

Cyclosporine Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 16.05.2024
3.0	06.07.2024	608885-00021	Date of first issue: 08.04.2016

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Cyclosporine Formulation
Other means of identification : Optimmune (A007869)
OPTIMMUNE OPHTHALMIC OINTMENT (51551)

Manufacturer or supplier's details

Company name of supplier : MSD
Address : 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
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
Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Carcinogenicity : Category 1B
Reproductive toxicity : Category 1B

GHS label elements

Hazard pictograms :



Signal Word : Danger

Hazard Statements : H350 May cause cancer.
H360Df May damage the unborn child. Suspected of damaging fertility.

Precautionary Statements : **Prevention:**
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
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.
Disposal:

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

Other hazards

None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)
Petrolatum	8009-03-8	≥ 50 -< 70
Cyclosporine	59865-13-3	≥ 0.1 -< 1

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.
May damage the unborn child. Suspected of damaging fertility.

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

Hazardous combustion products : Carbon oxides

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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 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

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- II**
- Hygiene measures : environment.
 : 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
 Self-reactive substances and mixtures
 Organic peroxides
 Explosives
 Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Petrolatum	8009-03-8	VLE-PPT (Mist)	5 mg/m ³	NOM-010-STPS-2014
		TWA (Inhalable particulate matter)	5 mg/m ³	ACGIH
Cyclosporine	59865-13-3	TWA	10 µg/m ³ (OEB 3)	Internal
		Wipe limit	100 µg/100 cm ²	Internal

- 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.

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Filter type	:	Combined particulates and organic vapor 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	:	ointment
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

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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 characteristics	:	
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

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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.

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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.
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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

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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

May damage the unborn child. Suspected of damaging fertility.

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

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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.

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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.
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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
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Bioaccumulative potential

No data available

Mobility in soil

No data available

Other adverse effects

No data available

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SECTION 13. DISPOSAL CONSIDERATIONS**Disposal methods**

Waste from residues	:	Do not dispose of waste into sewer. 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**NOM-002-SCT**

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**

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.	:	Not applicable
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The ingredients of this product are reported in the following inventories:

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

SECTION 16. OTHER INFORMATION

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Date format	:	dd.mm.yyyy

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Full text of other abbreviations

ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014	:	Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
ACGIH / TWA	:	8-hour, time-weighted average
NOM-010-STPS-2014 / VLE-	:	Time weighted average limit value
PPT	:	

AIIC - 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; TECl - 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

Sources of key data used to compile the Material Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

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

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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