Cyclosporine Formulation

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

1.1 Product identifier
   Trade name : Cyclosporine Formulation

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

1.3 Details of the supplier of the safety data sheet
   Company : MSD
             Walton Manor, Walton
             MK7 7AJ Milton Keynes - United Kingdom
   Telephone : 908-740-4000
   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)
   Carcinogenicity, Category 1B H350: May cause cancer.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   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:
SAFETY DATA SHEET
generated according to Regulation (EC) No. 1907/2006

Cyclosporine Formulation

Version 2.3
Revision Date: 23.03.2020
SDS Number: 610639-00011
Date of last issue: 13.09.2019
Date of first issue: 08.04.2016

P308 + P313 IF exposed or concerned: Get medical advice/attention.

Storage:
P405 Store locked up.

Hazardous components which must be listed on the label:
Cyclosporine

2.3 Other hazards
None known.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

Components

<table>
<thead>
<tr>
<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>Cyclosporine</td>
<td>59865-13-3</td>
<td></td>
<td></td>
<td>Acute Tox. 4; H302 Carc. 1B; H350 Repr. 1B; H360Df STOT RE 1; H372</td>
<td>&gt;= 0.1 - &lt; 0.3</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.

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.

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

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

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: 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 and personal protective equipment recommendations.
6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

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: 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 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.
7.2 Conditions for safe storage, including any incompatibilities

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

Advice on common storage: Do not store with the following product types:
- Strong oxidizing agents
- Organic peroxides
- Explosives
- Gases

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>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<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>

**Predicted No Effect Concentration (PNEC) according to Regulation (EC) No. 1907/2006:**

<table>
<thead>
<tr>
<th>Substance name</th>
<th>Environmental Compartment</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrolatum</td>
<td>Oral (Secondary Poisoning)</td>
<td>9.33 mg/kg food</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

**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**

**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
Cyclosporine Formulation

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>viscus liquid</td>
</tr>
<tr>
<td>Colour</td>
<td>colourless, to, light yellow</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Auto-ignition temperature</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.

9.2 Other information
Flammability (liquids) : No data available
Particle size : Not applicable

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 : Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid : None known.

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.

Components:
Cyclosporine:
Acute oral toxicity : LD50 (Rat): 1,480 mg/kg
Cyclosporine Formulation

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:

Cyclosporine:
Remarks: No data available
May irritate skin.

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

Components:

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:

Cyclosporine:
Remarks: May cause sensitisation of susceptible persons.

Germ cell mutagenicity
Not classified based on available information.

Components:

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:

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:

Cyclosporine:
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 off-spring 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 off-spring 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
**Repeated dose toxicity**

**Components:**

**Cyclosporine:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
<th>NOAEL</th>
<th>14 mg/kg</th>
<th>LOAEL</th>
<th>45 mg/kg</th>
<th>Application Route</th>
<th>Oral</th>
<th>Exposure time</th>
<th>90 Days</th>
<th>Target Organs: Kidney, Liver, Immune system</th>
<th>Symptoms: hair loss</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Monkey</th>
<th>NOAEL</th>
<th>20 mg/kg</th>
<th>LOAEL</th>
<th>60 mg/kg</th>
<th>Application Route</th>
<th>Oral</th>
<th>Exposure time</th>
<th>90 Days</th>
<th>Target Organs: Immune system</th>
<th>Symptoms: Gastrointestinal disturbance, Liver disorders, Kidney disorders</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
<th>LOAEL</th>
<th>15 mg/kg</th>
<th>Application Route</th>
<th>Oral</th>
<th>Exposure time</th>
<th>12 Months</th>
<th>Target Organs: Immune system</th>
<th>Symptoms: Changes in the blood count, Kidney disorders, Skin disorders, hair loss</th>
</tr>
</thead>
</table>

**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

**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 discussion with the waste disposal authorities.

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

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):
Conditions of restriction for the following entries should be considered:
Number on list 3
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

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Date of last issue: 13.09.2019
Date of first issue: 08.04.2016

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:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

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
H302: Harmful if swallowed.
H350: May cause cancer.
H360Df: May damage the unborn child. Suspected of damaging fertility.
H372: Causes damage to organs through prolonged or repeated exposure.

Full text of other abbreviations
Acute Tox.: Acute toxicity
Carc.: Carcinogenicity
Repr.: Reproductive toxicity
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
Cyclosporine Formulation

Version 2.3
Revision Date: 23.03.2020
SDS Number: 610639-00011
Date of last issue: 13.09.2019
Date of first issue: 08.04.2016

Goods by Road; AICS - Australian Inventory of Chemical Substances; 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 by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of Very High Concern; TCSI - Taiwan Chemical Substance Inventory; TRGS - Technical Rule for Hazardous Substances; TSCA - Toxic Substances Control Act (United States); UN - United Nations; vPvB - Very Persistent and Very Bioaccumulative

Further information

Classification of the mixture:

Carc. 1B H350

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.

GB / EN