MATERIAL SAFETY DATA SHEET

1. Identification

Product identifier

Product Name: Bortezomib for Injection

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name	Reliance Life Sciences Pvt. Ltd.
Address	Dhirubhai Ambani Life Sciences Center (DALC), R-282, TTC Area of MIDC, Thane – Belapur Road, Rabale, Navi Mumbai – 400701, Maharashtra, India.

Emergency phone number + 91-22-6767 8000

2. Hazard(s) identification

Classification of the chemical in accordance with CFR 1910.1200(d) (f):

GHS Pictograms:

GHS Class: Toxic, Category 3. Eye Damage, Category 1. Skin Irritant, Category 3. Reproductive hazard, Category 2.

Hazards not otherwise classified that have been identified during the classification process:

Emergency Overview: Bortezomib drug substance is a specific proteasome inhibitor used in anti-cancer treatments. DANGER! Toxic-Contains a pharmaceutically active ingredient. Handling should only be performed by personnel trained and familiar with handling of potent active pharmaceutical ingredients. Avoid skin contact, eye contact, and inhalation. Exercise due care: wear suitable protective clothing, gloves and eye /face protection.

Exposure Route: May be absorbed following ingestion, inhalation and through skin contact or contact with mucous membranes (this includes eyes).

Potential Health Effects:

Eye: Moderate to severe eye irritant

Skin: Moderate to severe skin eye irritant

Inhalation: 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.

Ingestion: Very toxic by ingestion

Chronic Effects: 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.

Target Organs: See Chronic Health Effects for potential target organ toxicity.

3. Composition/information on ingredients

Chemical Name	CAS#	Ingredient Percent
Excipients (Mannitol)	69-65-8	90% by weight
Bortezomib	390800-88-1	10% by weight

4. First-aid measures

Description of necessary 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 eye lids 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 swallowed, do NOT induce vomiting. Call a physician or poison control center immediately. Never give anything by mouth to a n unconscious person.

Indication of immediate medical attention and special treatment needed:

Note to Physicians: Material is a cytotoxic anticancer drug

5. Fire-fighting measures

Suitable and unsuitable extinguishing media:

Suitable Extinguishing Media: Use alcohol resistant foam, carbon dioxide, dry chemical, or water fog or spray when fighting fires involving this material.

Specific hazard arising from the chemical

Hazardous Combustion Byproducts: Carbon Monoxide and Nitrogen

Specific hazard arising from the chemical

Hazardous Combustion Byproducts: Carbon Monoxide and Nitrogen

Protective Equipment: As in any fire, wear Self-Contained Breathing Apparatus (SC BA), MSHA/NIO SH (approved or equivalent) and full protective gear.

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.

6. Accidental release measures

Environmental precautions:

Environmental Precautions: Dispose of all collected material as pharmaceutical biological/medical waste in accordance with applicable local, state and federal waste disposal regulations

Methods and materials for containment and cleaning up:

Spill Cleanup Measures: Liquid form; Absorb spill with inert material (e.g., dry sand or earth), then place in a chemical waste container. Provide ventilation. Clean up spills immediately observing precautions in the protective equipment section. After removal, flush spill area with soap and water to remove trace residue. Solid or powder form; do not raise dust. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize powder from entering the air. Add excess liquid to allow for the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak proof container suitable for disposal. After removal flush spill area with soap and water to remove trace residue.

7. Handling and storage precautions for safe

Precautions for safe handling:

Handling: Use with adequate ventilation. Wash thoroughly after handling. Avoid contact with eyes and skin. Avoid inhaling Dust, vapor, or mist. Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personnel protective equipment if needed).

Hygiene Practices: Wash thoroughly after handling. Conditions for safe storage, including any incompatibilities:

Storage:

Store at a controlled room temperature of 25ºC; excursions permitted from 15ºC to 30ºC. Retain vials in original package to protect from light.

8. Exposure controls

Guideline Info: None currently established by OSHA, NIOSH or ACGIH. Drug substance is highly toxic and potent

Appropriate engineering controls

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.

Individual protection measures

Eye /Face Protection: Wear appropriate protective glasses or splash goggles as described by 29 CFR 1910.133, OSHA eye and face protection regulation, or the European standard EN 166.

Skin Protection: Wear appropriate protective gloves and other protective apparel to prevent skin contact. Consult manufacturer's data for permeability data.

Respiratory Protection: ANIOSH 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.

Other Protective: Facilities storing or utilizing this material should be equipped with an eye wash and a deluge shower safety station. Decontaminate all protective equipment's after use. Exercise extreme care when working with sharps/needle/syringe/potent drugs.

9. Physical and chemical properties

Physical State Appearance:	White to off-white cake or powder.
Boiling Point:	Not determined
Melting Point:	Not determined
Density:	Not determined
Solubility:	Soluble in water
Vapor Density:	Not determined
Vapor pressure:	Not determined
Percent Volatile:	Not determined
Molecular Formula:	$C_{57}H_{69}B_3N_{12}O_9$ (Bortezomib drug substance)
Molecular Weight:	Mixture

Lower Flammable /Explosive Limit: Not determined

Upper Flammable /Explosive Limit: Not determined

Auto Ignition Temperature: Not determined

10. Stability and reactivity

Chemical Stability

Chemical Stability: Pharmacologically stable

Possibility of hazardous reactions:

Hazardous Polymerization: Not reported.

Conditions to avoid and incompatible material: Not known

11. Toxicological information

Inhalation: Not tested.

Ingestion: Not tested

Carcinogenicity: IARC, NTP, and OSHA studies not conducted

Mutagenicity: Bortezomib drug substance 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.

Reproductive Toxicity: 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 could affect male or female fertility.

Teratogenicity: Not conducted

Other Toxicological Information: Bortezomib is a cytotoxic antineoplastic compound that exerts its biological effects 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 is acutely lethal in animals, when delivered intravenously at sufficient dose and death is due to cardiovascular effects. Systemic therapeutic exposure to bortezomib in humans is associated with 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

12. Ecological information

Ecotoxicity

Ecotoxicity: No Data

Other adverse effects

Effect of Material on Aquatic Life: No Data

13. Disposal considerations

Description of waste:

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

14. Transport information

DOT Shipping Name:	Not regulated
DOT UN Number:	Not regulated
DOT Hazard Class:	Not regulated
DOT Packing Group:	Not regulated
IATA Shipping Name:	Not regulated
IATA UN Number:	Not regulated
IATA Hazard Class:	Not regulated
IATA Packing Group:	Not regulated

15. Regulatory information

Safety, health and environmental regulations specific for the product

TSCA Inventory Status: Not listed

SARA: No Data

California PROP 65: No Data

Canada WHMIS: Drugs are, however, if not a drug, the most appropriate classification for product would be Class D, Division 1, Subdivision A; based on its potential to be cytotoxic and a reproductive or developmental toxicant

Risk Phrases:	R 28 Very toxic if swallowed.
	R 38 Irritating to skin.
	R 41 Risk of serious damage to eyes.
	R 48 Toxic: danger of serious damage to health by prolonged exposure.
	R 62 Possible risk of impaired fertility.
	R 63 Possible risk of harm to the unborn child.
Safety Phrase:	S 24/25 Avoid contact with skin and eyes.
	S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
	S 28 After contact with skin, wash immediately with plenty of water.
	S 36/37/39 Wear suitable protective clothing, gloves and eye /face protection.

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

HMIS Ratings:

HMIS Health Hazard: 4

HMIS Fire Hazard: 1

HMIS Reactivity: 0

HMIS Personal Protection: X

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

End of Safety Data Sheet