



## SAFETY DATA SHEET

**Product code:** JANBEVELCADE

**Revision Date:** 28-Aug-2007

### 1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

**Supplier:**

J&J Pharmaceutical Research & Development  
A division of Janssen Pharmaceutica NV  
Turnhoutseweg 30  
2340 Beerse  
Belgium  
+32 14 602111

**Email:** RA-JANBE-SAFETYDA@JANBE.JNJ.COM

**Emergency telephone number:** +32 14 602444  
**Product name:** VELCADE for injection  
**Product code:** JANBEVELCADE  
**Synonyms:** Bortezomib for injection.

### 2. HAZARDS IDENTIFICATION

**General hazard information:** Cytotoxic drug.  
Very toxic if inhaled, in contact with skin and if swallowed.  
This product contains ingredients which may have reproductive effects.  
Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.  
Irritating to eyes, respiratory system and skin.

**Indication of danger:** T+ - Very toxic.



**Most important hazards**

**Risk Phrases:**

R26/27/28 - Very toxic by inhalation, in contact with skin and if swallowed.

R36/38 - Irritating to eyes and skin.

R48/23/24 - Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin.

**Carcinogenicity rating:**

**J & J** None.

**EC:** None.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

Components	CAS Number	Weight %	Synonyms	EINECS-No.	Classification
Mannitol	69-65-8	90		200-711-8	-
Bortezomib	179324-69-7	10			T+; R26/27/28 Xi; R36/38 T; R48/23/24

### 4. FIRST AID MEASURES

<b>Eye contact:</b>	In the case of contact with eyes, rinse immediately with plenty of water for 15 minutes and seek medical attention.
<b>Skin contact:</b>	After contact with skin, wash immediately with plenty of water. Immediately remove contaminated clothing and shoes and place in sealable, properly labeled waste disposal bag. Over bag into a sealable, properly labeled waste disposal bag. Material must be disposed of as hazardous drug waste. Seek medical attention if symptoms appear.
<b>Ingestion:</b>	If ingested, seek medical attention immediately and show the label.
<b>Inhalation:</b>	Move to fresh air immediately. If experiencing difficulty breathing, seek medical attention.
<b>Notes to physician:</b>	Treat symptomatically. Please refer to J&J OEL Monograph for Velcade (Bortezomib) on medical monitoring guidelines for personnel working with cytotoxic compounds.
<b>Protection of first-aiders:</b>	Please wear eye and skin protection.

### 5. FIRE-FIGHTING MEASURES

<b>Suitable extinguishing media:</b>	Water fog or mist. carbon dioxide (CO <sub>2</sub> ). dry powder. dry sand. foam.
<b>Extinguishing media which must not be used for safety reasons:</b>	None.
<b>Specific hazards:</b>	None.
<b>Special protective equipment for firefighters:</b>	Wear a self-contained breathing apparatus and full protective gear.
<b>Combustion products or resulting gases:</b>	Carbon dioxide (CO <sub>2</sub> ) Carbon monoxide Nitrogen oxides (NO <sub>x</sub> ) water

### 6. ACCIDENTAL RELEASE MEASURES

<b>Personal precautions:</b>	For milligram quantities: Disposable dust impervious protective suit and shoe covers. Full face negative pressure respirator with HEPA (ABEK-P3 in EU) cartridges. Two pairs of FDA approved "chemo" gloves. The outer glove shall be taped to the jumpsuit. For gram quantities: Clean-up personnel must wear self-contained breathing apparatus (SCBA) and totally encapsulated chemical resistant suit. Two pairs of FDA approved "chemo" gloves. The outer glove shall be taped to the jumpsuit. 2 pairs of gloves chemically-resistant to the decontamination solution/solvent. The outer glove shall be taped to the jumpsuit.
<b>Environmental precautions:</b>	Do not allow significant quantities of product to enter drains, sewers or public waterways.

## 6. ACCIDENTAL RELEASE MEASURES

**Methods for cleaning up:** Evacuate area.  
Next, use disposable towels moistened with an appropriate cleaning agent (i.e. solvent, detergent and water, etc.) to complete cleaning process. A designated HEPA vacuum can be used as an alternative cleaning method for large spills of powder. All waste must be placed in a sealable, properly labeled waste disposal bag. Over bag into a sealable, properly labeled waste disposal bag. Material must be disposed of as hazardous drug waste.

