SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Cyclosporine Formulation

Manufacturer or supplier's details
Company: MSD
Address: Rua Coronel Bento Soares, 530
          Cruzeiro - Sao Paulo - Brazil  CEP 12730-340
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Veterinary product

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Carcinogenicity: Category 1B

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms:  🍼

Signal Word: Danger
Hazard Statements: H350 May cause cancer.
Precautionary Statements:
Prevention:
P201 Obtain special instructions before use.
P280 Wear protective gloves/ protective clothing/ eye protec-
tion/ face protection.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/
attention.
Storage:
P405 Store locked up.

Other hazards which do not result in classification
None known.
SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Petrolatum</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
</tr>
<tr>
<td></td>
<td></td>
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</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. 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.

SECTION 5. FIRE-FIGHTING MEASURES

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Unsuitable extinguishing media: None known.
Specific hazards during fire fighting: Exposure to combustion products may be a hazard to health.
Hazardous combustion products: Carbon oxides

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.
- 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 spillages cannot be contained.

Methods and materials for containment and cleaning up:
- Soak up with inert absorbent material.
- For large spills, provide diking or other appropriate containment to keep material from spreading. If diked 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.

SECTION 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 vapors.
- Do not swallow.
- Avoid contact with eyes.
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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.

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 labeled 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
Organic peroxides
Explosives
Gases

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>Petrolatum</td>
<td>8009-03-8</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., dripless 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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Viscous liquid

Color: Colorless, to, light yellow

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: 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

Vapor pressure: No data available

Relative vapor 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
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.
Particle size: Not applicable

SECTION 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.

SECTION 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
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Version 3.1  Revision Date: 12.10.2021  SDS Number: 608873-00012  Date of last issue: 23.03.2020  Date of first issue: 08.04.2016

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

Cyclosporine:
Remarks : No data available
May irritate eyes.

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.
Respiratory sensitization
Not classified based on available information.

Components:

Petrolatum:
Test Type: Buehler Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative
Remarks: Based on data from similar materials

Cyclosporine:
Remarks: May cause sensitization 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 fetal development: Test Type: Embryo-fetal development  
Species: Rat  
Application Route: Skin contact

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Result: negative
Remarks: Based on data from similar materials

Cyclosporine:

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 fetal development:
- Test Type: Embryo-fetal 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 fetal weight., Fetal mortality., Retardations., Teratogenic effects.

- Test Type: Embryo-fetal 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 fetal weight., Fetal 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 y

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
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SECTION 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 (Daphnia magna (Water flea)): 10 mg/l Exposure time: 21 d Test substance: Water Accommodated Fraction Remarks: Based on data from similar materials

Persistence and degradability

Components:

Petrolatum:

Bioaccumulative potential
No data available

Mobility in soil
No data available

Other adverse effects
No data available

effects, Gastrointestinal disturbance
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
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.

Domestic regulation

ANTT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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

National List of Carcinogenic Agents for Humans - (LINACH)
Group 1: Carcinogenic to humans
Cyclosporine 59865-13-3

Brazil. List of chemicals controlled by the Federal Police: Not applicable

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

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA : 8-hour, time-weighted average

All abbreviations are at the end of the document.

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.