



MATERIAL SAFETY DATA SHEET

Product Name: Dacarbazine for Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address Hospira, Inc.
275 North Field Drive
Lake Forest, Illinois 60045
USA
Hospira Australia Pty Ltd
1 Lexia Place
Mulgrave VIC 3170
AUSTRALIA

Emergency Telephone #'s CHEMTREC: North America: 800-424-9300; International 1-703-527-3887;
Australia (02) 8014 4880

Hospira, Inc., Non-Emergency 224 212-2055

Product Name Dacarbazine for Injection, USP

Synonyms 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide; DTIC.

2. HAZARD INFORMATION / CLASSIFICATION

Emergency Overview Dacarbazine for Injection, USP, is a powder that contains dacarbazine, an anti-neoplastic drug that acts as an alkylating agent after metabolic activation by the liver. Dacarbazine is used to treat some types of cancers. It is a cytotoxic agent, and should be considered a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal tract, central nervous system, liver, skin, and the fetus.

Occupational Exposure Potential 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.

Signs and Symptoms This product should be considered irritating to the skin, eyes, and respiratory tract. In clinical use, adverse effects have included anorexia, severe nausea and vomiting, bone marrow depression, diarrhea, skin reactions, alopecia, abnormal ECG, hypotension, a flu-like syndrome, facial flushing and paraesthesia, headache, polyneuropathy, blurred vision, and seizures.

Medical Conditions Aggravated by Exposure Pre-existing hypersensitivity to dacarbazine. Pre-existing bone marrow, blood, gastrointestinal, central nervous system, liver, or skin ailments; or pregnancy.

Carcinogen Lists: **IARC:** Group 2B **NTP:** Suspected Human Carcinogen **OSHA:** Not listed

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Dacarbazine
Chemical Formula C₆H₁₀N₆O

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Dacarbazine	40-44	4342-03-4	NI3950000
Citric Acid Monohydrate	42-44	5949-29-1	GE7810000

Non-hazardous ingredients present at greater than 1% include mannitol.

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 product.
Fire & Explosion Hazard	None anticipated for this product.
Extinguishing Media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	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	<p>For spilled powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Collect the spilled powder using techniques that minimize powder migration. Clean affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations.</p> <p>If a spill occurs after reconstitution, absorb liquid with suitable material and clean affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations.</p>
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7. HANDLING AND STORAGE

Handling	<p>Dacarbazine is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastics agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic 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.</p> <p>Avoid ingestion, inhalation, skin contact, and eye contact. When handling the powder, 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 .</p>
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7. HANDLING AND STORAGE: continued

Storage No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for antineoplastic agents. For product protection, follow USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions Persons with known hypersensitivities to dacarbazine, 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	Exposure limits			
	OSHA-PEL	ACGIH-TLV	Hospira EEL	Other Limits
Dacarbazine	8-hr TWA: Not established	8-hr TWA: Not established	8-hr TWA: Not Established	NA
Citric Acid Monohydrate	8-hr TWA: Not established	8-hr TWA: Not established	8-hr TWA: Not Established	NA

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
 ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
 EEL: Employee Exposure Limit.
 TWA: 8-hour Time Weighted Average.
 STEL: 15-minute Short Term Exposure Limit.

Respiratory Protection Respiratory protection is normally not needed during intended product use. However, if the generation of dusts or 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 dust or 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 many antineoplastic agents. 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 When handling the dry powder, local exhaust ventilation is recommended 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	Dacarbazine is a colorless to ivory-colored crystalline solid.
Odor	Odorless
Odor Threshold:	NA
pH:	3-4 for a 1% solution when reconstituted
Melting point	202-205°C
Initial Boiling Point/Boiling Point Range	NA
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Evaporation Rate	NA
Specific Gravity	NA
Solubility	Slightly soluble in water and alcohol
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature	NA
Decomposition temperature	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined.
Chemical Stability	Stable under standard use and storage conditions. Dacarbazine is sensitive to light and heat; elevated temperatures may cause a color change from ivory to pink which is indicative of some decomposition.
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) and nitrogen oxides (NOx).
Hazardous Polymerization	Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity –

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Dacarbazine	100	LD50	Oral	2147	mg/kg	Rat
Dacarbazine	100	LD50	Oral	2032	mg/kg	Mouse
Dacarbazine	100	LD50	Intravenous	411	mg/kg	Rat
Dacarbazine	100	LD50	Intravenous	466	mg/kg	Mouse
Dacarbazine	100	LD50	Intraperitoneal	350	mg/kg	Rat
Dacarbazine	100	LD50	Intraperitoneal	567	mg/kg	Mouse
Citric Acid Monohydrate	100	LD50	Intraperitoneal	375	mg/kg	Rat

LD50 is the dosage producing 50% mortality.