## 7. HANDLING AND STORAGE

### Handling:

**Technical measures/precautions:**

**Safe handling advice:**

Handle and store per labeled instructions.

Work only in a designated area. Handle on easily cleanable, non-porous, smooth surfaces. Refer to Section 8 for exposure controls and personal protection.

### Storage:

**Technical measures/storage conditions:**

Store in tightly sealed containers. Protect from moisture. Primary containers shall be overpacked into Nalgene or other sealed unbreakable containers. Appropriate warning labels shall be affixed to both containers. Compounds shall be transported only when overpacked as described above and on carts or transport devices that minimize the risk of spills. Primary containers shall be tightly sealed immediately after use. Sealed primary containers shall be handled only with gloves. Contamination of the exterior of the primary container should be exposed.

**Incompatible products:**

No special restrictions on storage with other products.

### Specific use(s):

None under normal use.

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

### Exposure limits

Components	J&J - OEL (TWA - 8 hr)	J&J - OEL (STEL)	J&J - OEL (Ceiling)	J&J - PBOEL	ASL
Bortezomib (10%) 179324-69-7	530 ng/m <sup>3</sup>			Category 4 Repro	0.2 µg/m <sup>2</sup>

### Exposure controls / personal protection

#### **Engineering controls:**

Vented balance safety enclosures required for weighing/transferring or manipulating less than 200 milligram amount of dry solids. Glove box isolater required for greater than 200 milligram quantity manipulating of dry solids. All contaminant devices shall be exhausted directly following HEPA filtration.

Activities that can result in the generation or release of liquid aerosols, splatters or sprays require the use of the following containment devices:

- Directional laminar flow cabinets (vertical) equipped with HEPA filters.
- Type II B 2 biological safety cabinets.
- Glove box isolators.

Containment devices must be exhausted directly through a dedicated stack. Exhausted air may not be recirculated back to the room.

Directional laminar flow cabinets (vertical) shall also be used to control powder aerosols that may be released from vacuum ovens.

<b>Respiratory protection:</b>	Engineering Controls are required for handling Category 4 compounds. Respirators providing HEPA filtration (ABEK-P3 in EU) are required for dosing animals and for all related animal care activities, such as cage washing, handling excetera and bedding changes. Respirators shall also be used in the event of spills and for non-routine work activities, such as changing HEPA filters or cleaning biological safety cabinets. Please consult your local industrial hygienist to obtain the required respiratory protection and training if respirators are to be worn.
<b>Hand protection:</b>	Wear 2 pairs of nitrile gloves when handling as a solid or liquid formulation. When handling solutions, wear chemical-resistant gloves appropriate for the solvent(s) making up the solution.
<b>Eye protection:</b>	Wear eye and face protection. Safety glasses with side-shields recommended. Goggles recommended if potential exists for direct exposure to dust or splashes.
<b>Skin and body protection</b>	Wear disposable dust impervious protective suit and shoe covers.

## 9. PHYSICAL AND CHEMICAL PROPERTIES

### General Information

<b>Physical state:</b>	powder
<b>Colour:</b>	white

### Important Health Safety and Environmental Information

<b>Flash point:</b>	Not applicable	<b>pH:</b>	Not applicable
<b>Water solubility:</b>	± 80 mg/ml		

### Other information

<b>Melting point/range:</b>	165 °C
<b>Explosive properties:</b>	Not applicable

## 10. STABILITY AND REACTIVITY

<b>Chemical stability:</b>	Stable under recommended storage conditions.
<b>Materials to avoid:</b>	Strong oxidants.
<b>Conditions to avoid:</b>	Heat, flames and sparks. Avoid moisture.
<b>Hazardous polymerisation:</b>	Hazardous polymerisation does not occur.

## 11. TOXICOLOGICAL INFORMATION

### Acute toxicity

<b>Eye contact</b>	May cause severe eye irritation.	<b>Method</b>	Based on component data. (Bortezomib)
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<b>Skin contact</b>	Causes skin irritation. Very toxic in contact with skin.	<b>Method</b>	Based on component data. (Bortezomib)
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**Ingestion** Very toxic if swallowed.

Oral dose at 0.7 mg/kg in female monkeys was fatal, but not in male monkey tested at this dose. IV data indicates significant potential to be toxic or lethal at doses < 2 mg/kg in rats and mice.

