



Bristol-Myers Squibb Company

MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

BRISTOL-MYERS SQUIBB WORLDWIDE MEDICINES GROUP
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Product Identification **BicNU for IV Infusion**

Chemical Name (active ingredient): **1,2-bis(2-chloroethyl)-1-nitrosourea**

Synonym: **BCNU, Carmustine**

How Supplied: **BicNU is packaged as two vials. Each package includes a vial containing 100 mg carmustine and a vial containing 3 ml ethyl alcohol as a diluent.**

Product Use: **Cytotoxic antineoplastic agent**

Chemical Family: **Nitrosourea**

Molecular Formula: **C₅H₉C₁₂N₃**

CAS NUMBER: **154-93-8**

EMERGENCY CONTACTS

Transportation: **CHEMTREC (800)424-9300. For all international transportation emergencies call Chemtrec at (703) 527-3887, collect call accepted.**

EMERGENCY OVERVIEW: **Carmustine is a light yellow to white powder or a waxy congealed appearing substance (if an oily liquid, see package insert). Carmustine is a cytotoxic agent used in the treatment of certain neoplastic diseases. Highly toxic after oral exposure. Mutagen. Probable human carcinogen. It may adversely affect the fetus.**

Ethyl alcohol is a clear, colorless volatile liquid. Flammable. Irritant.

2. COMPOSITION/INFORMATION ON INGREDIENTS

COMPONENTS	HAZARDOUS (Y/N)	CONCENTRATION (wt %)	CAS NUMBER	EXPOSURE GUIDELINE
1 vial of carmustine	Y	100	154-93-8	none established
1 vial of ethyl alcohol	Y	100	64-17-5	1000 ppm (1)(2)

1 OSHA PEL = Occupational Safety and Health Administration - Permissible Exposure Limit

2 ACGIH TLV = American Conference of Governmental Industrial Hygienist - Threshold Limit Value

3. HEALTH HAZARDS IDENTIFICATION

EFFECTS OF OVEREXPOSURE

Routes of Entry:

1. **Inhalation:** If carmustine becomes airborne there is potential for inhalation. The extent of systemic absorption of carmustine is not known. If vials containing ethyl alcohol break or spill, vapors may be inhaled. Ethyl alcohol may be well absorbed after inhalation.



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

2. Skin contact: Exposure may occur via skin contact if vials break or spill and if gloves and protective clothing are not worn. Carmustine and ethyl alcohol may be absorbed through the skin, although the extent of systemic absorption is not known.

3. Ingestion: Ingestion of large quantities of this material in an occupational setting would not be expected to occur. Ingestion of trace amounts of the material might occur if material contacts the hands and hands are not washed prior to eating drinking or smoking. The extent of systemic absorption of carmustine after ingestion is not known. Ethyl alcohol may be well absorbed after ingestion.

Acute:

Ingestion: Carmustine was highly toxic in experimental animals following acute ingestion. Ethyl alcohol is a central nervous system depressant. Ingestion of large amounts may cause nausea, vomiting, confusion, loss of motor nerve control, shallow respiration, drowsiness, and possibly coma.

Inhalation: There is no information concerning the potential for carmustine to produce symptoms after inhalation. Most dusts may cause mechanical irritation (sneezing, tearing of the eyes) after high exposure. Acute inhalation of ethyl alcohol at ambient concentrations ranging from 1,000-10,000 ppm has caused temporary irritation of the upper respiratory tract and coughing and, if exposure is prolonged, central nervous system depression.

Skin Contact:

a. Toxic: There is no information concerning the potential of carmustine to produce symptoms after skin contact. Skin contact with small amounts of ethyl alcohol is not expected to produce systemic symptoms.

b. Irritation: Carmustine may cause a brown skin discoloration and burning sensation. Ethyl alcohol is a skin irritant, and direct contact may cause mild redness and burning.

c. Sensitization: Carmustine has been used in some topical formulations and hypersensitivity has been reported following daily topical use. Ethyl alcohol has occasionally been reported to produce contact dermatitis in some individuals.

Eye Contact: Carmustine should be handled as a potential eye irritant. It may cause conjunctivitis. Ethyl alcohol is an eye irritant. Vapors of ethyl alcohol at concentrations of 1,000-10,000 ppm may cause temporary eye irritation, with 15,000 ppm causing lacrimation. Direct contact with ethyl alcohol liquid may cause immediate burning and stinging.

