SAFETY DATA SHEET

SECTION 1 : IDENTIFICATION

Product Name:	**Bortezomib for Injection**
Synonyms:	None.
Product Use/Restriction:	Antineoplastic.
Manufacturer Name:	Fresenius Kabi USA, LLC
Address:	Three Corporate Drive Lake Zurich, Illinois 60047
General Phone Number:	(847) 550-2300
Customer Service Phone Number:	(888) 386-1300
Health Issues Information:	(800) 551-7176
SDS Revision Date:	February 04, 2016

SECTION 2 : HAZARD(S) IDENTIFICATION

GHS Pictograms:

Signal Word: DANGER.

GHS Class:
Reproductive toxicity. Category 1A.
Specific Target Organ Toxicity -STOT Repeated exposure RE. Category 2 (Nervous system).
Reproductive toxicity. Effects on or via lactation.

Hazard Statements:
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.

Precautionary Statements:
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/vapours/spray.
P263 - Avoid contact during pregnancy and while nursing.
P264 - Wash hands thoroughly after handling.
P270 - Do not eat, drink or smoke when using this product.
P280 - Wear protective gloves/protective clothing/eye protection/face protection.
P308+P313 - IF exposed or concerned: Get medical advice/attention.
P314 - Get medical advice/attention if you feel unwell.
P405 - Store locked up.
P501 - Dispose of contents/container in accordance with Local, State, Federal and Provincial regulations.

Route of Exposure: Inhalation Ingestion Eye contact Skin Absorption. Injection.

Potential Health Effects:
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, diarrheah.

Acute Health Effects:
The effects reported are from use of the drug product clinically or the testing of the drug substance in laboratory animals.
In patients given the drug, Bortezomib produces many of the acute offsets 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 effected 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 sellings.

Chronic Health Effects:
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.

Signs/Symptoms:
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 based on animal toxicity studies.

Target Organs:
Eyes, Skin, Respiratory system, Hematological system, Peripheral nervous system, Liver, Kidney, Reproductive system

SECTION 3 : COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS#	Ingredient Percent	EC Num.
Bortezomib	179324-69-7	9.09 by weight	
Mannitol	69-65-8	90.91 by weight	200-711-8

SECTION 4 : FIRST AID MEASURES

Eye Contact:	Immediately flush eyes with plenty of water for at least 15 to 20 minutes. Ensure adequate flushing of the eyes by separating the eyelids with fingers. Get immediate medical attention.
Skin Contact:	Immediately wash skin with plenty of soap and water for 15 to 20 minutes, while removing contaminated clothing and shoes. Get medical attention if irritation develops or persists.
Inhalation:	If inhaled, remove to fresh air. If not breathing, give artificial respiration or give oxygen by trained personnel. Seek immediate medical attention.
Ingestion:	If conscious, flush mouth out with water immediately. Call a physician or poison control center immediately. Do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person.
Other First Aid:	For Adverse Event Information, please call (800) 551-7176.

SECTION 5 : FIRE FIGHTING MEASURES

Flash Point:	Not established.
Flash Point Method:	Not established.
Auto Ignition Temperature:	Not established.
Lower Flammable/Explosive Limit:	Not established.
Upper Flammable/Explosive Limit:	Not established.
Fire Fighting Instructions:	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.
Extinguishing Media:	Use alcohol resistant foam, carbon dioxide, dry chemical, or water fog or spray when fighting fires involving this material. Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Protective Equipment:	As in any fire, wear Self-Contained Breathing Apparatus (SCBA), MSHA/NIOSH (approved or equivalent) and full protective gear.
Hazardous Combustion Byproducts:	Thermal decomposition products may include smoke and toxic fumes. Oxides of carbon, oxides of nitrogen and other organic substances may be formed. Other undetermined low molecular weight hydrocarbon compounds may be released in small quantities depending upon specific conditions of combustion.

SECTION 6 : ACCIDENTAL RELEASE MEASURES

Personal Precautions:	Evacuate area and keep unnecessary and unprotected personnel from entering the spill area. Avoid personal contact and breathing vapors or mists. Use proper personal protective equipment as listed in Section 8.
Environmental Precautions:	Avoid runoff into storm sewers, ditches, and waterways.
Methods for containment:	Contain spills with an inert absorbent material such as soil, sand or oil dry.
Methods for cleanup:	Absorb spill with inert material (e,g., dry sand or earth), then place in a chemical waste container. After removal, flush spill area with soap and water to remove trace residue.

SECTION 7 : HANDLING and STORAGE

Handling:	When handling pharmaceutical products, avoid all contact and inhalation of vapor, 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:	Unopened vials may be stored at controlled room temperature 20 - 25º C (68 - 77º F). Excursions permitted from 15 to 30º C (59 to 86º F). [See USP Controlled Room Temperature]. Retain in original package to protect from light.

SECTION 8: EXPOSURE CONTROLS, PERSONAL PROTECTION

Engineering Controls:	General ventilation is sufficient if this product is being used in a controlled medical setting (clinic, hospital, medical office) for its sole intended parenteral (injection) purpose. Otherwise, use appropriate engineering control such as process enclosures, local exhaust ventilation, or other engineering controls including use of a biosafety cabinet / fume hood to control airborne levels below recommended exposure limits.
Eye/Face Protection:	Chemical splash goggles. Wear a face shield also when splash hazard exist.
Skin Protection Description:	Protective laboratory coat, apron, or disposable garment recommended.
Hand Protection Description:	Wear appropriate protective gloves. Consult glove manufacturer's data for permeability data. Nitrile rubber or natural rubber gloves are recommended.
Respiratory Protection:	No personal respiratory protective equipment is normally required when this product is being used/administered by a licensed healthcare practitioner (i.e. an end-user such as a clinician / doctor / nurse) for its sole intended parenteral (injection) purpose in a controlled medical setting. The need for respiratory protection will vary according to the airborne concentrations and environmental conditions. A NIOSH approved air-purifying respirator with an organic vapor cartridge or canister may be permissible

	under certain circumstances. Consult the NIOSH web site (http://www.cdc.gov/niosh/npptl/topics/respirators/) for a list of respirator types and approved suppliers.
Other Protective:	Consult with local procedures for selection, training, inspection and maintenance of the personal protective equipment.

