SAFETY DATA SHEET

Cyclosporine Formulation

Version: 2.4
Revision Date: 12.10.2021
SDS Number: 610641-00012
Date of last issue: 23.03.2020
Date of first issue: 08.04.2016

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Cyclosporine Formulation

Manufacturer or supplier's details
Company: MSD
Address: Briahnager - Off Pune Nagar Road
Wagholi - Pune - India 412 207
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: Veterinary product

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Carcinogenicity: Category 1B

GHS label elements
Hazard pictograms:

Signal word: Danger
Hazard statements: H350 May cause cancer.

Precautionary statements: Prevention:
P203 Obtain, read and follow all safety instructions before use.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P318 IF exposed or concerned, get medical advice.

Storage:
P405 Store locked up.

Disposal:
SAFETY DATA SHEET

Cyclosporine Formulation

P501 Dispose of contents/container to an approved waste disposal plant.

Other hazards which do not result in classification
None known.

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></td>
<td>Petrolatum</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</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.

In case of skin contact: In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: Flush eyes with water as a precaution. Get medical attention if irritation develops and persists.

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

Most important symptoms and effects, both acute and delayed: May cause cancer.

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: Exposure to combustion products may be a hazard to health.

Hazardous combustion prod-
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.

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. Prevent spreading over a wide area (e.g. by containment or oil barriers). Retain and dispose of contaminated wash water. Local authorities should be advised if significant spills cannot be contained.

Methods and materials for containment and cleaning up: Soak up with inert absorbent material. For large spills, provide dyking or other appropriate containment to keep material from spreading. If dyked material can be pumped, store recovered material in appropriate container. Clean up remaining materials from spill with suitable absorbent. 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: See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe vapours. 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. Keep container tightly closed. Take care to prevent spills, waste and minimize release to the environment.
SAFETY DATA SHEET

Cyclosporine Formulation

Version | Revision Date: | SDS Number: | Date of last issue: | Date of first issue:
2.4     | 12.10.2021   | 610641-00012 | 23.03.2020          | 08.04.2016

Conditions for safe storage
- Keep in properly labelled containers.
- Store locked up.
- 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

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>Petrolatum</td>
<td>8009-03-8</td>
<td>TWA (Mist)</td>
<td>5 mg/m³</td>
<td>IN OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEL (Mist)</td>
<td>10 mg/m³</td>
<td>IN OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable particulate matter)</td>
<td>5 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>59865-13-3</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures
- Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., drip-less quick connections).
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
- Minimize open handling.

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: Chemical-resistant gloves

Remarks: Consider double gloving.

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.
- Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
Use appropriate degowning techniques to remove potentially contaminated clothing.

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

Appearance: viscous liquid

Colour: colourless, to, light yellow

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: No data available

Evaporation rate: No data available

Flammability (solid, gas): Not applicable

Flammability (liquids): No data available

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
10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: Can react with strong oxidizing agents.
Conditions to avoid: None known.
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:

Petrolatum:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Method: OECD Test Guideline 401
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity
Remarks: Based on data from similar materials

Cyclosporine:
Acute oral toxicity: LD50 (Rat): 1,480 mg/kg
LD50 (Mouse): 2,329 mg/kg
Acute inhalation toxicity : Remarks: No data available

Acute dermal toxicity : Remarks: No data available

Acute toxicity (other routes of administration) : LD50 (Mouse): 107 mg/kg
Application Route: Intravenous

LD50 (Rat): 25.8 mg/kg
Application Route: Intravenous

Skin corrosion/irritation
Not classified based on available information.

Components:

Petrolatum:
Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation
Remarks : Based on data from similar materials

Cyclosporine:
Remarks : No data available
May irritate skin.

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

Components:

Petrolatum:
Species : Rabbit
Method : OECD Test Guideline 405
Result : No eye irritation
Remarks : Based on data from similar materials

Cyclosporine:
Remarks : No data available
May irritate eyes.

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Petrolatum:
Test Type : Buehler Test
**SAFETY DATA SHEET**

**Cyclosporine Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
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- **Exposure routes**: Skin contact
- **Species**: Guinea pig
- **Result**: negative
- **Remarks**: Based on data from similar materials

**Cyclosporine**

**Remarks**: May cause sensitisation of susceptible persons.

**Germ cell mutagenicity**

Not classified based on available information.

**Components**

**Petrolatum**

- **Genotoxicity in vitro**
  - Test Type: Chromosome aberration test in vitro
  - Result: negative
  - Remarks: Based on data from similar materials

- **Genotoxicity in vivo**
  - Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - Species: Mouse
  - Application Route: Intraperitoneal injection
  - Method: OECD Test Guideline 474
  - Result: negative
  - Remarks: Based on data from similar materials

**Cyclosporine**

- **Genotoxicity in vitro**
  - Test Type: Bacterial reverse mutation assay (AMES)
  - Result: negative
  - Test Type: In vitro mammalian cell gene mutation test
  - Test system: Chinese hamster cells
  - Result: negative
  - Test Type: sister chromatid exchange assay
  - Result: positive

- **Genotoxicity in vivo**
  - Test Type: Micronucleus test
  - Species: Mouse
  - Application Route: Oral
  - Result: negative
  - Test Type: Chromosomal aberration
  - Species: Chinese hamster
  - Cell type: Bone marrow
  - Result: negative
  - Test Type: Chromosomal aberration
  - Species: Mouse
  - Result: negative
Carcinogenicity
May cause cancer.