Other: Carmustine, a cytotoxic agent, is reconstituted with ethyl alcohol and sterile water. It is generally intended for intravenous injection under the supervision of physicians experienced in cancer chemotherapy. Acute systemic exposure to BiCNU may produce delayed hematologic toxicity, nausea and vomiting, and ocular toxicity.

Chronic: Dose-dependent adverse effects associated with repeated, systemic exposure to BiCNU at therapeutic doses may include delayed hematologic toxicity, nausea and vomiting, pulmonary toxicity, mild and reversible hepatotoxicity, renal damage, and ocular toxicity. Although the carcinogenic potential has not been fully studied, acute leukemia and bone marrow dysplasia have been reported in patients receiving long-term therapy with nitrosurea derivatives.



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

Exposure Guideline Summary: Exposure guideline not established

Carcinogen Lists IARC: Group 2A NTP: Yes OSHA: No

Carmustine has been classified in Group 2A by IARC. A 2A designation indicates that IARC believes carmustine to be a probable human carcinogen, although there is limited human evidence. However, sufficient evidence of carcinogenicity in laboratory animals exists: carmustine administration has been associated with lung tumors, neurogenic tumors, and peritoneal cavity tumors in rats.

Target Organs: The hematopoietic system, gastrointestinal system, lungs, liver, kidney, skin and eyes are the major target organs. Other organ systems which undergo rapid cellular division may also be targets after systemic exposure.

Medical Conditions Aggravated by Exposure: Therapeutic doses of this material may aggravate blood disorders, gastrointestinal illnesses, pulmonary disease, kidney disease, or hepatic disease.

Medical Surveillance Recommendation: A pre-placement physical examination and history (noting any risk factors) for employees with potential exposure to BicNU is recommended. A complete blood count, including differential, a chest x-ray, pulmonary, liver and renal function tests may be taken to provide a baseline. Periodic follow-up examinations should be given in accordance with institutional policy, overseen by a physician thoroughly knowledgeable about both the toxicity of the substance and the extent of work place exposure. A permanent registry of all staff who routinely prepare or administer BicNU should be considered.

Staff members who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring workers' health.

4. FIRST AID MEASURES

Ingestion: Seek medical attention immediately. Induction of vomiting should be considered for significant ingestions if person is conscious and not experiencing convulsions. Never give anything by mouth to an unconscious person.

Inhalation: Remove exposed person to fresh air. If not breathing give artificial respiration. If breathing is difficult administer oxygen. Get medical attention.

Skin Contact: Immediate flush with large amounts of water. Use soap if available. Remove contaminated clothing, including shoes after flushing has begun. Get medical attention.

Eye Contact: Hold eyelids apart and flush with running water for at least 15 minutes. Get medical attention immediately.

Note to physicians: Carmustine is a mutagen and a probable human carcinogen. When administered parenterally, it is a toxic drug with a low therapeutic index.



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5. FIRE FIGHTING MEASURES

Flash point: Not determined for carmustine; 55 degrees F (13 degrees C) for ethyl alcohol.

Autoignition Temperature: Not determined for carmustine; 685 degrees F (363 degrees C) for ethyl alcohol.

Flammability Limits:

LEL: Not determined for carmustine;
3.3% for ethyl alcohol.

UEL: Not determined for carmustine;
19% for ethyl alcohol.

Combustibility of Dusts: Fine powders are considered to be combustible. Provide appropriate bonding and grounding protection to control static charges. Powder handling equipment such as dust collectors, dryers and mills may require additional protective measures (i.e. explosion venting).

Extinguishing Media: In case of fire use water, carbon dioxide, foam or dry chemical.

Firefighting Instructions: Firefighters should wear self contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Evacuate personnel to upwind direction, remove unneeded material and cool container(s) with water from a maximum distance.

Hazardous Combustion Products: May include CO, CO₂, HCl, and NO_x, and possibly some carcinogenic compounds.

Unusual Hazards: Highly toxic, mutagenic, antineoplastic drug. Avoid ingestion, inhalation and skin contact. Decontaminate protective equipment after use.

6. ACCIDENTAL RELEASE MEASURES

Spill/Clean-up: Small spills -- wipe liquids with absorbent gauze pads. Wipe solids with wet absorbent gauze. Clean, using detergent and water.

