

 <b>Pharmaceutical Division</b>	<b>Bortezomib for Injection</b>		<b>Safety Data Sheet (SDS)</b>	
	Effective Date: <b>09MAY2022</b>	SDS No.: <b>SDS053</b>	Revision No: <b>02</b>	Page <b>1 of 10</b>

### Section 1 - Identification


- (a) **Product Identifier:** Bortezomib for Injection
- (b) **Product Code:** 70860-225
- Common/Trade Name:** Bortezomib for Injection
- Chemical Name:** [(1R)-3-methyl-1-[[[(2S)-1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl] boronic acid
- Chemical Family:** Proteasome Inhibitor
- (c) **Product Use:** Pharmaceutical, Injectable
- Product Type:** Regulated Prescription Drug
- Container Information:** Vial
- (d) **Distributor:** Athenex Pharmaceutical Division, 10 N. Martingale Road, Suite 230, Schaumburg, IL 60173, 847-886-9515
- (e) **Emergency Telephone:** 855-273-0154

### Section 2 - Hazards Identification

(a)	<b>Classification:</b>	Reproductive toxicity. Category 1A Specific Target Organ Toxicity – STOT Repeated exposure RE. Category 2 (Nervous System) Reproductive toxicity. Effects on or via lactation.
(b)	<b>Signal Word:</b>	Danger
	<b>Hazard Statement</b>	H360 – May damage fertility or the unborn child. H373 – May cause damage to organs through prolonged or repeated exposure. H362 May cause harm to breast-fed children.
	<b>Symbols</b>	

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	<b>Precautionary Statement(s)</b>	<p><b>Prevention:</b> P201 - Obtain special instructions before use.  P202 - Do not handle until all safety precautions have been read and understood.  P260 – Do not breathe dust/fume/gas/mist/vapors/spray.  P263 – Avoid contact during pregnancy and while nursing.  P280 - Wear protective gloves. Wear eye or face protection. Wear protective clothing.  P270 - Do not eat, drink or smoke when using this product.  P264 - Wash hands thoroughly after handling</p> <p><b>Response:</b> P308 + P313 - IF exposed or concerned: Get medical attention.  P314 – Get medical advice/attention if you feel unwell.</p> <p><b>Storage:</b> P405 - Store locked up.</p> <p><b>Disposal:</b> P501 - Dispose of contents and container in accordance with all local, regional, national, and international regulations.</p>
(c)	<b>Description of Hazards</b>	<p><i>Potential Health Effects:</i> This product is intended for therapeutic use only when prescribed by a physician. Potential adverse reactions from prescribed doses and overdoses are described in the package insert. Handling should only be performed by personnel trained and familiar with handling of potent active pharmaceutical ingredients. May cause irritation to eyes, skin and respiratory tract, nausea, vomiting, rash, diarrhea.</p> <p><i>Acute Health Effects:</i> The effects reported are from use of the drug product clinically or the testing of the drug substance in laboratory animals.</p> <p>In patients given the drug, Bortezomib produces many of the acute effects typical of drugs that kill rapidly growing cells, including effects on the hematological system, fatigue, nausea, vomiting, diarrhea, and fever. Other organ systems reported to be affected include the respiratory tract (shortness of breath), and nervous system (headache, dizziness, and peripheral neuropathy). Some of the acute effects may be delayed in onset, such as the effects on the hematological system, which are characterized by decreased white blood cells, platelets and red blood cells, and may occur several days or weeks following the acute exposure. These effects may potentially occur from acute (severe spill) or repeated overexposure in occupational settings.</p> <p><i>Chronic Health Effects:</i> based on other antineoplastic agents and data on Bortezomib, the spectrum of effects after chronic exposure would be expected to be similar to those after acute exposure. Initial repeated dose studies in laboratory animals have shown similar effects as acute studies.</p> <p><i>Target Organs:</i> Eyes, Skin, Respiratory system, Hematological system, peripheral nervous system, liver, kidney, reproductive system.</p>
(d)	<b>Unknown Acute Toxicity</b>	N/A

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### Section 3 – Composition / Information on Ingredients


(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure	(c) CAS No.	(d) Impurities / Stabilizing Additives
Bortezomib	Bortezomib	3.5 mg	390800-88-1	N/A
Mannitol, USP	Mannitol	35 mg	69-65-8	N/A

### Section 4 – First Aid Measures

- Eye Exposure:** Immediately flush eyes with plenty of water for 15 – 20 minutes. Ensure adequate flushing of the eyes by separating the eyelids with fingers. Get immediate medical attention.
- Skin Exposure:** Immediately wash skin with plenty of soap and water for 15-20 minutes, while removing contaminated clothing and shoes. Get medical attention if irritation develops or persists.
- Ingestion:** If swallowed, do NOT induce vomiting. Call a physician or poison control center immediately. Never give anything by mouth to an unconscious person.
- Inhalation:** If inhaled, remove to fresh air. If not breathing, give artificial respiration or give oxygen by trained personnel. Seek immediate medical attention.
- Notes to Physician:** Material is a cytotoxic anticancer drug

### Section 5 – Fire-fighting Measures

- (a) **Extinguishing Media** Use alcohol resistant foam, carbon dioxide, dry chemical or water fog or spray when fighting fires.
- (b) **Hazardous Combustion Byproducts:** Carbon monoxide and nitrogen oxides.

