SAFETY DATA SHEET

1. Identification

Product identifier **Bendamustine Hydrochloride**

Other means of identification

Catalog number 1065221

CAS number 3543-75-7

Chemical name 4-[5-[Bis(2-chloroethyl)amino]-1-methylbenzimidazol-2-yl]butanoic acid hydrochloride

Recommended use Specified quality tests and assay use only.

Recommended restrictions Not for use as a drug. Not for administration to humans or animals.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name U. S. Pharmacopeia

Address 12601 Twinbrook Parkway
Rockville
MD
20852-1790
United States

Telephone RS Technical Services 301-816-8129

Website www.usp.org

E-mail RSTECH@usp.org

Emergency phone number CHEMTREC within US & Canada 1-800-424-9300
CHEMTREC outside US & Canada +1 703-527-3887

2. Hazard(s) identification

Physical hazards Not classified.

Health hazards

Acute toxicity, oral	Category 3
Germ cell mutagenicity	Category 1
Carcinogenicity	Category 1
Reproductive toxicity	Category 1
Specific target organ toxicity, repeated exposure	Category 1 (bone marrow)

Environmental hazards Not classified.

OSHA defined hazards Not classified.

Label elements

Signal word Danger

Hazard statement Toxic if swallowed. May cause genetic defects. May cause cancer. May damage fertility or the unborn child. Causes damage to organs (bone marrow) through prolonged or repeated exposure.

Precautionary statement

Prevention Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Wear protective gloves/protective clothing/eye protection/face protection. Do not breathe dust. Wash thoroughly after handling.

Response If swallowed: Immediately call a poison center/doctor. Rinse mouth. If exposed or concerned: Get medical advice/attention.

Storage Store locked up.

Disposal Dispose of contents/container in accordance with local/regional/national/international regulations.

Hazard(s) not otherwise classified (HNOC) None known.

Supplemental information Potent pharmacologically active material.

3. Composition/information on ingredients

Substance

Chemical name	Common name and synonyms	CAS number	%
Bendamustine Hydrochloride		3543-75-7	100

4. First-aid measures

Inhalation Move to fresh air. Call a physician if symptoms develop or persist.

Skin contact Rinse skin with water/shower. Get medical attention if irritation develops and persists.

Eye contact Rinse with water. Get medical attention if irritation develops and persists.

Ingestion Call a physician or poison control center immediately. Rinse mouth. Do not induce vomiting without advice from poison control center. If vomiting occurs, keep head low so that stomach content doesn't get into the lungs. Do not use mouth-to-mouth method if substance is ingested. Induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device.

Most important symptoms/effects, acute and delayed Bone marrow suppression. Potent pharmacologically active material. Occupational exposure to small amounts may cause physiological effects.

Indication of immediate medical attention and special treatment needed Provide general supportive measures and treat symptomatically. Monitor hematologic abnormalities. Monitor cardiac rhythm.

General information Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposures. In the United States, the national poison control center phone number is 1-800-222-1222. If person is not breathing, give artificial respiration. If breathing is difficult, give oxygen if available. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention.

5. Fire-fighting measures

Suitable extinguishing media Water. Foam. Dry chemical or CO2. Use fire-extinguishing media appropriate for surrounding materials.

Unsuitable extinguishing media None known.

Specific hazards arising from the chemical No unusual fire or explosion hazards noted.

Special protective equipment and precautions for firefighters Wear suitable protective equipment.

Fire fighting equipment/instructions Use water spray to cool unopened containers. As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing.

Specific methods Use standard firefighting procedures and consider the hazards of other involved materials.

General fire hazards No unusual fire or explosion hazards noted.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures Keep unnecessary personnel away. Wear appropriate personal protective equipment. Avoid inhalation of dust from the spilled material. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation. For personal protection, see section 8 of the SDS.

Methods and materials for containment and cleaning up For waste disposal, see section 13 of the SDS. Avoid the generation of dusts during clean-up. Sweep up or vacuum up spillage and collect in suitable container for disposal. Clean surface thoroughly to remove residual contamination.

Environmental precautions Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling As a general rule, when handling USP Reference Standards, avoid all contact and inhalation of dust, mists, and/or vapors associated with the material. Clean equipment and work surfaces with suitable detergent or solvent after use. After removing gloves, wash hands and other exposed skin thoroughly. Select and use containment devices and personal protective equipment based on a risk assessment of material potency and exposure potential.

Conditions for safe storage, including any incompatibilities Store in tight container as defined in the USP-NF. This material should be handled and stored per label instructions to ensure product integrity.

