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
Telefax : 908-735-1496

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 protection/ face protection.
Response: P308 + P313 IF exposed or concerned: Get medical advice/ attention.
Storage: P405 Store locked up.
SAFETY DATA SHEET
Cyclosporine Formulation

Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Petrolatum</td>
<td>8009-03-8</td>
<td>Acute toxicity (Oral), Category 4</td>
<td>&gt;= 50 -&lt; 70</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
<td>59865-13-3</td>
<td>Acute toxicity (Oral), Category 4, Carcinogenicity, Category 1B, Reproductive toxicity, Category 1B, Specific target organ toxicity - repeated exposure (Kidney, Liver, Immune system), Category 1</td>
<td>&gt;= 0,1 -&lt; 0,3</td>
</tr>
</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

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 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 and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided.
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 or spray mist.
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.

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:

Material: 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 reac-
tions : 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
Cyclosporine Formulation

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
- 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
Cyclosporine Formulation

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:
- 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
   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

<table>
<thead>
<tr>
<th>Components:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine:</td>
</tr>
<tr>
<td>Target Organs</td>
</tr>
<tr>
<td>Assessment</td>
</tr>
</tbody>
</table>

Repeated dose toxicity

<table>
<thead>
<tr>
<th>Components:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrolatum:</td>
</tr>
<tr>
<td>Species</td>
</tr>
<tr>
<td>NOAEL</td>
</tr>
<tr>
<td>Application Route</td>
</tr>
<tr>
<td>Exposure time</td>
</tr>
</tbody>
</table>

| 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

<table>
<thead>
<tr>
<th>Components:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine:</td>
</tr>
<tr>
<td>Inhalation</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

Cyclosporine Formulation

Version 3.0  Revision Date: 23.03.2020  SDS Number: 608873-00011  Date of last issue: 13.09.2019
Date of first issue: 08.04.2016

Skin contact: Remarks: May irritate skin.
Eye contact: Symptoms: Eye irritation, eye pain
Ingestion: Symptoms: Kidney disorders, Tremors, hypertension, blood effects, Gastrointestinal disturbance

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:
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
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

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

International Regulations

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

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

AICS - Australian Inventory of Chemical Substances; 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 - Transport of Dangerous Goods; 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.

BR / Z8