

Safety Data Sheet (SDS) According to the REACH Regulation (EC) No. 1907/2006

Issuing Date: 2014-05-20

Revision Date: 2024-02-23

Version: 4

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Product No 2204
Product name Bortezomib

Contains

| | | |
|---|------------------|---------------|
| Chemical name | Index No. | CAS No |
| [(1R)-3-methyl-1-[[[(2S)-3-phenyl-2-(pyrazine-2-yl)propanoyl]amino]butyl]boronic acid (90 - 100%) | Not Listed | 179324-69-7 |

| | |
|-------------------------|--|
| Formula | C ₁₉ H ₂₅ BN ₄ O ₄ |
| Molecular Weight | 384.24 g/mol |

1.2. Relevant identified uses of the substance or mixture and uses advised against

Identified uses For Research Use Only. Not for Use in Diagnostic Procedures.

1.3. Details of the supplier of the safety data sheet

| | |
|---------------------------------------|---------------------------------|
| Importer | Manufacturer |
| Cell Signaling Technology Europe B.V. | Cell Signaling Technology, Inc. |
| Dellaertweg 9b | 3 Trask Lane |
| 2316 WZ Leiden | Danvers, MA 01923 |
| The Netherlands | United States |
| TEL: +31 (0)71 7200 200 | TEL: +1 978 867 2300 |
| FAX: +31 (0)71 891 0019 | FAX: +1 978 867 2400 |

| | |
|-----------------------|--------------------|
| Website | www.cellsignal.com |
| E-mail Address | info@cellsignal.eu |

1.4. Emergency telephone number

CHEMTREC 24 hours a day, 7 days a week, 365 days a year
 +1 703 527 3887 (INTERNATIONAL) +1 800 424 9300 (NORTH AMERICA)

Europe 112

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Regulation (EC) No. 1272/2008

| | |
|----------------------------|---------------------|
| Acute oral toxicity | Category 1 - (H300) |
|----------------------------|---------------------|

| | |
|--|---------------------|
| Skin corrosion/irritation | Category 2 - (H315) |
| Serious eye damage/eye irritation | Category 2 - (H319) |
| Reproductive toxicity | Category 2 - (H361) |
| Specific target organ toxicity - repeated exposure (STOT RE) | Category 1 - (H372) |

2.2. Label elements



Signal word

Danger

Hazard statement(s)

H300 - Fatal if swallowed.
H315 - Causes skin irritation.
H319 - Causes serious eye irritation.
H361 - Suspected of damaging fertility or the unborn child.
H372 - Causes damage to organs through prolonged or repeated exposure.

Precautionary statement(s)

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.
P264 - Wash face, hands and any exposed skin thoroughly after handling.
P270 - Do not eat, drink or smoke when using this product.
P280 - Wear protective gloves/protective clothing/eye protection/face protection.
P301 + P310 - IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
P302 + P352 - IF ON SKIN: Wash with plenty of soap and water.
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308 + P313 - IF exposed or concerned: Get medical advice/attention.
P314 - Get medical advice/attention if you feel unwell.
P330 - Rinse mouth.
P332 + P313 - If skin irritation occurs: Get medical advice/attention.
P337 + P313 - If eye irritation persists: Get medical advice/attention.
P362 + P364 - Take off contaminated clothing and wash it before reuse.
P405 - Store locked up.
P501 - Dispose of contents/container to an approved waste disposal plant.

2.3. Other hazards

Avoid release to the environment.

For the full text of the H-phrases & EUH-phrases mentioned in this Section, see Section 16

SECTION 3: Composition/information on ingredients

3.1 Substances

Synonyms

Bortezomib;
Velcade®;
PS-341;

| | |
|------------------------|--|
| Formula | Boronic acid, (3-methyl-1-((1-oxo-3-phenyl-2-((pyrazinylcarbonyl)amino)propyl)amino)butyl)-, (S-(R*,S*))- |
| Chemical nature | C ₁₉ H ₂₅ BN ₄ O ₄ Monoconstituent substance |

| Chemical name | CAS No | Weight-% | EC No | Classification (1272/2008) | REACH Registration Number |
|--|-------------|----------|-------|--|---------------------------|
| [(1R)-3-methyl-1-[[[(2S)-3-phenyl-2-(pyrazine-2-carbonylamino)propanoyl]amino]butyl]boronic acid | 179324-69-7 | 100 | - | Acute Tox. 1 (H300) Skin Irrit. 2 (H315) Eye Dam. 1 (H318) Repr. 2 (H361) STOT RE 1 (H372) | no data available |