Aspiration Hazard	None anticipated from normal handling of this product .
Dermal Irritation/Corrosion	None anticipated from normal handling of this product . Inadvertent skin contact with this product may produce irritation and redness.
Ocular Irritation/Corrosion	None anticipated from normal handling of this product . Inadvertent eye contact with this product is anticipated to produce irritation, redness and discomfort.
Dermal or Respiratory Sensitization	None anticipated from normal handling of this product. In clinical use, erythematous and urticarial rashes have been observed infrequently. Rarely, photosensitivity reactions have occurred.
Reproductive Effects	Administration of dacarbazine to male rats at dosages up to 50 mg/kg twice/week for nine weeks had no effect on fertility. Administration of dacarbazine to female rats for two weeks prior to mating at dosages up to 30 mg/kg/day had no adverse effects on fertility. Administration of a single dosage of 800 or 1,000 mg/kg dacarbazine to pregnant rats on day 11 or 12 of gestation produced skeletal reduction defects, some cleft palates, and encephaloceles. Similarly, intraperitoneal administration of dacarbazine to pregnant rats throughout organogenesis produced an increase in resorptions, a decrease in litter size, and an increase in skeletal anomalies at doses from 30 mg/kg/day and higher. Major malformations in the rat offspring were increased at maternal doses of 50 and 70 mg/kg/day. In pregnant rabbits, maternal doses of 10 mg/kg/day produced abortion and an increase in major malformations. The no-observed-adverse-effect dosage was 5 mg/kg/day in the study in rabbits.
Mutagenicity	Dacarbazine was positive in the Ames test for mutagenicity. Dacarbazine was also positive for genotoxicity in vitro in rodent cell assays.
Carcinogenicity	Oral or intraperitoneal administration of dacarbazine to rats produced tumors in the mammary glands, thymus, spleen and brain. Dacarbazine is listed by IARC as Group 2B, and by NTP as a suspect human carcinogen.
Target Organ Effects	This product 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 tract, central nervous system, liver, skin, and the fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined for product. Citric Acid LC50 (96 hrs, static) = 1516 - 2600 mg/L in freshwater fish EC50(72 hrs) \approx 120 mg/L in Daphnia magna EC3 (7 days) = 640 mg/L in algae
Persistence/Biodegradability	Not determined for product. Citric acid is considered readily biodegradable. Approximately 98% was degraded after 48 hours (OECD Guideline 302B, domestic, non-adapted sewage).
Bioaccumulation	Not determined for product.
Mobility in Soil	Not determined for product.

13. DISPOSAL CONSIDERATIONS

Waste Disposal	All waste materials must be properly characterized by the waste generator. Disposal of all pharmaceuticals 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
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

TSCA Status	Exempt
CERCLA Status	Not listed
SARA 302 Status	Not listed
SARA 313 Status	Not listed
RCRA Status	Not listed
PROP 65 (Calif.)	This product is, or contains chemical(s) known to the State of California to cause developmental toxicity. This product is or contains chemical(s) known to the State of California to cause cancer.

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

U.S. OSHA Classification Possible Irritant
Reproductive Toxin
Carcinogen
Target Organ Toxin

GHS Classification* *Where medicinal products are not exempt, the recommended GHS workplace classification for this product is as follows:

Hazard Class	Acute Oral Toxicity	Eye Irritation	Skin Irritation	Toxic to Reproduction	Mutagenicity	Target Organ Toxicity	Carcinogenicity
Hazard Category	5	2B	2	2	2	2	2
Symbol	NA	NA					
Signal Word	Warning	Warning	Warning	Warning	Warning	Warning	Warning
Hazard Statement	May be harmful if swallowed	Causes eye irritation	Causes skin irritation	Suspected of damaging fertility or the unborn child	Suspected of causing genetic defects if ingested.	May cause damage to the bone marrow, gastrointestinal tract, central nervous system, liver, and skin through prolonged or repeated exposure.	Suspected of causing cancer if ingested.

GHS Precautionary Statements:

- Prevention:** Do not eat, drink or smoke when using this product.
Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood.
Use personal protective equipment as required.
Avoid breathing dust or vapors.
In case of inadequate ventilation wear respiratory protection.
Wear protective gloves.
Wash hands thoroughly after handling.
Contaminated work clothing should not be allowed out of the workplace.
- Response:** IF SWALLOWED: Call a POISON CENTER or doctor if you feel unwell.
IF INHALED: If breathing is difficult, remove to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms call a POISON CENTER or a doctor.
IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs, seek medical attention. Take off contaminated clothing and wash before reuse.
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.
If exposed or concerned, get medical attention.

15. REGULATORY INFORMATION: continued

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the active drug substance dacarbazine.

Classification(s): Irritant Toxic for Reproduction Category 2 Mutagen Category 2 Carcinogen Category 2

Symbol:



Indication of Danger: Xi T T T

Risk Phrases:

R36/37/38 - Irritating to eyes, respiratory system and skin
 R45 - May cause cancer
 R46 - May cause heritable genetic damage
 R48/25 - Danger of serious damage to health by prolonged exposure if swallowed
 R60 - May impair fertility
 R61 - May cause harm to the unborn child
 R64 - May cause harm to breastfed babies

Safety Phrases:

S22: Do not breathe dust
 S24: Avoid contact with the skin
 S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.

16. OTHER INFORMATION

Notes: NA

- 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

16. OTHER INFORMATION: continued

MSDS Coordinator: Global Occupational Toxicology
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Disclaimer:

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