Lupin Pharmaceuticals, Inc.

SAFETY DATA SHEET

Section 1: Identification

Material

Cyclosporine Opthalmic Emulsion 0.05%

Manufacturer

Allergan Sales, LLC
8301 Mars Dr,
Waco, Texas (TX) 76712-6578
United States

Distributor

Lupin Pharmaceuticals, Inc.
111 South Calvert Street,
Harborplace Tower, 21st Floor,
Baltimore, Maryland 21202
United States
Tel. 001-410-576-2000
Fax. 001-410-576-2221

Section 2: Hazard(s) Identification

OSHA Regulatory Status

This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Acute toxicity - Inhalation (Dusts/Mists)

Category 4

Label Elements

Warning
Hazard Statement
H332 – Harmful if Inhaled

Precautionary statements

P261 - Avoid breathing dust/fume/gas/mist/vapors/spray
P271 - Use only outdoors or in a well-ventilated area
P304 + P340 - IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
P312 - Call a POISON CENTER or doctor if you feel unwell

Other Information

Exempt under the criteria of the Federal OSHA Hazard Communication Standard 20 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limit may be surpassed, than can be considered hazardous

Section 3: Composition/Information on Ingredients

Chemical Name	CAS No.	EINECS	Weight-%
Water	7732-18-5	231-791-2	60 - 100*
GLYCERINE USP (96%)	56-81-5	200-289-5	1 - 5*
Polysorbate 80	9005-65-6	N/A	1 - 5*
Castor Oil	8001-79-4	232-293-8	0.1 - 1*
Cyclosporine	59865-13-3	N/A	<0.1*
*The exact percentage (concentration) of composition has been withheld as a trade secret.			

Section 4: First-Aid Measures

Ingestion	Consult a physician if necessary.
Inhalation	Remove to fresh air.
Skin Contact	Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.
Eye Contact	Rinse immediately with plenty of water and seek medical advice.

NOTES TO HEALTH PROFESSIONALS

Note to Physicians

Risk-benefit should be considered when the following medical problems exist: Cardiac disease or hypervolemia (sudden expansion of extracellular fluid may lead to congestive heart failure); Confused mental states or severe dehydration; diabetes mellitus (existing dehydration may affect patient); Renal disease (accumulation may lead to overexpansion of extracellular fluid and circulatory overload).

Transient hepatotoxicity and nephrotoxicity may occur which should resolve following drug withdrawal. Oral doses of cyclosporine up to 10 g (about 150 mg/kg) have been tolerated with relatively minor clinical consequences, such as vomiting, drowsiness, headache, tachycardia and, in a few patients, moderately severe, reversible impairment of renal function. However, serious symptoms of intoxication have been reported following accidental parenteral overdosage with cyclosporine in premature neonates. General supportive measures and symptomatic treatment should be followed in all cases of overdosage. Cyclosporine is not dialyzable to any great extent, nor is it cleared well by charcoal hemoperfusion.

Section 5: Fire-Fighting Measures

Suitable extinguishing media	Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Unsuitable extinguishing media	None known.
Specific hazards arising from the chemical	Fire may produce irritating, corrosive and/or toxic gases.
Explosion data	
Sensitivity to Mechanical Impact	Not impact sensitive
Sensitivity to Static Discharge	Fine dust dispersed in air, in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
Protective equipment and precautions for firefighters	As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

Section 6: Accidental Release Measures

Personal Precautions	Use personal protection recommended in Section 8. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing.
Environmental Precautions	See Section 12 for additional ecological information.
Clean-up Methods	Avoid creating dust.
Methods for containment	Prevent further leakage or spillage if safe to do so.

Section 7: Handling and Storage

Handling — Avoid contact with skin, eyes or clothing. Avoid generation of dust. Do not eat, drink or smoke when using this product.

Storage — Store at 15°-25°C (59°-77°F)

Section 8: Exposure Controls/Personal Protection

Control parameters

Exposure Guidelines

Chemical Name	ACGIH TLV	OSHA PEL	NIOSH IDLH	Allergan OEL (ug/m3)
GLYCERINE USP (96%) 56-81-5	N/A	TWA: 15 mg/m3 mist, total particulate TWA: 5 mg/m3 mist, respirable fraction (vacated) TWA: 10 mg/m3 mist, total particulate (vacated) TWA: 5 mg/m3 mist, respirable fraction	N/A	N/A
Cyclosporine 59865-13-3	N/A	N/A	N/A	N/A

Appropriate engineering controls

Engineering Controls — The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used.
Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/face protection — No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, safety glasses should be considered.

Skin and body protection — During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. Use appropriate protective clothing for the task (e.g., lab coat, etc.).

Respiratory protection — Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

Section 9: Physical and Chemical Properties

Physical Form — Cyclosporine ophthalmic emulsion is packaged in sterile, preservative-free single-use vials.
Each vial contains 0.4 mL fill in a 0.9 mL LDPE vial; 30 or 60 vials are packaged in a polypropylene tray with an aluminum peelable lid. The entire contents of each tray (30 vials or 60 vials) must be dispensed intact.