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**(c) Special Protective Equipment / Precautions:**

As in any fire, wear Self-Contained Breathing Apparatus (SCBA), MSHA/NIOSH (approved or equivalent) and full protective gear.  
Evacuate area of unprotected personnel. Use cold water spray to cool fire exposed containers to minimize risk of rupture. Do not enter confined fire space without full protective gear. If possible, contain fire run-off water.

### Section 6 - Accidental Release Measures

**Spill:** Contain spills with an inert, absorbent material such as soil, sand, or oil dry, then place in a chemical waste container. After removal, flush spill area with soap and water to remove trace residue.

**Release to Air:** Avoid personal contact and breathing vapors or mists.

**Release to Water:** Avoid runoff into storm sewers, ditches, and waterways.

### Section 7 - Handling and Storage

**General Handling:** When handling pharmaceutical products, avoid all contact and inhalation of vapors, mists and/or fumes. Use with adequate ventilation. Use only in accordance with directions. Handling should only be performed by personnel trained and familiar with handling of potent active pharmaceutical ingredients.


**Storage Conditions:** Unopened vials may be stored at controlled room temperature 25°C (77°F); excursions permitted between 15°C and 30°C (59°F and 86°F). Retain in original package to protect from light.

### Section 8 - Exposure Controls / Personal Protection

**(a) Exposure Limits:** None

**(b) Engineering Controls**

Use appropriate engineering control such as process enclosures, local exhaust ventilation, or other engineering controls to control airborne levels below recommended exposure limits. Good general ventilation should be sufficient to control airborne levels. Where such systems are not effective wear suitable personal protective equipment, which performs satisfactorily and meets OSHA or other recognized standards. Consult with local procedures for selection, training, inspection and maintenance of the personal protective equipment.


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**(c) Individual Protection Measures**

Respiratory Protection:	A NIOSH approved air-purifying respirator with an organic vapor cartridge or canister may be permissible under certain circumstances where airborne concentrations are expected to exceed exposure limits. Protection provided by air purifying respirators is limited. Use a positive pressure air supplied respirator if there is any potential for an uncontrolled release, exposure levels are not known, or any other circumstances where air purifying respirators may not provide adequate protection.
Eye Protection:	Chemical splash goggles. Wear a face shield also when splash hazard exist.
Skin Protection:	Protective laboratory coat, apron, or disposable garment recommended. Wear appropriate protective gloves. Consult glove manufacturer's data for permeability data. Nitrile rubber or natural rubber gloves are recommended.
Other Protective Equipment:	Facilities storing or utilizing this material should be equipped with an eyewash and a deluge shower safety station. Decontaminate all protective equipment after use. Exercise extreme care when working with sharps/needles/syringes and potent drugs.

**Section 9 - Physical and Chemical Properties**

<b>(a) Appearance</b>	White to off-white cake or powder.
<b>(b) Odor</b>	Not available
<b>(c) Odor Threshold</b>	Not available
<b>(d) pH</b>	Not available
<b>(e) Melting Point:</b>	140 – 150 °C
<b>(f) Initial Boiling Point:</b>	Not available
<b>(g) Flash Point</b>	Not available
<b>(h) Evaporation Rate:</b>	Not available
<b>(i) Flammability</b>	Not available
<b>(j) Upper Lower Flammability or Explosion Limits</b>	Not available
<b>(k) Vapor Pressure:</b>	Not available
<b>(l) Vapor Density:</b>	Not available
<b>(m) Relative Density</b>	Not available

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<b>(n)</b>	<b>Solubility(ies)</b>	Soluble in water (3.3 to 3.8 mg/mL at pH range of 2 to 6.5)
<b>(o)</b>	<b>Partition Coefficient: n-octanol/water</b>	Not available
<b>(p)</b>	<b>Auto-ignition Temperature</b>	Not available
<b>(q)</b>	<b>Decomposition Temperature</b>	Not available
<b>(r)</b>	<b>Viscosity</b>	Not available

**Section 10 - Stability and Reactivity**

<b>(a)</b>	<b>Reactivity</b>	Stable under normal conditions of use.
<b>(b)</b>	<b>Chemical Stability</b>	Stable at normal temperatures and pressures
<b>(c)</b>	<b>Possibility of Hazardous Reactions</b>	Hazardous polymerization does not occur
<b>(d)</b>	<b>Conditions to Avoid</b>	Protect from light
<b>(e)</b>	<b>Incompatible Materials</b>	Avoid contact with oxidizing agents
<b>(f)</b>	<b>Hazardous Decomposition Products</b>	Carbon oxides. Nitrogen oxides (NO <sub>x</sub> )

