Daptomycin Injection Formulation - 2nd Generation

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

1.1 Product identifier
   Trade name: Daptomycin Injection Formulation - 2nd Generation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company: MSD
   Shotton Lane
   NE23 3JU Cramlington NU - Great Britain
   Telephone: 44 1 670 59 30 00
   Telefax: 908-735-1496
   E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Specific target organ toxicity - repeated exposure, Category 2
   H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Hazard pictograms:  

   Signal word: Warning

   Hazard statements: H373 May cause damage to organs through prolonged or repeated exposure.

   Precautionary statements: Response:
   P314 Get medical advice/attention if you feel unwell.
Hazardous components which must be listed on the label:
Daptomycin

2.3 Other hazards
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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daptomycin</td>
<td>103060-53-3</td>
<td></td>
<td></td>
<td>STOT RE 2; H373 (muscle, Kidney, Nervous system)</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

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).

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: May cause damage to organs through prolonged or repeated
4.3 Indication of any immediate medical attention and special treatment needed

Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture

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

5.3 Advice for firefighters

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

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

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

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

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 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.

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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)

Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational Exposure Limits

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
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<td>103060-53-3</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TWA</td>
<td>0.4 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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

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.

Hand protection
Material: Chemical-resistant gloves

Skin and body protection: Work uniform or laboratory coat.

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
Equipment should conform to NS EN 143

Filter type: Particulates type (P)

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SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance: lyophilised cake

Colour: light brown

Odour: No data available

Odour Threshold: No data available

pH: 6.5 - 7.3
(as aqueous solution)

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.

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: No data available

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: Not applicable

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.
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

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Version 2.4  Revision Date: 10.10.2020  SDS Number: 690893-00012  Date of last issue: 23.03.2020
Date of first issue: 19.05.2016

9.2 Other information
- Flammability (liquids): No data available
- Particle size: No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
- Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
- Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
- Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
- Information on likely routes of exposure: Inhalation, Skin contact, Ingestion, Eye contact

Acute toxicity
Not classified based on available information.

Skin corrosion/irritation
Not classified based on available information.

Components:

Daptomycin:
- Species: Rabbit
- Result: Mild skin irritation
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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:**

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

**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 through prolonged or repeated exposure.

**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  
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

SECTION 12: Ecological information

12.1 Toxicity
No data available

12.2 Persistence and degradability
No data available

12.3 Bioaccumulative potential
No data available

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods
Product : Dispose of in accordance with local regulations.
According to the European Waste Catalogue, Waste Codes are not product specific, but application specific.
Waste codes should be assigned by the user, preferably in
### SECTION 14: Transport information

14.1 **UN number**
- Not regulated as a dangerous good

14.2 **UN proper shipping name**
- Not regulated as a dangerous good

14.3 **Transport hazard class(es)**
- Not regulated as a dangerous good

14.4 **Packing group**
- Not regulated as a dangerous good

14.5 **Environmental hazards**
- Not regulated as a dangerous good

14.6 **Special precautions for user**
- Not applicable

14.7 **Transport in bulk according to Annex II of Marpol and the IBC Code**
- Remarks: Not applicable for product as supplied.

### SECTION 15: Regulatory information

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

- **REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII)**: Not applicable
- **REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59)**: Not applicable
- **REACH - List of substances subject to authorisation (Annex XIV)**: Not applicable
- **Regulation (EC) No 1005/2009 on substances that deplete the ozone layer**: Not applicable
- **Regulation (EU) 2019/1021 on persistent organic pollutants (recast)**: Not applicable
- **Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals**: Not applicable

**Other regulations:**

Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is...
The components of this product are reported in the following inventories:

AICS : not determined

DSL : not determined

IECSC : not determined

15.2 Chemical safety assessment

A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information : Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements

H373 : May cause damage to organs through prolonged or repeated exposure in contact with skin.

Full text of other abbreviations

STOT RE : Specific target organ toxicity - repeated exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RID - Regulations concerning the International Carriage of Dangerous Goods.
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<table>
<thead>
<tr>
<th>Version</th>
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<td>19.05.2016</td>
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Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bio-accumulative

Further information

Classification of the mixture: STOT RE 2  H373
Classification procedure: Calculation method

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.

NO / EN