SAFETY DATA SHEET

Ceftolozane / Tazobactam Injection Formulation

Version 2.13  Revision Date: 12.10.2021  SDS Number: 438908-00015  Date of last issue: 23.03.2020
Date of first issue: 06.01.2016

Section 1: Identification

Product name: Ceftolozane / Tazobactam Injection Formulation

Manufacturer or supplier's details
Company: MSD
Address: 33 Whakatiki Street - Private Bag 908
Upper Hutt - New Zealand
Telephone: +1-908-740-4000
Emergency telephone number: +1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

Section 2: Hazard identification

GHS Classification
Respiratory sensitisation: Category 1
Specific target organ toxicity - repeated exposure: Category 2 (Kidney, Liver)

GHS label elements
Hazard pictograms:

Signal word: Danger

Hazard statements:
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H373 May cause damage to organs (Kidney, Liver) through prolonged or repeated exposure.

Precautionary statements:
Prevention:
P260 Do not breathe dust.
P284 Wear respiratory protection.

Response:
P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P342 + P311 If experiencing respiratory symptoms: Call a POISON CENTER/ doctor.
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Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

Section 3: Composition/information on ingredients

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane</td>
<td>689293-68-3</td>
<td>&gt;= 30 -&lt; 60</td>
</tr>
<tr>
<td>Tazobactam</td>
<td>89786-04-9</td>
<td>&gt;= 10 -&lt; 30</td>
</tr>
</tbody>
</table>

Section 4: First-aid measures

General advice : In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled : If inhaled, remove to fresh air.
If not breathing, give artificial respiration.
If breathing is difficult, give oxygen.
Get medical attention.

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water.
Get medical attention if symptoms occur.

In case of eye contact : If in eyes, rinse well with water.
Get medical attention if irritation develops and persists.

If swallowed : If swallowed, DO NOT induce vomiting.
Get medical attention if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed : May cause allergy or asthma symptoms or breathing difficulties if inhaled.
May cause damage to organs through prolonged or repeated exposure.
Excessive exposure may aggravate preexisting asthma and other respiratory disorders (e.g. emphysema, bronchitis, reactive airways dysfunction syndrome).
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders : First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician : Treat symptomatically and supportively.
Section 5: Fire-fighting measures

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.

Hazardous combustion products: Carbon oxides
Metal oxides
Chlorine compounds
Nitrogen oxides (NOx)

Specific extinguishing methods: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.

Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

Hazchem Code: 2Z

Section 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.
Section 7: Handling and storage

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: Do not breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Already sensitised individuals should consult their physician regarding working with respiratory irritants or sensitisers. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage: Keep in properly labelled containers. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents

Section 8: Exposure controls/personal protection

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane</td>
<td>689293-68-3</td>
<td>TWA</td>
<td>1000 µg/m³ (OEB 1)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tazobactam</td>
<td>89786-04-9</td>
<td>TWA</td>
<td>250 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: DSEN, RSEN

Wipe limit: 100 µg/100 cm²

Further information: RSEN

**Engineering measures**

Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

**Personal protective equipment**

**Respiratory protection**

If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

- **Filter type**: Particulates type

**Hand protection**

- **Material**: Chemical-resistant gloves

**Eye protection**

Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**Skin and body protection**

- **Work uniform or laboratory coat**.

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**Section 9: Physical and chemical properties**

- **Appearance**: powder
- **Colour**: No data available
- **Odour**: No data available
- **Odour Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
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</table>

flammmability limit

Vapour pressure : No data available
Relative vapour density : No data available
Relative density : No data available
Density : No data available

Solubility(ies)
Water solubility : No data available

Partition coefficient: n-octanol/water : No data available
Auto-ignition temperature : No data available
Decomposition temperature : No data available

Viscosity
Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available
Particle size : No data available

Section 10: Stability and reactivity

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.
Conditions to avoid : Heat, flames and sparks.
Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

Section 11: Toxicological information

Exposure routes : Inhalation
Skin contact
Ingestion
Eye contact
Acute toxicity
Not classified based on available information.