Large spills -- cover liquid with absorbent sheets, spill-control pads or pillows.

Cover powder with damp cloth or towels. Clean, using detergent and water. Product and contaminated materials are hazardous waste (D001) due to the ethyl alcohol. Incineration is recommended.

7. HANDLING AND STORAGE

Handling Precautions: Ship and store under refrigeration. Do not break vials or spill contents. See relevant guidance for handling of cytotoxic materials.

Container Requirements: Must conform with all federal and international regulations. Packaging Group II. See also 49 CFR 173.4. Incompatible with polyvinyl chloride containers.

Storage Conditions: Should be stored under refrigeration (2 to 8 degrees C). When stored in original container, drug is stable to the expiration date on the label of the product.



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8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

Ventilation Requirements: Local mechanical exhaust ventilation recommended to minimize employee exposure. Control exposure by enclosure to processes whenever possible. A biological safety cabinet (BSC) should be used for preparation of this drug, or as determined appropriate by industrial hygienist.

Respiratory Protection: When engineering controls are not sufficient to control exposure, or if BSC is not available, wear an approved dust respirator with high efficiency dust filter, or powered air-purifying respirator; self-contained breathing apparatus should be available for emergency use or when the PEL for ethyl alcohol is exceeded.

Eye Protection: Wear chemical safety goggles. (ANSI Z87.1).

Protective Gloves: Wear disposable surgical latex gloves rather than polyvinyl chloride (PVC) gloves. Gloves should be changed regularly and removed immediately after overt contamination. Double gloving is recommended for cleaning up spills.

Special Clothing: Wear impervious disposable coveralls with closed front, long sleeves and elastic cuffs, and boots to protect from dusts, splashes, or sprays. Remove disposable clothing prior to leaving the work area.

Hygiene: Wash hands, forearms, and face thoroughly after handling compounds and before eating, smoking, using lavatory, and at the end of day.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance/Physical State/Color: Carmustine is a light yellow to white powder or a waxy congealed appearing substance (carmustine decomposes to an oily liquid at temperatures of 30.5 degrees C or warmer). Ethyl alcohol is a clear, colorless volatile liquid.

Boiling point: Not available for carmustine; 173 degree F (78 degrees C) for ethyl alcohol.

Evaporation rate: Not applicable to carmustine; 1.4 for ethyl alcohol (carbon tetrachloride = 1).

Flash point: Not available for carmustine; 55 degrees F (13 degrees C) for ethyl alcohol.

Freezing point: Not available for carmustine.

Melting point: 87 degrees F (30.5 degrees C) for carmustine (with decomposition); -179 degrees F (-117 degrees C) for ethyl alcohol)

Octanol/water partition coefficient: Not available for carmustine.

Odor (threshold): Not available for carmustine; pleasant odor with 5-10 ppm odor threshold for ethyl alcohol.

pH: 5.6-6 for reconstituted BiCNU solution.

Solubility: Carmustine is 0.4% by weight soluble in water, 50% by weight soluble in alcohol, and highly soluble in lipids. Ethyl alcohol is miscible with water.



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PHYSICAL AND CHEMICAL PROPERTIES (CONTINUED)

Specific gravity: Not applicable to carmustine; 0.7893 for ethyl alcohol.

Vapor density: Not applicable to carmustine; 1.59 for ethyl alcohol.

Vapor Pressure: Not applicable to carmustine; 40 mm Hg at 19 degrees C for ethyl alcohol.

Viscosity: Not applicable to carmustine; 1.22 cp at 20 degrees C for ethyl alcohol.

10. STABILITY AND REACTIVITY

Stability: When stored in original container and kept in refrigerator (2-8 degrees C), carmustine is stable to the expiration date indicated on the label of the product. If heated to 87 degrees F, the drug will appear as an oil film in the vial. This is an indication of decomposition. Ethyl alcohol is stable under normal temperatures and pressures.

Incompatibilities: Carmustine is incompatible with polyvinyl chloride containers. Ethyl alcohol is a flammable liquid, and should be kept away from oxidizers, open flames, sparks, or other potential sources of ignition.

Conditions of Reactivity: Not applicable to the packaged product or to the product when used in accordance with directions provided on the package insert.

