accidental injection. Do not eat, drink or smoke when handling. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

### 16. OTHER INFORMATION

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