

V#448 Ivax Pharmaceuticals - Rx
3663499



Safety Data Sheet
Technical Engineering department

Name CYCLOSPORINE		Number of document BDL-SV\TE\010\05 - A
Number of replaced document BDL-SV\TE\010\01\02	Number of source document ZŘ 0093/05	Efficacy from 24. 2. 2005
Czech version elaborated by: Eva Kašingová <i>[Signature]</i>		
Translated by: Eva Kašingová <i>[Signature]</i>		
Approved by: Date: 20.5.2005 <i>[Signature]</i> Director of Technical Engineering Department		
Date: 15.6.2005 Issued by: <i>[Signature]</i>		

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1 Identification of the substance/preparation and of the manufacturer/supplier:

1.1 Identification of the substance or preparation

- 1.1.1 Chemical name of the substance/trade name of the product: Cyclosporine
- 1.1.2 Other name of the substance or preparation: Cyclosporinum, ciclosporine A
- 1.1.3 CAS-No: 59865-13-3
- 1.1.4 ES (EINECS)-No: -

1.2 Application of the substance or preparation: material for production of medicinal preparation

1.3 Identification of the manufacturer/supplier

- 1.3.1 Company: IVAX Pharmaceuticals Inc.
- 1.3.2 Address: Ostravská 29/305, 747 70 Opava 9, Czech republic
- 1.3.3 Telephone Number: ++420-653-64 1111
- 1.3.4 Fax: ++420-653-64 2150
- 1.3.5 e-mail: eva_kasingova@ivax-cz.com

1.4 Emergency telephone number and address: Toxicological information centre
 Na Bojišti 1
 128 08 Prague 2, Czech republic
 ++420-2-24 91 92 93
 ++420-2-24 91 54 02
 ++420-2-24 91 45 75
 tis@mbox.cesnet.cz

2 Composition information on ingredients:

Product contains following hazardous ingredients in concentration:

chemical name	CAS-No		concentration %	symbol(s)	R- phrase(s)
	ES (EINECS)-No.	index No.			
	cyclo-(3-hydroxy- N, 4-dimethyl - I -2-amino -6-octenoyl - α-aminobutyryl -N- methylglycyl - - methyl -leucyl-Lvalyl- N-methyl-Lleucyl -Lalanyl - D- alanyl - N - methyl -L-leucyl -N- methyl- L leucyl - N - methyl -L - valyl)	59865-13-3			

3 Hazard specification of substance or preparation

3.1 Classification substance or preparation according law:

Health risks for man: after overexposure, risk of effects on organism immunity, central nervous system damages, nephrotoxicity, hepatotoxicity, allergic skin reaction.

Hazard risks to environment: considering the low solubility of cyclosporine in water, adverse effects due to its release to the environment are not expected

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3.2 Most important adverse effects bear on possible unsuitable use:

Physical chemical: airborne organic dust together with electrostatic discharges can explode
Effects on man health: do not use for personal usage. This substance is set for other products preparation only
Effects on environment: in unsuitable use does not present risk for environment

3.3 Additional risks: none**4 First aid measures****4.1 Immediate medical aid:** is necessary, cyclosporine is toxic**4.2 First aid measures**

After inhalation: immediately leave area of inhalation, rinse thoroughly eyes and mucous membranes of upper respiratory tract

After skin contact: remove contaminated clothes, wash powder from skin with wet tampons, thoroughly wash skin with soap and water

After eye contact: rinse opened eyes for at least 15 minutes under running water

After ingestion: rinse out mouth, after swallowing bigger amounts induce stomach wound

4.3 Professional medical aid: in all cases seek medical advice and give information of preparation and exposure

5 Fire-fighting measures**5.1 Suitable extinguishing material:** water mist, foam**5.2 Unsuitable extinguishing material:** compressed CO₂ - danger of dust generation

5.3 Special risks: avoid dust generation (airborne organic dust together with electrostatic discharges can explode. In case of dust generation apply water mist).

5.4 Special protective equipment for fire fighters: self - contained breathing apparatus, protective clothing

6 Accidental release measures

6.1 Personal precautions: avoid overexposure to substance. Use personal protective equipment presented in point 8. Avoid dust generation. Wash thoroughly area of release.

6.2 Environmental precautions: place of escape exhaustive clean. Avoid release to the environment, water drainage and sewage system.

6.3 Methods for cleaning/disposal: clean up mechanically, sweep up carefully, collect in duplicate, entire labeled packing (PE bag, drum, container). Store for disposal, protect from release and steal.

