

Dacarbazine for Injection, USP

1. PRODUCT IDENTIFICATION

Product Name Dacarbazine for Injection, USP
Product Use Medical Treatment; Metastatic Malignant Melanoma and Hodgkin's Disease

Manufacturer Address Teva Parenteral Medicines, Inc.
 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.newsicor.com>

Common Names DTIC; DTIC-Dome®
Chemical Name 5-(3,3-Dimethyl-1-triazeno) imidazold-4-carboxamide
Chemical Formula C₆H₁₀N₆O
Chemical Family Imidazole
How Supplied 100 or 200 mg in vials

Date of Preparation: December 4, 2005

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	EXPOSURE LIMITS IN AIR					
		Wt%	ACGIH		OSHA		Other
			TLV	CEIL	PEL	CEIL	
Dacarbazine, USP	4342-03-4	40-45	NE	NE	NE	NE	NE
Citric Acid, Anhydrous	77-92-9	40-45	NE	NE	NE	NE	NE
Mannitol	7732-18-5	10-20	NE	NE	NE	NE	NE

NE - Not Established

C - Ceiling Limit

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 colorless to ivory colored powder. It is a cytotoxic agent and a probable cancer hazard. Eye and skin irritant. May cause damage to the bone marrow, blood, and liver. 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 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 swelling and damage to the eyes and redness, itching burning and damage to the skin. May cause allergic skin reactions.

Ingestion: Ingestion is not an anticipated route of occupational exposure. However, the active ingredient, Dacarbazine, is slightly 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 decreased blood platelets and white blood cells, anemia, nausea, vomiting, fever, muscle pain, rash, hair loss, irritation of the respiratory tract and photosensitivity 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 decreased blood platelets and white blood cells, anemia, nausea, vomiting, fever, muscle pain, rash, hair loss, irritation of the respiratory tract and photosensitivity may occur.

Cancer: Dacarbazine is considered probably carcinogenic (see Section 11).

Chronic: Dacarbazine is considered a potential developmental toxicant (see Section 11).

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

Pre-Existing Medical Conditions: Pre-existing skin, liver, bone marrow and blood 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 cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, 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: Dacarbazine 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: This material decomposes explosively between 250 and 255°C

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: 1 (Slight)
 Reactivity: 0 (Least)

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6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Wet material to prevent dusting and absorb 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

DACARBAZINE 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 refrigerated at temperatures between 2-8°C (36-46°F). 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):	>1
Specific Gravity (water = 1):	ND	Melting/Freezing Point:	250°C (482°F) Decomposes
Solubility in Water:	Slightly	Boiling Point:	NA
Vapor Pressure, mm Hg @ 25°C.	NA	pH:	NA)
Odor Threshold: Odorless			
Appearance and Color: Colorless to ivory colored powder			

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 strong oxidizers, strong acids and strong bases. Avoid exposure to light (especially sun light) and heat.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Oxides of carbon and nitrogen.

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11. TOXICOLOGICAL INFORMATION

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

Oral LD50(rat) = 2147 mg/kg	Oral LD50(mouse) = 2032 mg/kg
IP LD50 (mouse) = 567 mg/kg	IV LD50 (rat) = 411 mg/kg
IP LD50(rat) = 350 mg/kg	IV LD50 (mouse) = 466 mg/kg

Suspected Cancer Agent: Following oral or intraperitoneal administration to rats, in as little as eighteen weeks dacarbazine produced tumors at various sites, including mammary gland, thymus, spleen, and brain. Carcinogenicity has been reported in different animal species; however, at present there is inadequate evidence for the carcinogenicity of dacarbazine in humans, and the compound is classified as a group 2B, probable human carcinogen. It is listed as carcinogenic by NTP and IARC.

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

Sensitization to the Product: Dermatological reactions have infrequently been observed with chronic exposure to this compound. Specific data on repeated skin contact occupationally was not identified.

Target Organ(s): Hematopoietic depression is the most common toxicity with dacarbazine and involves primarily the leukocytes and platelets, although anemia may sometimes occur. Leukopenia and thrombocytopenia may be severe enough to cause death. Hepatic toxicity accompanied by hepatic vein thrombosis and hepatocellular necrosis resulting in death has been reported.

Reproductive Toxicity Information: Listed below is information concerning the effects of Dacarbazine 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: Dacarbazine is reportedly mutagenic to cultured rodent cells and bacteria (Ames bacterial cell test, mouse lymphoma assay), and weakly induced sister chromatid exchanges in Chinese hamster ovary cells in vitro. In one study, dacarbazine did not induce sister chromatid exchanges in the lymphocytes of treated patients.

Embryotoxicity/Teratogenicity: After intraperitoneal administration to rats at the end of pregnancy, dacarbazine produced tumors in offspring. Increased frequencies of central nervous system, limb, and craniofacial anomalies were observed in rats treated with a single dose 22-220 times the usual human dose of dacarbazine on days 11 or 12 gestation. In rabbits, a daily dose seven times the human daily dose given on days 6-15 of gestation resulted in fetal skeletal anomalies.

Reproductive Toxicity: Chemotherapy with drug regimens that include dacarbazine do not typically cause more than transient gonadal dysfunction.

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

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12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: It is anticipated that this compound will decompose into a variety of organic compounds.

Effect of Materials on Plants or Animals: This product may be harmful to contaminated plant and animal life. See Section 11 (Toxicological Information) for additional information.

Effect of Chemicals on Aquatic Life: This product may be harmful to aquatic plant and animal life in contaminated bodies of water.

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: Dacarbazine 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 and developmental effects - Dacarbazine.

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: Dacarbazine 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): DANGER! Cytotoxic Agent and Probable Cancer Hazard. Eye and skin irritant. May cause damage to the bone marrow, blood, and liver. 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. Dacarbazine should be administered under the supervision of a qualified physician. Avoid accidental injection. Do not eat, drink or smoke when handling Dacarbazine. Clean up spills promptly.

16. OTHER INFORMATION

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