Components:

Ceftolozane:
Acute toxicity (other routes of administration):
  LD50 (Rat): > 2,000 mg/kg
  Application Route: Intravenous
  LD50 (Mouse): > 1,500 mg/kg
  Application Route: Intravenous
  LD50 (Dog): > 2,000 mg/kg
  Application Route: Intravenous

Tazobactam:
Acute oral toxicity:
  LD50 (Rat): > 5,000 mg/kg
  LD50 (Mouse): > 5,000 mg/kg

Acute toxicity (other routes of administration):
  LD50 (Rat): > 5,000 mg/kg
  Application Route: Intravenous
  LD50 (Mouse): > 5,000 mg/kg
  Application Route: Intravenous
  LD50 (Dog): > 5,000 mg/kg
  Application Route: Intravenous

Skin corrosion/irritation
Not classified based on available information.

Serious eye damage/eye irritation
Not classified based on available information.

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Components:

Ceftolozane:
  Test Type: Maximisation Test
  Species: Guinea pig
  Result: Sensitiser

Tazobactam:
  Result: Sensitiser
Chronic toxicity

Germ cell mutagenicity
Not classified based on available information.

Components:

Ceftolozane:
Genotoxicity in vitro:
   Test Type: Bacterial reverse mutation assay (AMES)
   Result: negative

   Test Type: Chromosome aberration test in vitro
   Result: negative

   Test Type: In vitro mammalian cell gene mutation test
   Result: positive

   Test Type: In vitro mammalian cell gene mutation test
   Result: negative

Genotoxicity in vivo:
   Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
   Species: Mouse
   Result: negative

   Test Type: Unscheduled DNA synthesis (UDS) test with mammalian liver cells in vivo
   Species: Mouse
   Result: negative

Tazobactam:
Genotoxicity in vitro:
   Test Type: Bacterial reverse mutation assay (AMES)
   Result: negative

   Test Type: In vitro mammalian cell gene mutation test
   Test system: mouse lymphoma cells
   Result: positive

   Test Type: Chromosome aberration test in vitro
   Test system: Chinese hamster fibroblasts
   Result: negative

Genotoxicity in vivo:
   Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
   Species: Mouse
   Application Route: Intraperitoneal injection
   Result: negative

   Test Type: Unscheduled DNA synthesis (UDS) test with mammalian liver cells in vivo
   Species: Mouse
   Result: negative
Carcinogenicity
Not classified based on available information.

Reproductive toxicity
Not classified based on available information.

Components:

Ceftolozane:
Effects on fertility : Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Intravenous injection
Fertility: NOAEL: 1,000 mg/kg body weight
Result: No effects on fertility

Effects on foetal development : Test Type: Embryo-foetal development
Species: Mouse
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 2,000 mg/kg body weight
Remarks: No significant adverse effects were reported

Tazobactam:
Effects on fertility : Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Intraperitoneal injection
Fertility: NOAEL: 640 mg/kg body weight

Effects on foetal development : Test Type: Embryo-foetal development
Species: Rat
Application Route: Intraperitoneal injection
Developmental Toxicity: NOAEL: 40 mg/kg body weight
Result: Effects on early embryonic development

        Test Type: Embryo-foetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 3,000 mg/kg body weight
Result: No effects on foetal development

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Kidney, Liver) through prolonged or repeated exposure.
Components:

Ceftolozane:
Target Organs: Kidney
Assessment: May cause damage to organs through prolonged or repeated exposure.

Tazobactam:
Target Organs: Liver
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity
Components:

Ceftolozane:
Species: Rat
NOAEL: 1,000 mg/kg
Application Route: Intravenous
Exposure time: 28 days
Target Organs: Kidney
Symptoms: No adverse effects

Species: Dog
LOAEL: 300 mg/kg
Exposure time: 28 days
Target Organs: Kidney

Tazobactam:
Species: Rat
NOAEL: 40 mg/kg
Application Route: Intraperitoneal
Exposure time: 6 Months
Target Organs: Liver

Species: Dog
NOAEL: 40 mg/kg
LOAEL: 80 mg/kg
Application Route: Intraperitoneal
Exposure time: 6 Months
Target Organs: Liver

Aspiration toxicity
Not classified based on available information.