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7 Handling and storage

7.1 Handling

7.1.1 Preventive measures for safety handling: handle with product only in original package (commonly metal or PE container including PE bag). Use personal protective agents.

7.1.2 Preventive measures for environment protective: avoid dust generation

7.1.3 Special demand for handling: none

7.2 Storage

7.2.1 Conditions for safety storage: store in original closed package (usually metal or plastic container with insert PE bag). Samples up to 100 g can be stored in double PE bag. Protect from light. Store at dry place. Storage temperature up to +25 °C. Transport temperature up to +40 °C.

7.2.2 Special demand for storage: do not store together with flammables and ignition sources.

7.3 Special use (at finished piece): cyclosporine is not finished piece

8 Exposure controls and personal protection

8.1 Exposure limits: for included material are appointed following acceptable exposition limits (PEL) and highest concentration in workplace (NPK-P):

chemical name of substance	mg.m ⁻³	
	PEL	NPK-P
cyclosporine	-	0.02

limiting value of biological exposure tests:

not determined

recommended monitor procedure:

not determined

8.2 Exposure restraint:

8.2.1 Exposure restraint of employees

Applicable operation: before breaks and after handling wash thoroughly hands

Technical regulation measures: ensure adequate ventilation/exhaust on workplace and storage areas

Collective protective equipment: not determined

Individual protective equipment: use following protective equipment:

Respiratory protection: mask or filter P3 with supported breathing, in emergency respirator P3

Eye protection: protective goggles

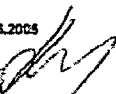
Hand protection: rubber gloves

Skin protection: protective clothes (e.g. Tyvek or RACAL), closed work shoes

8.3 Exposure restraint of environment: contaminated protective equipments must be consider as dangerous waste

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9 Information about physical and chemical properties

9.1 Common information:

Form (20 °C): solid (fine crystalline powder)
 Colour: white
 Odour (smell): odourless

9.2 Information for health protection, safety and environment:

pH value: not determined
 Boiling point: not determined
 Flash point (°C): not determined
 Flammability: formation fo explosive dust/air mixtures is possible
 Auto-ignition: not auto-ignite
 Explosion limits: upper (% v/v): not determined
 Oxidative properties: not oxidant
 Vapour pressure: not applicable
 Density: bulk density 400 kg.m⁻³
 shaken bulk density 480 kg.m⁻³
 Solubility in water: insoluble (substance is highly hydrphobic)
 fats: readily soluble in fats
 organic solvents: readily soluble in acetone, methanol, ethanol, chloroform and dichlormethane, badly soluble in saturated hydrocarbons, insoluble in hexane
 Partition coefficient Pow: not determined
 Viscosity: not applicable
 Density of steams: not determined
 Speed of evaporation: not determined

9.3 Additional information:

Mix: not determined
 Conductance: not determined
 Melting point: 148-151°C
 Class of gas: not applicable
 Ignition temperature (°C): not determined

10 Information about stability and reactivity

10.1 Conditions by which is product stable: product is stable, non-reactive and inexplusive under normal conditions (room temperatures) and conditions presented in product documentation and this safety sheet.

10.2 Conditions to be avoid: higher temperatures, sources of ignition

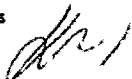
10.3 Substances to be avoid: oxidizing agents, alkali metals and aluminium