**Inhalation** May be very toxic if inhaled.

### Sub-Chronic / Chronic Toxicity

## 11. TOXICOLOGICAL INFORMATION

Application Route	Species	Dosing	Result
Intravenous (IV) administration			effects consistent with cytotoxic drugs (i.e. gastrointestinal (GI) Tract, blood, liver)
<b>Specific effects</b>			
Target Organ(s)	gastrointestinal tract, liver, reproductive system , eyes, skin, blood, kidney		
Reproductive effects	Resulted in impaired fertility in animal studies.		
Developmental effects	Developmental studies in rats and rabbits resulted in embryo/fetal death only at maternally toxic dosages, but no direct toxicity to the embryo/fetus.		
carcinogenic effects	Not available.		
Genotoxic effects	Not mutagenic. Not clastogenic.		
Method	microbial (Ames) mutagenicity assay in vivo rodent micronucleus bone marrow assay in vitro chromosomal aberrations assay (chinese hamster ovary cells)		

## 12. ECOLOGICAL INFORMATION

### Ecotoxicity

Ecotoxicity effects:	This product has no known eco-toxicological effects.
Aquatic toxicity effects:	This product has no known aquatic toxicological effects.
Persistence / degradability:	Unknown on product.
Bioaccumulation:	Unknown on product.
Degradation:	Unknown on product.

## 13. DISPOSAL CONSIDERATIONS

Waste from residues / unused products:	Waste disposal must be in accordance with appropriate US, Federal, State and International regulations. This product, if unaltered by use, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority.
Contaminated packaging:	Empty packing materials should be handled according to local current procedures or according to local by-laws or national laws.

## 14. TRANSPORT INFORMATION

### IATA/ICAO

ID/UN No.:	UN 3249
Proper shipping name	UN 3249, Medicine, toxic, solid n.o.s. (containing bortezomib), 6.1, II
Hazard class:	6.1
Packing group:	PG II
IATA - label:	Toxic (6.1)

### IMO/IMDG

UN/Id No.:	UN3249
Proper shipping name	UN 3249, Medicine, toxic, solid n.o.s. (containing bortezomib), 6.1, II
Hazard class:	6.1
Packing group:	PG II

## 14. TRANSPORT INFORMATION

IMDG-labels: Toxic (6.1)

### ADR/RID

ADR/RID UN/Id No.: UN 3249  
Proper shipping name UN 3249, Medicine, toxic, solid n.o.s. (containing bortezomib), 6.1, II  
Hazard class/item No. letter: 6.1, PG II  
ADR/RID-labels: Toxic (6.1)  
TREM-card: 61GT2-II

## 15. REGULATORY INFORMATION

Indication of danger: T+ - Very toxic.

Contains: Bortezomib

T+



### R -phrase(s)

R26/27/28 - Very toxic by inhalation, in contact with skin and if swallowed.  
R36/38 - Irritating to eyes and skin.  
R48/23/24 - Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin.

### S -phrase(s)

S26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.  
S28 - After contact with skin, wash immediately with plenty of water and soap.  
S38 - In case of insufficient ventilation, wear suitable respiratory equipment.  
S45 - In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)  
S53 - Avoid exposure - obtain special instructions before use.  
S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

## 16. OTHER INFORMATION

### This data sheet contains changes from the previous version in section(s):

Changes since the last publication are highlighted in red followed by three asterisks (\*\*\*)

**Additional advice:** Consult your supplier if the material is to be used for special applications such as in the food industry or for hygiene, medical or surgical end-use.

### Text of R phrases mentioned in Section 2 and 3

R26/27/28 - Very toxic by inhalation, in contact with skin and if swallowed.  
R36/38 - Irritating to eyes and skin.  
R48/23/24 - Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin.

### Literary reference:

1. MSDS Velcade: supplier Millenium Pharmaceuticals, Inc dd May, 14, 2003.
2. EC direction 67/548 and all adaptations.
3. PbOEL/OEL global list
4. IATA (regulations dangerous goods transported by air)
5. IMDG (regulations of dangerous goods transported by boat)
6. EC guidelines for labeling
7. ADR 2007

**MSDS Format:** European Format.  
This Material Safety Data Sheet was prepared in accordance with Regulation (EC) No 1907/2006.

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**End of Safety Data Sheet**