SAFETY DATA SHEET

Daptomycin Injection Formulation - 2nd Generation

Version 2.6  Revision Date: 2020/10/10  SDS Number: 679932-00011  Date of last issue: 2019/09/13

Date of first issue: 2016/05/19

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Daptomycin Injection Formulation - 2nd Generation

Manufacturer or supplier's details

Company: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone: 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

2. HAZARDS IDENTIFICATION

GHS Classification
Specific target organ toxicity - repeated exposure (Dermal): Category 2 (muscle, Kidney, Nervous system)

GHS label elements

Hazard pictograms:

Signal word: Warning
Hazard statements: H373 May cause damage to organs (muscle, Kidney, Nervous system) through prolonged or repeated exposure in contact with skin.

Precautionary statements:

Response: P314 Get medical advice/ attention if you feel unwell.
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.

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>Sucrose</td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
</tr>
</tbody>
</table>

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. Get medical attention if symptoms occur.

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 damage to organs through prolonged or repeated exposure in contact with skin. 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.

5. FIREFIGHTING 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.
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.

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 Advice on safe handling : Use only with adequate ventilation. Do not get on skin or clothing. Do not breathe dust, fume, gas, mist, vapours or spray. Do not swallow. Avoid contact with eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
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 labelled containers.
Store in accordance with the particular national regulations.

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

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>Sucrose</td>
<td>57-50-1</td>
<td>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
</tbody>
</table>

Further information: Adopted in Year 1996, Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals

<table>
<thead>
<tr>
<th></th>
<th>TWA</th>
<th>10 mg/m³</th>
<th>ACGIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptomycin</td>
<td>TWA</td>
<td>0.4 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

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.

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.

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearance</strong></td>
<td>Lyophilised cake</td>
</tr>
<tr>
<td><strong>Colour</strong></td>
<td>Light brown</td>
</tr>
<tr>
<td><strong>Odour</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Odour Threshold</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>6.5 - 7.3 (as aqueous solution)</td>
</tr>
<tr>
<td><strong>Melting point/freezing point</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Initial boiling point and boiling range</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Flash point</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Evaporation rate</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Flammability (solid, gas)</strong></td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td><strong>Flammability (liquids)</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Upper explosion limit / Upper flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Lower explosion limit / Lower flammability limit</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Vapour pressure</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Relative vapour density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Relative density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Density</strong></td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Solubility(ies)</strong></td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td><strong>Partition coefficient: n-octanol/water</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Auto-ignition temperature</strong></td>
<td>No data available</td>
</tr>
</tbody>
</table>
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.
Particle size : No data available

10. STABILITY AND REACTIVITY
Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reac-
tions : May form explosive dust-air mixture during processing, han-
dling 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.

11. TOXICOLOGICAL INFORMATION
Information on likely routes of exposure : Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
Not classified based on available information.

Components:
Sucrose:
Acute oral toxicity : LD50 (Rat): 29,700 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:
Daptomycin:
Species : Rabbit
Result : Mild skin irritation

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

Daptomycin:
Species: Rabbit
Result: Mild eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Germ cell mutagenicity
Not classified based on available information.

Components:

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

Daptomycin:
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
Test system: mouse lymphoma cells
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
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: Hamster
Application Route: Intraperitoneal injection
Result: negative
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Carcinogenicity
Not classified based on available information.

Reproductive toxicity
Not classified based on available information.

Components:

Daptomycin:
Effects on fertility: Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Intravenous injection  
Fertility: NOAEL: 150 mg/kg body weight  
Result: No effects on fertility

Effects on foetal development: Test Type: Embryo-foetal development  
Species: Rat  
Application Route: Intravenous injection  
Developmental Toxicity: NOAEL: 75 mg/kg body weight  
Result: No significant adverse effects were reported

Test Type: Embryo-foetal development  
Species: Rabbit  
Application Route: Intravenous injection  
Developmental Toxicity: NOAEL: 75 mg/kg body weight  
Result: No significant adverse effects were reported

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (muscle, Kidney, Nervous system) through prolonged or repeated exposure in contact with skin.

Components:

Daptomycin:
Target Organs: muscle, Kidney, Nervous system  
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Daptomycin:
Species: Dog  
NOAEL: 20 mg/kg  
LOAEL: 40 mg/kg  
Application Route: Intravenous  
Exposure time: 3 Months  
Target Organs: Skeletal muscle

Species: Monkey
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NOAEL: 10 mg/kg
Application Route: Intravenous
Exposure time: 1 Months
Remarks: No significant adverse effects were reported

Species: Dog
Application Route: Intravenous
Exposure time: 28 Days
Target Organs: Skeletal muscle, Nervous system
Symptoms: muscle twitching

Species: Juvenile dog
LOAEL: 50 mg/kg
Application Route: Intravenous
Exposure time: 28 Days
Target Organs: Skeletal muscle, Nervous system

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Daptomycin:
General Information: Symptoms: Rash, Diarrhoea, vaginitis

12. ECOLOGICAL INFORMATION

Ecotoxicity
No data available

Persistence and degradability
No data available

Bioaccumulative potential

Components:

Sucrose:
Partition coefficient: n-octanol/water: Pow: < 1

Mobility in soil
No data available

Other adverse effects
No data available

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 han-
14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

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

15. REGULATORY INFORMATION

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

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered : Not applicable

Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : Not applicable

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
16. OTHER INFORMATION

Further information

Date format: yyyymm/dd

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ID OEL: Indonesia. Occupational Exposure Limits
ACGIH / TWA: 8-hour, time-weighted average
ID OEL / NAB: Long term exposure limit

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
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intended manner of handling, use, processing and storage, including an assessment of the ap-
propriateness of the SDS material in the user’s end product, if applicable.

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