Hazardous Decomposition Products: May include CO, CO₂, HCl, NO_x and possibly some carcinogenic compounds.

Hazardous Polymerization: Will not occur.

Explosion data relative to mechanical impact: No specific data.

Explosion data relative to static discharge: No specific data.

11. TOXICOLOGICAL INFORMATION (for carmustine)

RTECS NUMBER (U.S.): YS2625000

ACUTE:

LD 50:

Acute oral LD50 (rat) = 20 mg/kg;
Acute oral LD50 (mouse) = 19 mg/kg;
Acute ip LD50 (rat) = 17.42 mg/kg;
Acute ip LD50 (mouse) = 21.26 mg/kg;
Acute iv LD50 (rat) = 13.8 mg/kg;
Acute iv LD50 (mouse) = 45 mg/kg;
Acute im LD50 (rat) = 79.6 mg/kg;
Acute im LD50 (mouse) = 86.3 mg/kg;
Acute sc LD50 (rat) = 83.2 mg/kg;
Acute sc LD50 (mouse) = 24 mg/kg.

LC 50: No information.

CHRONIC:

Carcinogenicity: Carmustine has been shown to be carcinogenic in rats and



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TOXICOLOGICAL INFORMATION (CONTINUED)

mice, and has been associated with a marked increase in the incidence of tumors when administered to these animals in dosages equivalent to the usual human dosage. Although the carcinogenic potential has not been fully studied, acute leukemia and bone marrow dysplasia have been reported in patients receiving long-term therapy with nitrosurea derivatives.

Mutagenicity: Carmustine was reported to cause mutations in genetic toxicity studies. Compounds which are mutagens may have potential to cause cancer or other reproductive effects.

Teratogenicity: Carmustine may cause fetal harm when administered to pregnant women. Carmustine has been shown to be teratogenic in rats and embryotoxic in rats and rabbits receiving dosages equivalent to the usual human dosage.

Reproductive Effects: Carmustine has been shown to affect fertility in male rats receiving the drug at dosages somewhat higher than the usual human dosage.

Toxicological synergistic products: None known.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information: No information.

Chemical Fate Information: No information.

13. DISPOSAL CONSIDERATIONS

Disposal: Dispose of in accordance with National, State, Local and applicable country regulations. Product and contaminated materials are hazardous waste (D001) due to the ethyl alcohol. Incineration at an approved facility is recommended.

14. TRANSPORT INFORMATION

DOMESTIC

Hazard Class (UN NUMBER): 3 (UN 1992)
Proper shipping name: Chemical kit, poison
Label requirements: Flammable Liquid, poison
Placard requirements: Flammable Liquid
Limited Quantity Exemption: See 49 CFR 173.4

INTERNATIONAL

Hazard Class (UN NUMBER or PIN NUMBER): 3 (UN 1992)
Proper shipping name: Chemical kit, poison
Label requirements: Flammable Liquid, poison
Placard requirements: Flammable Liquid
Limited Quantity Exemption: Not applicable.

15. REGULATORY/STATUTORY INFORMATION -- not meant to be all inclusive

U.S. Federal: None noted

International: None noted

EC Labeling: None noted



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REGULATORY/STATUTORY INFORMATION (CONTINUED)

California: Contains carmustine which is subject to California Proposition 65 carcinogen and reproductive toxin warning and release requirements.

16. OTHER INFORMATION

12-7-2000: The MSDS dated 1-7-93 was revised to change telephone numbers.

Therapeutic agents are intended for use under direction of a physician and/or under the conditions of use described on the label. As a general precaution, personnel who handle drug substances should avoid contact (ingestion, inhalation, skin and eye contact) with these substances.

This material safety data sheet is intended for use by personnel who handle this material as part of their job responsibilities. It does not address the therapeutic use of this material. Information concerning the therapeutic use of this drug substance should be obtained from formulated product package inserts and other appropriate references.

Federal law prohibits dispensing without prescription. See package insert for recommended medical use. See OSHA Instruction PUB. 8-1.1 for additional work practice guidelines for handling this material. Copies are available from OSHA, Room N3651, 200 Constitution Avenue, N.W., Washington, DC 20210.

The information contained in this MSDS is believed to be accurate and represents the best information available at the time of preparation. However, we make no warranty, express or implied, with respect to such information, and we assume no liability from its use.