EXPOSURE GUIDELINES

Mannitol :

Guideline ACGIH:	TLV-TWA: 2 mg/m3 TLV-STEL: 6 mg/m3

SECTION 9 : PHYSICAL and CHEMICAL PROPERTIES

Physical State:	Lyophilized powder.
Color:	White
Odor:	Not determined.
Odor Threshold:	Not determined.
Boiling Point:	Not determined.
Melting Point:	Not determined.
Specific Gravity:	Not determined.
Solubility:	Not determined.
Vapor Density:	Not determined.
Vapor Pressure:	Not determined.
Evaporation Rate:	Not determined.
pH:	Not determined.
Viscosity:	Not determined.
Flash Point:	Not established.
Flash Point Method:	Not established.
Auto Ignition Temperature:	Not established.
VOC Content:	Not determined.

SECTION 10 : STABILITY and REACTIVITY

Chemical Stability:	Stable under normal temperatures and pressures.
Hazardous Polymerization:	Not reported.
Conditions to Avoid:	Protect from light.
Incompatible Materials:	Avoid contact with oxidizing agents.
Special Decomposition Products:	Carbon oxides. Nitrogen oxides (NOx).

SECTION 11 : TOXICOLOGICAL INFORMATION

Bortezomib :

Ingestion:	No single dose oral toxicity studies in rats or mice. Most studies conducted either by intravenous or intraperitoneal administration. In one study in the monkey, an oral dose of 0.7 mg/kg was fatal in a female monkey, but not in a male monkey tested at this dose. Based on this limited data and intravenous data indicating significant potential to be toxic or lethal at doses < 2 mg/kg in rats and mice, bortezomib should be considered highly acutely toxic.
Sensitization:	Moderate to severe skin irritant based on studies in rabbits. Considered to be severe eye irritant based on the skin irritation study. No studies assessing allergic skin potential.
Chronic Effects:	Repeated Dose Studies: Administration by intravenous injection has produced effects consistent with other cytotoxic drugs including effects on the gastrointestinal tract, hematological system, liver, peripheral nervous system, kidney and liver.
Mutagenicity:	Studies evaluating gene mutation were negative (Ames gene mutation assay). Positive in vitro chromosomal aberration study in Chinese hamster ovary cells most likely due to pharmacological mechanism of action. Not a clastogen in vivo (mouse micronucleus test),
Reproductive Toxicity:	Bortezomib has not been evaluated for reproductive toxicity (effects on fertility). Repeated dose studies in laboratory animals have caused degenerative changes in the ovary and testes.
Teratogenicity:	Developmental Toxicity: At low doses in laboratory animal (< 0.05 mg/kg/day by injection) during gestation, Bortezomib at maternally toxic doses was embryo lethal and embryo toxic but did not cause a significant increase in malformations in the rat and rabbit. Because of the embryo lethal effects at low doses, it should be considered a reproductive toxicant but not a teratogenic agent.
Other Toxicological Information:	Intravenous - mouse TDLo: 6 mg/kg/3W (intermittent) [Tumorigenic - active as anti-cancer agent] Intravenous - Primate monkey LDLo: 0.3 mg/kg [Cardiac - pulse rate Vascular - BP lowering not characterized in autonomic section] Intraperitoneal - mouse TDLo: 5 mg/kg/14D (intermittent) [Vascular - structural changes in vessels Tumorigenic - active as anti-cancer agent] Unreported - Human : 0.147 mg/kg/2W (intermittent) [Peripheral Nerve and Sensation - sensory change involving peripheral nerve]

Mannitol :

Ingestion:	Oral - Rat LD50 - Lethal dose, 50 percent kill: 13500 mg/kg [Details of toxic effects not reported other than lethal dose value] (RTECS)

SECTION 12 : ECOLOGICAL INFORMATION

Effect of Material On Aquatic Life:	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 federal, state and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill should be discharged in an environmentally safe manner, e.g. appropriately permitted municipal or on cite wastewater treatment facility.

SECTION 14 : TRANSPORT INFORMATION

DOT Shipping Name:	Medicine, solid, toxic, n.o.s.
DOT UN Number:	UN3249
DOT Hazard Class:	6.1
DOT Packing Group:	II
IATA Shipping Name:	Medicine, solid, toxic, n.o.s.
IATA UN Number:	UN3249
IATA Hazard Class:	6.1
IATA Packing Group:	II

SECTION 15 : REGULATORY INFORMATION

Mannitol :

TSCA Inventory Status:	Listed
Canada DSL:	Listed
EC Number:	200-711-8

SECTION 16 : ADDITIONAL INFORMATION

HMIS Ratings:

HMIS Health Hazard:	3*
HMIS Fire Hazard:	1
HMIS Reactivity:	1
HMIS Personal Protection:	X

SDS Revision Date:	February 04, 2016
SDS Revision Notes:	"GHS Update"
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