30 Vials 0.4 mL each - NDC 68180-214-30
60 Vials 0.4 mL each - NDC 68180-214-60

Physical state — Liquid
Appearance — Liquid

Color	No information available
Odor	No information available
Odor threshold	No information available
Property	
pH	No information available
Melting point/ Freezing point	No information available
Boiling point/ Boiling Range	No information available
Flash point	No information available
Evaporation rate	No information available
Flammability (solid, gas)	No information available
Flammability Limit in Air	No information available
Upper flammability limit:	No information available
Lower flammability limit:	No information available
Vapor pressure	No information available
Vapor density	No information available
Specific Gravity	No information available
Water solubility	No information available
Solubility in other solvents	No information available
Partition coefficient	No information available
Autoignition temperature	No information available
Decomposition temperature	No information available
Explosive properties	No information available
Oxidizing properties	No information available
Other Information	
Molecular weight	No information available
VOC Content (%)	No information available
Density	No information available
Bulk density	No information available

Section 10: Stability and Reactivity

Reactivity	Not defined As Reactive substance
Chemical stability	Stable under normal conditions.
Possibility of Hazardous Reactions	None under normal processing.
Conditions to avoid	Aerosol formation.
Incompatible materials	None known based on information supplied.
Hazardous Decomposition Products	None known based on information supplied

Section 11: Toxicological Information

Information on likely route of exposure

Acute toxicity

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
Water	> 90 mL/kg (Rat)	N/A	N/A
GLYCERINE USP (96%)	= 12600 mg/kg (Rat)	> 10 g/kg (Rabbit)	> 570 mg/m³ (Rat) 1 h
Polysorbate 80	= 34500 µL/kg (Rat)	N/A	N/A
Cyclosporine	= 1480 mg/kg (Rat)	N/A	N/A

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Chemical Name	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Effects on or via lactation
GLYCERINE USP (96%)	Not mutagenic in the standard battery of tests.	This product does not contain any carcinogens or potential carcinogens as listed by OSHA, IARC or NTP.	This product does not contain any known or suspected reproductive hazards.	It is not known whether the drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this drug is administered to nursing mothers.

Chemical Name	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Effects on or via lactation
Polysorbate 80	No information available.	Not suspected of being a human carcinogen.	This product does not contain any known or suspected reproductive hazards.	It is not known whether the drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this drug is administered to nursing mothers.
Cyclosporine	Not mutagenic in the standard battery of tests.	Carcinogenicity studies were carried out in male and female rats and mice. In the 78-week mouse study, at doses of 1, 4, and 16 mg/kg/day, evidence of a statistically significant trend was found for lymphocytic lymphomas in females, and the incidence of hepatocellular carcinomas in mid-dose males significantly exceeded the control value. In the 24–month rat study, conducted at 0.5, 2, and 8 mg/kg/day, pancreatic islet cell adenomas significantly exceeded the control rate in the low-dose level. The hepatocellular carcinomas and pancreatic islet cell adenomas were not dose related.	Animal studies have shown reproductive toxicity in rats and rabbits. Cyclosporine gave no evidence of mutagenic or teratogenic effects in the standard test systems with oral application (rats up to 17 mg/kg and rabbits up to 30 mg/kg per day orally). cyclosporine has been shown to be embryo- and fetotoxic in rats and rabbits when given in doses 2-5 times the human dose. At toxic doses (rats at 30 mg/kg/day and rabbits at 100 mg/kg/day), cyclosporine was embryo- and fetotoxic as indicated by increased pre- and postnatal mortality and reduced fetal weight together with related skeletal retardations. In the well-tolerated dose range (rats at up to 17 mg/kg/day and rabbits at up to 30 mg/kg/day), cyclosporine proved to be without any embryolethal or teratogenic effects.	Detectable amounts of this compound have been identified in the milk of nursing women receiving this drug. Caution should be exercised when taking this compound is administered to nursing women.

Numerical measures of toxicity - Product Information

The following values are calculated based on chapter 3.1 of the GHS document.
ATEmix (inhalation-dust/mist) 4.9 mg/l

Section 12: Ecological Information

Ecotoxicity

1.51% of the mixture consists of components(s) of unknown hazards to the aquatic environment

Chemical Name	Algae/aquatic plants	Fish	Crustacea
GLYCERINE USP (96%) 56-81-5	N/A	51 - 57: 96 h Oncorhynchus mykiss mL/L LC50 static	500: 24 h Daphnia magna mg/L EC50

Chemical Name	Persistence and	Bioaccumulation	Mobility	Partition coefficient
GLYCERINE USP (96%) 56-81-5	N/A	N/A	N/A	-1.76

Other adverse effects No information available

Section 13: Disposal Considerations

Waste treatment method

Disposal of wastes Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated packaging	Do not reuse container. Dispose of contents/containers in accordance with local regulations.

Section 14: Transport Information

DOT	Not regulated
TDG	Not regulated
ICAO (air)	Not regulated
IATA	Not regulated
IMDG	Not regulated
ADR	Not regulated
ADN	Not regulated

Section 15: Regulatory Information

International Inventories

TSCA	Not Listed
DSL/NDSL	Not Listed
EINECS/ELINCS	Not Listed

Legend :
TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances

US Federal Regulations

Carcinogenicity — This product contains one or more substances which are classified by IARC as carcinogenic to humans (Group I), probably carcinogenic to humans (Group 2A) or possibly carcinogenic to humans (Group 2B)

Chemical Name	ACGIH	IARC	NTP	OSHA
Cyclosporine 59865-13-3	-	Group 1	Known	X

SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

Acute health hazard	No
Chronic Health Hazard	No
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)
This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA
This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material

US State Regulations

California Proposition 65
This product contains the following Proposition 65 chemicals

Chemical Name	California Proposition 65
Cyclosporine - 59865-13-3	Carcinogen

U.S. State Right-to-Know Regulations

Chemical Name	New Jersey	Massachusetts	Pennsylvania
GLYCERINE USP (96%) 56-81-5	X	X	X

Section 16: Other Information

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.

Lupin shall not be held liable for any damage resulting from handling or from contact with the above product. Lupin reserves the right to revise this SDS.