**Section 11 - Toxicological Information**

<b>(a)</b>	<b>Likely Routes of Exposure</b>	Ingestion, inhalation, skin contact, mucous membranes.
<b>(b)</b>	<b>Symptoms related to the physical, chemical and toxicological characteristics</b>	<i>Eye:</i> Moderate to severe eye irritant <i>Skin:</i> Moderate to severe skin eye irritant <i>Inhalation:</i> Inhalation data not identified. Based on the high acute toxicity reported in non-clinical IV studies, a potential for toxicity via the inhaled route cannot be excluded. <i>Ingestion:</i> Very toxic by ingestion

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<b>(c)</b>	<p><b>Delayed and immediate effects and chronic effects from short- and long-term exposure</b></p>	<p>Repeated occupational overexposure may cause fatigue and fever, and effects on the hematological (decreases in hemoglobin/anemia, blood counts and platelets), gastrointestinal (nausea, diarrhea, vomiting, abdominal pain), and nervous systems (headache, peripheral neuropathy). May affect fertility and fetal development based on mechanism and animal toxicity studies.</p> <p><i>Mutagenicity:</i> Bortezomib API showed clastogenic activity in the in vitro chromosomal aberration assay using Chinese hamster ovary cells, but bortezomib was not genotoxic in the in vitro mutagenicity assay (Ames test), or in the in vivo micronucleus assay in mice.</p> <p><i>Reproductive Toxicity:</i> Fertility studies have not been performed, but degenerative effects have been observed in the ovaries and testes of rats in a 6 month toxicity study. Bortezomib API could affect male or female fertility.</p> <p><i>Teratogenicity:</i> Not conducted</p>
<b>(d)</b>	<p><b>Other Toxicological Information</b></p>	<p>Bortezomib API is a cytotoxic antineoplastic compound that exerts its biological effects by inhibiting the activity of the proteasome, a macromolecular complex found in all cells that plays a critical role in protein homeostasis. In local tolerance studies bortezomib showed minimal tissue irritancy; however direct skin contact should be avoided. Bortezomib API is acutely lethal in animals, when delivered intravenously at sufficient doses, and death is due to cardiovascular effects. Systemic, therapeutic exposure to bortezomib in humans is associated with a variety of adverse events, including peripheral neuropathy, hypotension, cardiac disorders, pulmonary disorders, reversible posterior leukoencephalopathy syndrome (RPLS), gastrointestinal disturbances (nausea, diarrhea, constipation, vomiting, decreased platelet count and neutrophil counts in the blood, tumor lysis syndrome, and liver disturbances.</p>


**Acute Toxicity:** Not available.

**Hazardous Chemical Listings**

NTP: Not Listed

IARC: Not Listed

OSHA: Not Listed

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**Section 12 - Ecological Information**

<b>(a)</b>	<b>Ecotoxicity</b>	No Data Available
<b>(b)</b>	<b>Persistence and degradability</b>	No Data Available
<b>(c)</b>	<b>Bioaccumulative potential</b>	No Data Available
<b>(d)</b>	<b>Mobility in soil</b>	No Data Available
<b>(e)</b>	<b>Other Adverse Effects</b>	No Data Available

**Section 13 - Disposal Considerations**

**Waste Disposal:** All wastes containing the material should be properly labeled. Dispose of any waste residues according to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

**Section 14 - Transport Information**

**DOT**

DOT Shipping Name:	Not Regulated.
DOT UN Number	Not Regulated.
DOT Hazard Class	Not Regulated.
DOT Packing Group	Not Regulated.


**IATA**

IATA Shipping Name:	Not Regulated.
IATA UN Number	Not Regulated.
IATA Hazard Class	Not Regulated.
IATA Packing Group	Not Regulated.

**Section 15 - Regulatory Information**

Below is selected regulatory information chosen primarily for possible Athenex Pharmaceutical Division usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.



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**U.S. Regulations:**

TSCA – Not regulated

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

**Section 16 - Other Information**


As of the date of effectiveness, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:

Athenex Pharmaceutical Division  
10 N. Martingale Road, Suite 230  
Schaumburg, IL 60173  
847-886-9515

**Glossary:** This glossary contains definitions of general terms used in SDSs. Not all of these Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AICS	Australian Inventory of Chemical Substances
AIHA	American Industrial Hygiene Association
ANSI	American National Standards Institute
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
DSL	Domestic Substances List
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of Notified Chemical Substances
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEPA	High Efficiency Particulate Air (Filter)
HMIS	Hazardous Materials Identification System
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport
IMO	International Maritime Organization

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KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NDSL	Non-Domestic Substances List
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPDES	National Pollutant Discharge Elimination System
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations
USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)
WHMIS	Workplace Hazardous Materials Information System