For the full text of the R-phrases mentioned in this Section, see Section 16

SECTION 4: First aid measures

4.1. Description of first aid measures

| | |
|-----------------------------------|---|
| General advice | Immediate medical attention is required. Show this safety data sheet to the doctor in attendance. If symptoms persist, call a physician. |
| Inhalation | Immediate medical attention is required. IF INHALED: Remove to fresh air and keep at rest in a position comfortable for breathing. If not breathing, give artificial respiration. |
| Skin contact | Immediate medical attention is required. Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. |
| Eye contact | Rinse thoroughly with plenty of water, also under the eyelids. Keep eye wide open while rinsing. |
| Ingestion | Clean mouth with water and afterwards drink plenty of water. Immediate medical attention is required. Never give anything by mouth to an unconscious person. |
| Protection of first-aiders | Use personal protective equipment. Avoid contact with skin, eyes and clothing. |

4.2. Most important symptoms and effects, both acute and delayed

Nausea. Diarrhea. thrombocytopenia. Neutropenia. peripheral neuropathy. Fatigue. anemia. Constipation. Vomiting. rash. Pyrexia. Anorexia. Neuralgia. Leukopenia. Lymphopenia.

4.3. Indication of any immediate medical attention and special treatment needed

| | |
|---------------------------|------------------------|
| Notes to physician | Treat symptomatically. |
|---------------------------|------------------------|

SECTION 5: Firefighting measures

5.1. Extinguishing media

| | |
|---------------------------------------|--|
| Suitable Extinguishing Media | Use extinguishing measures that are appropriate to local circumstances and the surrounding environment |
| Unsuitable Extinguishing Media | No information available |

5.2. Special hazards arising from the substance or mixture

Thermal decomposition can lead to release of irritating gases and vapors.

5.3. Advice for firefighters

Wear self-contained breathing apparatus and protective suit. Wear self contained breathing apparatus for fire fighting if necessary.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel Use personal protective equipment. Keep people away from and upwind of spill/leak. Evacuate personnel to safe areas.

For emergency responders Use personal protection recommended in Section 8.

6.2. Environmental precautions

Do not flush into surface water or sanitary sewer system.

6.3. Methods and material for containment and cleaning up

Methods for containment Prevent further leakage or spillage if safe to do so. Cover powder spill with plastic sheet or tarp to minimize spreading. Dike far ahead of liquid spill for later disposal.

Methods for cleaning up Use personal protective equipment. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Take up mechanically, placing in appropriate containers for disposal. Avoid dust formation. Soak up with inert absorbent material. Take precautionary measures against static discharges.

6.4. Reference to other sections

See Sections 8 & 13 for additional information.

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Avoid contact with skin, eyes and clothing. Wear personal protective equipment. Prevent the formation of vapors, mists and aerosols. Do not eat, drink or smoke when using this product. Use only in area provided with appropriate exhaust ventilation.

7.2. Conditions for safe storage, including any incompatibilities

Keep away from direct sunlight.

7.3. Specific end use(s)

Use as a laboratory reagent.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

The product does not contain any hazardous materials with occupational exposure limits established.

8.2. Exposure controls

Appropriate engineering controls

Showers, eyewash stations, and ventilation systems.