8. Exposure controls/personal protection

Occupational exposure limits

The following constituents are the only constituents of the product which have a PEL, TLV or other recommended exposure limit. At this time, the other constituents have no known exposure limits.

Exposure limit values

Industrial Use

Material	Type	Value
Bendamustine Hydrochloride (CAS 3543-75-7)	TWA	0.001 mg/m3

Biological limit values No biological exposure limits noted for the ingredient(s).

Appropriate engineering controls No open handling. For laboratory operations, use approved ventilation or containment system (biological safety cabinet, ventilated balance enclosure, glovebox). Control exposures to below the occupational exposure level (if available). Select and use containment devices and personal protective equipment based on a risk assessment of exposure potential. Cover all containers for solutions and slurries while being transferred.

Individual protection measures, such as personal protective equipment

Eye/face protection Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

Skin protection

Hand protection Consider double gloves. Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Other Train employees in proper gowning and degowning practices. Wear disposable lab coat, disposable sleeve covers and two pair of gloves as appropriate for the task. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use. Do not wear protective garments in common areas (e.g., cafeterias) or out-of-doors.

Respiratory protection Use a powered air-purifying respirator (PAPR) with HEPA filters, disposable outerware and head cover for spill cleanup. Chose respiratory protection appropriate to the task and the level of existing engineering controls.

Thermal hazards Wear appropriate thermal protective clothing, when necessary.

General hygiene considerations Pharmacological effects may be seen with occupational exposure. Handling practices in this SDS are recommendations for laboratory use of reference standards. Procedures for any other uses or quantities should be determined after an appropriate assessment.

9. Physical and chemical properties

Appearance Appearance descriptions are general information and not specific to any USP lot.

Physical state Solid.

Form Solid.

Color White.

Odor Odorless.

Odor threshold Not available.

pH Not available.

Melting point/freezing point 334.4 °F (168 °C)

Initial boiling point and boiling range Not available.

Flash point Not available.

Evaporation rate Not available.

Flammability (solid, gas) Not available.

Upper/lower flammability or explosive limits

Flammability limit - lower (%) Not available.

Flammability limit - upper (%) Not available.

Explosive limit - lower (%) Not available.

Explosive limit - upper (%) Not available.

Vapor pressure < 0.0000001 kPa at 25 °C

Vapor density Not available.

Relative density Not available.

Solubility(ies)

Solubility (water) Insoluble (at pH 7).

Auto-ignition temperature Not available.

Decomposition temperature Not available.

Viscosity Not available.

Other information

Chemical family	Nitrogen mustard.
Molecular formula	C16H22Cl3N3O2
Molecular weight	394.72
pH in aqueous solution	3 - 4 (2.5 g/L)

10. Stability and reactivity

Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.
Conditions to avoid	Contact with incompatible materials.
Incompatible materials	None known.
Hazardous decomposition products	Irritating and/or toxic fumes or gases. Emits toxic fumes under fire conditions. NOx, Cl-.

11. Toxicological information

Information on likely routes of exposure

Inhalation	This material may cause: Systemic effects.
Skin contact	This material may cause: Systemic effects.
Eye contact	Knowledge about health hazard is incomplete.
Ingestion	Toxic if swallowed. Based on information from therapeutic use, this material may cause: Bone marrow suppression.
Symptoms related to the physical, chemical, and toxicological characteristics	Alkylating antineoplastics: Gastrointestinal disturbances. Hair loss. Central nervous system depression. Loss of appetite. Mouth sores.

Information on toxicological effects

Acute toxicity Toxic if swallowed.

Product	Species	Test Results
Bendamustine Hydrochloride (CAS 3543-75-7)		
Acute		
Oral		
LD50	Mouse	250 mg/kg
	Rat	200 mg/kg

Skin corrosion/irritation Knowledge about health hazard is incomplete.

Serious eye damage/eye irritation Knowledge about health hazard is incomplete.

Respiratory or skin sensitization

Respiratory sensitization	Knowledge about health hazard is incomplete.
Skin sensitization	Knowledge about health hazard is incomplete.

Germ cell mutagenicity May cause genetic defects.
Alkylating antineoplastic agents have been shown to increase genotoxic effects in both occupational and therapeutic exposures.

Mutagenicity

Ames test.
Result: Positive.
Mutagenicity, In vitro clastogenicity assay in human lymphocytes.
Result: Positive.
Mutagenicity, In vitro sister chromatid exchange assay
Result: Positive.
Mutagenicity, In vivo rat bone marrow micronucleus assay.
Result: Positive.

