SECTION 1. IDENTIFICATION

Product name : Ceftolozane / Tazobactam Injection Formulation

Manufacturer or supplier's details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
          Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)

Combustible dust
Respiratory sensitization : Category 1

Specific target organ toxicity - repeated exposure : Category 2 (Kidney, Liver)

GHS label elements
Hazard pictograms :

Signal Word : Danger

Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
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.
P285 In case of inadequate ventilation wear respiratory protection.

Response:
P304 + P341 IF INHALED: If breathing is difficult, remove person to fresh air and keep comfortable for breathing.
P342 + P311 If experiencing respiratory symptoms: Call a doc-
DISPOSAL:
P501 Dispose of contents and container to an approved waste disposal plant.

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td>Mixture</td>
<td>Ceftolozane</td>
</tr>
<tr>
<td></td>
<td>Tazobactam</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

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
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 fire fighting:
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 fire-fighters:
In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

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 sensitized individuals should consult their physician regarding working with respiratory irritants or sensitizers.
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.

Conditions for safe storage:
Keep in properly labeled 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

Ingredients 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>
</tbody>
</table>

Further information: DSEN, RSEN

| Tazobactam | 89786-04-9 | TWA | 250 µg/m³ (OEB 2) | Internal |

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: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

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.

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Color: No data available
Odor: No data available
Odor 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
SAFETY DATA SHEET

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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

Vapor pressure : No data available

Relative vapor density : No data available

Relative density : No data available

Density : No data available

Solubility(ies) : No data available

Water solubility : No data available

Partition coefficient: n-octanol/water : No data available

Autoignition 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 : No hazardous decomposition products are known.
SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

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 sensitization

Skin sensitization
Not classified based on available information.

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

Components:

Ceftolozane:
Test Type: Maximization Test
Species: Guinea pig
Result: Sensitizer

Tazobactam:
Result: Sensitizer

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.
IARC: No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA: No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP: No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

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

Test Type: Embryo-fetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 1,000 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 fetal development:
- Test Type: Embryo-fetal development
- Species: Rat
- Application Route: Intraperitoneal injection
- Developmental Toxicity: NOAEL: 40 mg/kg body weight
- Result: Effects on early embryonic development.

- Test Type: Embryo-fetal development
- Species: Rat
- Application Route: Intravenous injection
- Developmental Toxicity: NOAEL: 3,000 mg/kg body weight
- Result: No effects on fetal 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: Diarrhea, Fever, Headache, Nausea, Skin irritation, Gastrointestinal discomfort

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
Method: OECD Test Guideline 201
NOEC (Anabaena flos-aquae): 0.0018 mg/l
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
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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 (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: 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
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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.

Domestic regulation

49 CFR
UN/ID/NA number: UN 3077
Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Ceftolozane, Tazobactam)
Class: 9
Packing group: III
Labels: CLASS 9
ERG Code: 171
Marine pollutant: yes (Ceftolozane, Tazobactam)
Remarks: Above applies only to containers over 119 gallons or 450 liters., Shipment by ground under DOT is non-regulated; however it may be shipped per the applicable hazard classification to facilitate multi-modal transport involving ICAO (IATA) or IMO.

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

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.
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SARA 311/312 Hazards:  
- Combustible dust  
- Respiratory or skin sensitization  
- Specific target organ toxicity (single or repeated exposure)

SARA 313:  
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know

Ceftolozane  689293-68-3  
L-Arginine hydrochloride  1119-34-2  
Tazobactam  89786-04-9  
Sodium chloride  7647-14-5

The ingredients of this product are reported in the following inventories:  
- AICS: not determined  
- DSL: not determined  
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information

NFPA 704:  
- Flammability: 1  
- Health: 0  
- Instability: 0  
- Special hazard

HMIS® IV:  
- HEALTH: * 2  
- FLAMMABILITY: 3  
- PHYSICAL HAZARD: 0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/'" represents the absence of a chronic hazard.

Full text of other abbreviations
SAFETY DATA SHEET

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Version: 7.3
Revision Date: 10/12/2021
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Date of last issue: 03/23/2020
Date of first issue: 01/06/2016

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.

US / Z8

Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 10/12/2021