Individual protection measures, such as personal protective equipment

Eye/face protection Tightly fitting safety goggles.

| | |
|-------------------------------|--|
| Skin protection | Wear protective gloves and protective clothing |
| Hand protection | Impervious gloves. |
| Other | Impervious gloves. Impervious clothing. Long sleeved clothing. |
| Respiratory protection | In case of inadequate ventilation wear respiratory protection. |

Environmental Exposure Controls

No information available.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

| | | |
|---|---------------------------------|--------------------------------|
| Physical state | Solid - Powder | |
| Color | White | |
| Odor | No information available | |
| Property | Values | Remarks • Method |
| pH | 2-6.5 | @ 0.0033 - 0.0038 g/L in water |
| Melting point/freezing point | 124-140 °C | |
| Boiling point or initial boiling point and boiling range | No information available | No information available |
| Flash point | No information available | No information available. |
| Evaporation rate | No information available | No information available |
| Flammability | No information available | No information available |
| Upper/lower flammability or explosive limits | Lower: No information available | No information available |
| Vapor pressure | No information available | No information available |
| Relative vapor density | No information available | No information available |
| Density and/or relative density | No information available | No information available |
| Solubility | Partly soluble | |
| Partition coefficient: n-octanol/water | 2.0 | estimated |
| Autoignition temperature | No information available | No information available |
| Decomposition temperature | No information available | No information available. |
| Viscosity | No information available | No information available |
| Explosive properties | No information available | No information available |
| Oxidizing properties | No information available | No information available |

9.2. Other information

| | |
|-------------------------------------|---|
| Softening point | No information available |
| Molecular Weight | 384.24 g/mol |
| Solubility in other solvents | Soluble in dimethyl sulfoxide (DMSO) @ 200 mg/mL, Soluble in ethanol (EtOH) @ 200 mg/mL |
| VOC content | No information available |
| Liquid Density | No information available |

SECTION 10: Stability and reactivity

10.1. Reactivity

No information available.

10.2. Chemical stability

Stable under normal conditions.

10.3. Possibility of hazardous reactions

Hazardous polymerization
Hazardous reactions

Hazardous polymerization does not occur.
None under normal processing

10.4. Conditions to avoid

None known based on information supplied.

10.5. Incompatible materials

No information available.

10.6. Hazardous decomposition products

None under normal use conditions.

SECTION 11: Toxicological information

11.1. Information on hazard classes as defined in Regulation (EC) No 1272/2008

This material should only be handled by, or under the close supervision of, those properly qualified in the handling and use of potentially hazardous chemicals. It should be borne in mind that the toxicological and physiological properties of this compound is not well defined.

Acute Toxicity

In humans, fatal outcomes following the administration of more than twice the recommended therapeutic dose have been reported, which were associated with the acute onset of symptomatic hypotension and thrombocytopenia. Studies in monkeys and dogs showed that intravenous bortezomib doses as low as 2 times the recommended clinical dose were associated with increases in heart rate, decreases in contractility, hypotension, and death. In dog studies, a slight increase in the corrected QT interval was observed at doses resulting in death. In monkeys, doses of 3.0 mg/kg and greater (approximately twice the recommended clinical dose) resulted in hypotension starting at 1 hour post-administration, with progression to death in 12 to 14 hours following drug administration.

Information on likely routes of exposure**Inhalation**

There is no data available for this product.

Eye contact

May cause irreversible damage to eyes.

Skin contact

Irritating to skin. May be harmful in contact with skin.

Ingestion

Very toxic if swallowed. Target Organ Effects. Reproductive Toxicity.

Symptoms

Nausea. Diarrhea. thrombocytopenia. Neutropenia. peripheral neuropathy. Fatigue. anemia. Constipation. Vomiting. rash. Pyrexia. Anorexia. Neuralgia. Leukopenia. Lymphopenia.

Skin corrosion/irritation

Causes skin irritation.

Serious eye damage/eye irritation

Risk of serious damage to eyes.

Sensitization

No information available.

Mutagenic effects

No information available.

Carcinogenicity

No information available.

Reproductive toxicity

In a 6-month rat toxicity study, degenerative effects in the ovary were observed at doses = 0.3 mg/kg and degenerative changes in the testes occurred at 1.2 mg/kg. Pregnant rabbits given bortezomib during organogenesis at a dose of 0.05 mg/kg experienced significant post-implantation loss and decreased number of live fetuses. Live fetuses from these litters also showed significant decreases in fetal weight.

STOT - single exposure
STOT - repeated exposure

No information available.