Carcinogenicity May cause cancer.
Secondary malignancies are potential delayed effects of alkylating antineoplastic agents. Risk seems to increase with long-term use. There is no clear indication whether the effect is related to their mutagenic potential or immunosuppressive action.

12.5 - 25 mg/kg/day Carcinogenicity
Result: Positive: Peritoneal sarcomas.
Species: Mouse
Test Duration: 4 days
62.5 mg/kg/day Carcinogenicity
Result: Positive: Mammary carcinomas and pulmonary adenomas.
Species: Rat
Test Duration: 4 days

IARC Monographs. Overall Evaluation of Carcinogenicity

Not listed.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not regulated.

US. National Toxicology Program (NTP) Report on Carcinogens

Not listed.

Reproductive toxicity May damage fertility or the unborn child.
Alkylating antineoplastic agents have been associated with severe birth defects when administered to mothers during pregnancy. Adverse fertility effects have been observed during therapy treatment in males and females. The effects appear to be dose related and length of therapy and may be irreversible.

Reproductivity

20 mg/kg Reproductivity / Developmental, administered intraperitoneally during gestation.
Result: Positive: Embryo and fetal lethality, and malformations in the offspring.
Species: Rat
70 mg/kg Reproductivity / Developmental, administered intraperitoneally during organogenesis.
Result: Positive: Fetotoxicity and malformations in the offspring. No maternal toxicity noted.
Species: Mouse

Specific target organ toxicity - single exposure Knowledge about health hazard is incomplete.

Specific target organ toxicity - repeated exposure Causes damage to organs (bone marrow) through prolonged or repeated exposure.

Aspiration hazard Based on available data, the classification criteria are not met.

Further information Potent pharmacologically active material. Occupational exposure to small amounts may cause physiological effects.

12. Ecological information

Ecotoxicity The product is not classified as environmentally hazardous. However, this does not exclude the possibility that large or frequent spills can have a harmful or damaging effect on the environment.

Persistence and degradability No data is available on the degradability of this product.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Other adverse effects No other adverse environmental effects (e.g. ozone depletion, photochemical ozone creation potential, endocrine disruption, global warming potential) are expected from this component.

13. Disposal considerations

Disposal instructions Dispose in accordance with all applicable regulations. Under RCRA, it is the responsibility of the user of the product to determine, at the time of disposal, whether the product meets RCRA criteria for hazardous waste.

Local disposal regulations Dispose in accordance with all applicable regulations.

Hazardous waste code The waste code should be assigned in discussion between the user, the producer and the waste disposal company.

Waste from residues / unused products Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).

Contaminated packaging Since emptied containers may retain product residue, follow label warnings even after container is emptied.

14. Transport information

DOT

UN number	UN2811
UN proper shipping name	Toxic solid, organic, n.o.s. (Bendamustine Hydrochloride)
Transport hazard class(es)	
Class	6.1
Subsidiary risk	-
Packing group	III

IATA

UN number	UN2811
UN proper shipping name	Toxic solid, organic, n.o.s. (Bendamustine Hydrochloride)
Transport hazard class(es)	
Class	6.1
Subsidiary risk	-
Packing group	III
Other information	
Passenger and cargo aircraft	Allowed with restrictions.
Cargo aircraft only	Allowed with restrictions.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not applicable.

DOT; IATA

General information It is the shipper's responsibility to determine the correct transport classification at the time of shipment.

15. Regulatory information

US federal regulations This product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories Immediate Hazard - Yes
Delayed Hazard - Yes
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 302 Extremely hazardous substance

Not listed.

SARA 311/312 Hazardous chemical Yes

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

US state regulations California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Australia	Australian Inventory of Chemical Substances (AICS)	No
Canada	Domestic Substances List (DSL)	No
Canada	Non-Domestic Substances List (NDSL)	No
China	Inventory of Existing Chemical Substances in China (IECSC)	No
Europe	European Inventory of Existing Commercial Chemical Substances (EINECS)	No
Europe	European List of Notified Chemical Substances (ELINCS)	No
Japan	Inventory of Existing and New Chemical Substances (ENCS)	No
Korea	Existing Chemicals List (ECL)	No
New Zealand	New Zealand Inventory	No
Philippines	Philippine Inventory of Chemicals and Chemical Substances (PICCS)	No
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)
A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date 09-26-2016

Revision date 02-23-2018

Version # 02

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