Experience with human exposure
Components:

Ceftolozane:
Ingestion: Symptoms: Diarrhoea, Fever, Headache, Nausea, Skin irrita-
### Tazobactam:

**Inhalation**: Remarks: May cause allergy or asthma symptoms or breathing difficulties if inhaled.

### Section 12: Ecological information

#### Ecotoxicity

**Components:**

**Ceftolozane:**

- **Toxicity to algae/aquatic plants**
  - EC50 (Anabaena flos-aquae): 0.0401 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - NOEC (Anabaena flos-aquae): 0.0018 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

- **Toxicity to fish (Chronic toxicity)**
  - NOEC (Pimephales promelas (fathead minnow)): 10 mg/l
  - Exposure time: 32 d
  - Method: OECD Test Guideline 210

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**
  - NOEC (Daphnia magna (Water flea)): 9.6 mg/l
  - Exposure time: 21 d
  - Method: OECD Test Guideline 211

- **Toxicity to microorganisms**
  - EC50: > 1,000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209
  - NOEC: 560 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - Method: OECD Test Guideline 209

**Tazobactam:**

- **Toxicity to algae/aquatic plants**
  - EC50 (Anabaena flos-aquae): 0.96 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - NOEC (Anabaena flos-aquae): 0.44 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201

- **Toxicity to fish (Chronic toxicity)**
  - NOEC (Pimephales promelas (fathead minnow)): 10.6 mg/l
  - Exposure time: 32 d
  - Method: OECD Test Guideline 210

- **Toxicity to daphnia and other aquatic invertebrates**
  - NOEC (Daphnia magna (Water flea)): 9.6 mg/l
aquatic invertebrates (Chronic toxicity)  
Exposure time: 21 d  
Method: OECD Test Guideline 211

Toxicity to microorganisms  
EC50: > 1,000 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

NOEC: 1,000 mg/l  
Exposure time: 3 h  
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

Persistence and degradability

Components:

Ceftolozane:  
Biodegradability: Result: Not readily biodegradable.  
Method: OECD Test Guideline 301D

Tazobactam:  
Biodegradability: Result: Not readily biodegradable.  
Method: OECD Test Guideline 301D

Bioaccumulative potential

Components:

Ceftolozane:  
Partition coefficient: n-octanol/water  
log Pow: -0.21

Tazobactam:  
Partition coefficient: n-octanol/water  
log Pow: -0.63

Mobility in soil

Components:

Ceftolozane:  
Distribution among environmental compartments  
log Koc: 3.3  
Method: OECD Test Guideline 106

Tazobactam:  
Distribution among environmental compartments  
log Koc: 0.87

Other adverse effects
No data available
Section 13: Disposal considerations

Disposal methods
- Waste from residues: Dispose of in accordance with local regulations.
- Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

Section 14: Transport information

International Regulations

UNRTDG
- UN number: UN 3077
- Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ceftolozane, Tazobactam)
  - Class: 9
  - Packing group: III
  - Labels: 9

IATA-DGR
- UN/ID No.: UN 3077
- Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Ceftolozane, Tazobactam)
  - Class: 9
  - Packing group: III
  - Labels: Miscellaneous
  - Packing instruction (cargo aircraft): 956
  - Packing instruction (passenger aircraft): 956
  - Environmentally hazardous: yes

IMDG-Code
- UN number: UN 3077
- Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ceftolozane, Tazobactam)
  - Class: 9
  - Packing group: III
  - Labels: 9
  - EmS Code: F-A, S-F
  - Marine pollutant: yes

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

NZS 5433
- UN number: UN 3077
- Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
Class: 9
Packing group: III
Labels: 9
Hazchem Code: 2Z

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

Section 15: Regulatory information

Safety, health and environmental regulations/legislation specific for the substance or mixture

HSNO Approval Number
HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

HSW Controls
Certified handler certificate not required.
Tracking hazardous substance not required.
Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further information.

The components of this product are reported in the following inventories:

AICS: not determined
DSL: not determined
IECSC: not determined

Section 16: Other information

Further information

Date format: dd.mm.yyyy

Full text of other abbreviations

AIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized Sys-
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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 is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

NZ / EN