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

1.1. Product identifier

Product No: 2204
Product name: Bortezomib
Reach registration number: This substance/mixture contains only ingredients which have been registered, or are exempt from registration, according to Regulation (EC) No. 1907/2006.

Chemical Name: \((1R)-3\text{-methyl-1-}[[2S]-3\text{-phenyl-2\text{-}(pyrazine-2\text{-carbonylamino)propanoyl]amino]butyl}][boronic acid
\newline(90 - 100%)

Index No.: Not Listed
CAS No: 179324-69-7

Formula: \(\text{C}_{19}\text{H}_{25}\text{BN}_{4}\text{O}_{4}\)
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

1.3. Details of the supplier of the safety data sheet

Importer (Applicable in EU only): Cell Signaling Technology Europe B.V.
Schuttersveld 2
2316 ZA Leiden
The Netherlands
TEL: +31 (0)71 7200 200
FAX: +31 (0)71 891 0098
Website: www.cellsignal.com
E-mail Address: info@cellsignal.eu

Manufacturer: Cell Signaling Technology, Inc.
3 Trask Lane
Danvers, MA 01923
United States
TEL: +1 978 867 2300
FAX: +1 978 867 2400

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)

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Regulation (EC) No. 1272/2008

<table>
<thead>
<tr>
<th>Hazard Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute oral toxicity</td>
<td>Category 1 - (H300)</td>
</tr>
<tr>
<td>Skin corrosion/irritation</td>
<td>Category 2 - (H315)</td>
</tr>
</tbody>
</table>
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
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

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;
Boronic acid,
(3-methyl-1-((1-oxo-3-phenyl-2-((pyrazinyl(carbonyl)amino)propyl)amino)butyl)-, (S-)(R*,S*)-

Formula
C₁₉H₂₅B₄N₄O₄

Chemical nature
Monoconstituent substance.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>CAS No</th>
<th>Weight %</th>
<th>EC No</th>
<th>Classification</th>
<th>REACH</th>
</tr>
</thead>
</table>
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


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. Provide regular cleaning of equipment, work area and clothing. Wash hands before breaks and immediately after handling the product.

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

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
   Hand protection  Impervious gloves.
   Other
Respiratory protection  Impervious gloves. Impervious clothing. Long sleeved clothing.

Environmental Exposure Controls
No information available.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state  Solid
Appearance  Powder
Color  White
2204 Bortezomib

<table>
<thead>
<tr>
<th>Property</th>
<th>Values</th>
<th>Remarks • Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>2-6.5</td>
<td>@ 0.0033 - 0.0038 g/L in water</td>
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<td>Melting point/freezing point</td>
<td>124-140 °C</td>
<td>No information available</td>
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<td>Initial boiling point and boiling range</td>
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<td></td>
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<tr>
<td>Flash point</td>
<td></td>
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</tr>
<tr>
<td>Evaporation rate</td>
<td></td>
<td>No information available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
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</tr>
<tr>
<td>Upper flammability limit</td>
<td></td>
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</tr>
<tr>
<td>Lower flammability limit</td>
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</tr>
<tr>
<td>Vapor pressure</td>
<td></td>
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</tr>
<tr>
<td>Vapor density</td>
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</tr>
<tr>
<td>Relative density</td>
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<tr>
<td>Solubility</td>
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<tr>
<td>Partition coefficient: n-octanol/water</td>
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</tr>
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<td>Decomposition temperature</td>
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<td>Viscosity</td>
<td></td>
<td>No information available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td></td>
<td>No information available</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td></td>
<td>No information available</td>
</tr>
</tbody>
</table>

9.2. Other information

<table>
<thead>
<tr>
<th>Property</th>
<th>Values</th>
<th>Remarks • Method</th>
</tr>
</thead>
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<tr>
<td>Softening point</td>
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</tr>
<tr>
<td>Molecular Weight</td>
<td>384.24 g/mol</td>
<td></td>
</tr>
<tr>
<td>Solubility in other solvents</td>
<td>Soluble in dimethyl sulfoxide (DMSO) @ 200 mg/mL, Soluble in ethanol (EtOH) @ 200 mg/mL</td>
<td></td>
</tr>
<tr>
<td>VOC content</td>
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</tr>
<tr>
<td>Density</td>
<td></td>
<td>No information available</td>
</tr>
</tbody>
</table>

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 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 toxicological effects

Page 5 / 9
2204 Bortezomib

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**

**Skin corrosion/irritation**
- Causes skin irritation.

**Serious eye damage/eye irritation**
- Risk of serious damage to eyes.

**Sensitization**
- No information available.

**Mutagenic effects**
- The weight of evidence demonstrates that this material is not genotoxic. Bortezomib showed clastogenic activity (structural chromosomal aberrations) in the in vitro chromosomal aberration assay using Chinese hamster ovary cells. Bortezomib was not genotoxic when tested in the in vitro mutagenicity assay (Ames test) and in vivo micronucleus assay in mice.

**Carcinogenic effects**
- 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**
- No information available.

**STOT - repeated exposure**
- 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.

**Other information**
- No information available.

SECTION 12: Ecological information

**12.1. Toxicity**
- No information available.

**12.2. Persistence and degradability**
2204 Bortezomib

No information available.

12.3. Bioaccumulative potential

Bioaccumulation: Not likely to bioaccumulate.
Bioconcentration factor (BCF): No information available.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Octanol-Water Partition Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1R)-3-methyl-1-[(2S)-3-phenyl-2-(pyrazine-2-carbonylamino)propanoyl]amino[butyl]boronic acid</td>
<td>2.0</td>
</tr>
</tbody>
</table>

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. 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 EmS No.**: F-A, S-A
14.7 **Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**: 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 Classification Code**: T2
    **Tunnel Restriction Code**: (C/E)

**IATA**
2204 Bortezomib

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  
ERG code  6L  

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/NDSL  -  
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:  2018-04-09  

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.