In a repeat dose toxicity study in monkeys, myocardial hemorrhage, inflammation, and necrosis were observed. In animals, severe anemia and thrombocytopenia, and gastrointestinal, neurological and lymphoid system toxicities were observed during chronic dosing. Neurotoxic effects of bortezomib included axonal swelling and degeneration in peripheral nerves, dorsal spinal roots, and tracts of the spinal cord, multifocal hemorrhage and necrosis in the brain, eye, and heart.

Target Organ Effects

Cardiovascular system, Gastrointestinal tract (GI), Hematopoietic System, Central nervous system (CNS), Peripheral Nervous System (PNS).

Aspiration Hazard

No information available.

11.2. Information on other hazards

No information available.

SECTION 12: Ecological information**12.1. Toxicity**

No information available.

12.2. Persistence and degradability

No information available

12.3. Bioaccumulative potential**Bioaccumulation**

Not likely to bioaccumulate.

| Chemical name | Octanol-Water Partition Coefficient |
|--|-------------------------------------|
| [(1R)-3-methyl-1-[[[(2S)-3-phenyl-2-(pyrazine-2-carbonylamino)propanoyl]amino]butyl]boronic acid | 2.0 |

Bioconcentration factor (BCF)

No information available.

12.4. Mobility in soil

Is predicted to have low mobility in the environment.

12.5. Results of PBT and vPvB assessment

No information available.

12.6. Endocrine disrupting properties

This product does not contain any known or suspected endocrine disruptors

12.7. Other adverse effects

No information available

SECTION 13: Disposal considerations**13.1. Waste treatment methods****Waste from residues / unused products**

Dispose of in accordance with local regulations.

Contaminated packaging

Empty containers should be taken to an approved waste handling site for recycling or

disposal.

Other information

According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user based on the application for which the product was used.

SECTION 14: Transport information

IMDG/IMO

| | |
|--|---|
| 14.1 UN number | UN2811 |
| 14.2 UN proper shipping name | Toxic solid, organic, n.o.s. (Bortezomib) |
| 14.3 Transport hazard class(es) | 6.1 |
| 14.4 Packing group | I |
| 14.5 Environmental hazards | None |
| 14.6 Special precautions for user | None |
| 14.7 Maritime transport in bulk according to IMO instruments | Not regulated |

ADR/RID

| | |
|-----------------------------------|---|
| 14.1 UN number | UN2811 |
| 14.2 UN proper shipping name | Toxic solid, organic, n.o.s. (Bortezomib) |
| 14.3 Transport hazard class(es) | 6.1 |
| 14.4 Packing group | I |
| 14.5 Environmental hazards | None |
| 14.6 Special precautions for user | None |

IATA

| | |
|-----------------------------------|---|
| 14.1 UN number | UN2811 |
| 14.2 UN proper shipping name | Toxic solid, organic, n.o.s. (Bortezomib) |
| 14.3 Transport hazard class(es) | 6.1 |
| 14.4 Packing group | I |
| 14.5 Environmental hazards | None |
| 14.6 Special precautions for user | None |

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture**Candidate List of Substances of Very High Concern for Authorization Information**

This product does not contain Substances of Very High Concern (SVHC).

SEVESO Directive Information

H1 - ACUTE TOXIC

International inventories

| | |
|---------------|---|
| TSCA 8(b) | - |
| DSL/NDL | - |
| EINECS/ELINCS | - |
| ENCS | - |
| IECSC | - |
| KECL | - |
| PICCS | - |
| AICS | - |

International inventories legend

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances
PICCS - Philippines Inventory of Chemicals and Chemical Substances
AICS - Australian Inventory of Chemical Substances

15.2. Chemical safety assessment

For this substance a chemical safety assessment has not been carried out

| |
|--------------------------------------|
| SECTION 16: Other information |
|--------------------------------------|

Full text of H-Statements referred to under Sections 2 and 3

H300 - Fatal if swallowed
H315 - Causes skin irritation
H319 - Causes serious eye irritation
H361 - Suspected of damaging fertility or the unborn child
H372 - Causes damage to organs through prolonged or repeated exposure

| | |
|----------------------------------|---|
| Classification procedure: | Expert judgment and weight of evidence determination. |
| Issuing Date: | 2014-05-20 |
| Revision Date: | 2024-02-23 |

Disclaimer

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.