Components:

Petrolatum:
Species: Rat
Application Route: Ingestion
Exposure time: 2 Years
Result: negative

Cyclosporine:
Species: Mouse
Application Route: Oral
Exposure time: 78 weeks
LOAEL: 4 mg/kg body weight
Result: positive
Target Organs: Liver, lymphatic system

Species: Rat
Application Route: Oral
Exposure time: 2 Years
LOAEL: 0.5 mg/kg body weight
Result: positive
Target Organs: Pancreas

Species: Humans
Result: May cause cancer.
Target Organs: Immune system, Skin
Remarks: Information taken from reference works and the literature.

Carcinogenicity - Assessment: May cause cancer.

Reproductive toxicity
Not classified based on available information.

Components:

Petrolatum:
Effects on fertility: Test Type: Reproduction/Developmental toxicity screening test
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Skin contact
Result: negative
Remarks: Based on data from similar materials

Cyclosporine:
SAFETY DATA SHEET

Cyclosporine Formulation

Effects on fertility:
- Test Type: One-generation reproduction toxicity study
  - Species: Rat
  - Application Route: Oral
  - General Toxicity F1: LOAEL: 15 mg/kg body weight
  - Result: No effects on fertility, Effect on reproduction capacity

  Test Type: Fertility
  - Species: Rat, males
  - Application Route: Subcutaneous
  - Fertility: LOAEL: 10 mg/kg body weight
  - Result: Reduced fertility

Effects on foetal development:
- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 30 mg/kg body weight
  - Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, Reduced foetal weight, foetal mortality, Retardations, Teratogenic effects

  Test Type: Embryo-foetal development
  - Species: Rabbit
  - Developmental Toxicity: LOAEL: 100 mg/kg body weight
  - Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses, Reduced foetal weight, foetal mortality, Retardations, Teratogenic effects

  Test Type: Development
  - Species: Rabbit
  - Application Route: Subcutaneous
  - Developmental Toxicity: LOAEL: 10 mg/kg body weight
  - Target Organs: Kidney
  - Result: Visceral malformations

  Test Type: Development
  - Species: Rat
  - Application Route: Intravenous
  - Developmental Toxicity: LOAEL: 12 mg/kg body weight
  - Target Organs: Heart
  - Result: Visceral malformations

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Components:

Cyclosporine:
- Target Organs: Kidney, Liver, Immune system
- Assessment: Causes damage to organs through prolonged or repeated exposure.
Repeated dose toxicity

**Components:**

**Petrolatum:**
- **Species:** Rat
- **NOAEL:** 5,000 mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 2 yr

**Cyclosporine:**
- **Species:** Rat
  - **NOAEL:** 14 mg/kg
  - **LOAEL:** 45 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 90 Days
  - **Target Organs:** Kidney, Liver, Immune system
  - **Symptoms:** hair loss

- **Species:** Monkey
  - **NOAEL:** 20 mg/kg
  - **LOAEL:** 60 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 90 Days
  - **Target Organs:** Immune system
  - **Symptoms:** Gastrointestinal disturbance, Liver disorders, Kidney disorders

- **Species:** Dog
  - **LOAEL:** 15 mg/kg
  - **Application Route:** Oral
  - **Exposure time:** 12 Months
  - **Target Organs:** Immune system
  - **Symptoms:** Changes in the blood count, Kidney disorders, Skin disorders, hair loss

**Aspiration toxicity**

Not classified based on available information.

**Experience with human exposure**

**Components:**

**Cyclosporine:**
- **Inhalation:** Remarks: May cause irritation of respiratory tract.
- **Skin contact:** Remarks: May irritate skin.
- **Eye contact:** Symptoms: Eye irritation, eye pain
- **Ingestion:** Symptoms: Kidney disorders, Tremors, Hypertension, blood effects, Gastrointestinal disturbance
## 12. ECOLOGICAL INFORMATION

### Ecotoxicity

**Components:**

**Petrolatum:**

- **Toxicity to fish:** LL50 (Pimephales promelas (fathead minnow)): > 100 mg/l
  - Exposure time: 96 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 203
  - Remarks: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates:** EC50 (Daphnia magna (Water flea)): > 10,000 mg/l
  - Exposure time: 48 h
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials

- **Toxicity to algae/aquatic plants:** NOEL (Pseudokirchneriella subcapitata (green algae)): > = 100 mg/l
  - Exposure time: 72 h
  - Test substance: Water Accommodated Fraction
  - Method: OECD Test Guideline 201
  - Remarks: Based on data from similar materials

- **Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):** NOEC: 10 mg/l
  - Exposure time: 21 d
  - Species: Daphnia magna (Water flea)
  - Test substance: Water Accommodated Fraction
  - Remarks: Based on data from similar materials

### Persistence and degradability

**Components:**

**Petrolatum:**

- **Biodegradability:** Result: Not readily biodegradable.
  - Biodegradation: 31%
  - Exposure time: 28 d
  - Method: OECD Test Guideline 301F
  - Remarks: Based on data from similar materials

### Bioaccumulative potential

No data available

### 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 handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

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 IMO instruments
Not applicable for product as supplied.

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

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

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

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

16. OTHER INFORMATION

Further information


Date format: dd.mm.yyyy

Full text of other abbreviations

ACGIH: USA. ACGIH Threshold Limit Values (TLV)
IN OEL: India. Permissible levels of certain chemical substances in work environment.
SAFETY DATA SHEET

Cyclosporine Formulation

Table: Safety Data Sheet Details

<table>
<thead>
<tr>
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<th>Revision Date</th>
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ACGIH / TWA : 8-hour, time-weighted average
IN OEL / TWA : Time-Weighted Average Concentration (TWA) (8 hrs.)
IN OEL / STEL : Short-term exposure Limit STEL (15 min)

AllIC - 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 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; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; 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; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TECI - Thailand Existing Chemicals 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 Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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.

IN / EN