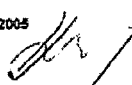
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<p>10.4 Hazardous decomposition products: toxic fumes and gases (CO, CO₂, NO_x) can release under fire conditions.</p> <p>Demand and attendance of stabilizers: none Eventuality of hazardous exothermic reactions: is not possible Optionally account change of physical condition for safety: is not changed Optionally hazardous products of decomposition, which grow in contact with water: are not Eventuality of decomposition at unstable products: under normal conditions the material is not decomposition</p> <p>11 Toxicological information</p> <p>11.1 Acute toxicity</p> <table style="width: 100%; border: none;"> <tr> <td style="padding-left: 20px;">- LD₅₀, oral, rat (mg.kg⁻¹):</td> <td style="text-align: right;">>1480</td> </tr> <tr> <td style="padding-left: 20px;">- LD₅₀, oral, mouse (mg.kg⁻¹):</td> <td style="text-align: right;">2329</td> </tr> <tr> <td style="padding-left: 20px;">- LD₅₀, oral dog (mg.kg⁻¹):</td> <td style="text-align: right;">not determined</td> </tr> <tr> <td style="padding-left: 20px;">- LD₅₀, dermal, rat /rabbit (mg.kg⁻¹):</td> <td style="text-align: right;">not determined</td> </tr> <tr> <td style="padding-left: 20px;">- LC₅₀, inhalation, rat/rabbit aerosols/particles (mg. kg⁻¹):</td> <td style="text-align: right;">not determined</td> </tr> <tr> <td style="padding-left: 20px;">- LC₅₀, inhalation, rat, gases/vapors (ppm):</td> <td style="text-align: right;">not determined</td> </tr> </table> <p>11.2 Subchronic-chronic toxicity</p> <p>Sensitization: eventuality cutaneous allergic reaction after ingestion Narcotic effects: may cause halucination as consequence hypomagnezemy which is do effects of cyclosporin (USP DI, Martindale) Carcinogenity: cyclosporine has been reported to be carcinogen, based on IARC classification, and probable carcinogenic, based on laboratory animal tests. EC classification of cyclosporine is carcinogenic category 1, in case of oral or intravenous immunosupressant doses, administrated after organ transplantations. (IARC) Mutagenity: laboratory studies have shown mutagenic effects. Mutagen in mammalian systems. Possible risk of congenital malformation in the fetus. Toxicity for reproduction: based on animal studies cyclosporine has been reported to be probably toxic for reproduction Experience on man: substance is toxic Laboratory test animals: based on animal studies on rats, mice and rabbits, exposure to cyclosporine leads to diarrhea. After overexposure doses on rats, high rate of fetus mortality has been reported. Swallowing lead to leukemia on mice. Additional information: none</p> <p>12 Ecological information</p> <p>12.1 Ekotoxicita:</p> <p>Toxicity for water organism:</p> <table style="width: 100%; border: none;"> <tr> <td style="padding-left: 20px;">LC₅₀, 96 h, fish (mg/l):</td> <td style="text-align: right;">data not available</td> </tr> <tr> <td style="padding-left: 20px;">EC₅₀, 24 h, daphnia (mg/l):</td> <td style="text-align: right;">data not available</td> </tr> <tr> <td style="padding-left: 20px;">IC₅₀, 72 h, algae (mg/l):</td> <td style="text-align: right;">data not available</td> </tr> <tr> <td style="padding-left: 20px;">LC₅₀, 96 h, other water organism (mg/l):</td> <td style="text-align: right;">data not available</td> </tr> </table>		- LD ₅₀ , oral, rat (mg.kg ⁻¹):	>1480	- LD ₅₀ , oral, mouse (mg.kg ⁻¹):	2329	- LD ₅₀ , oral dog (mg.kg ⁻¹):	not determined	- LD ₅₀ , dermal, rat /rabbit (mg.kg ⁻¹):	not determined	- LC ₅₀ , inhalation, rat/rabbit aerosols/particles (mg. kg ⁻¹):	not determined	- LC ₅₀ , inhalation, rat, gases/vapors (ppm):	not determined	LC ₅₀ , 96 h, fish (mg/l):	data not available	EC ₅₀ , 24 h, daphnia (mg/l):	data not available	IC ₅₀ , 72 h, algae (mg/l):	data not available	LC ₅₀ , 96 h, other water organism (mg/l):	data not available
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<p>Toxicity for additional environment: data not available soil microorganism: birds: bees: plants: inhibiting effects to microorganism:</p> <p>12.2 Mobility: data not available Known or expected distribution to component of environment: Surface tension: Adsorption or desorption:</p> <p>12.3 Degradability: residues from accidental release biodegrade quickly</p> <p>12.4 Bioakumulacy potential: Ability acumulation at biota and getting along of food chain: not determined K_{ow}: not determined BDF: not determined</p> <p>12.5 Additional information: data not available</p> <p>13 Direction for disposal substance or preparation</p> <p>13.1 Safety handling with substance: handle with product only in original package (commonly metal or PE container including PE bag). Cyclosporin is toxic - use personal protective agents.</p> <p>13.2 Disposal methods of substance and package: mechanically sweep up to the alternative labelled packaging (see point 6). Decontaminate tools and appliances washing with tampons soaked in ethanol. Tampons used for collecting powder and decontamination dispose similarly. Dispose product by incineration in chartered industrial waste incinerate plant. Before incineration, resolve product in suitable solvent or oil - it is forbidden to incinerate product as a form of powder.</p> <p>13.3 Legal rule of waste: dispose in compliance with legally valid laws and regulations, by authorised persons/companies.</p> <p>14 Transport information</p> <p>14.1 Preventive measures by transport: transport in original closed package, transport temperature up to +25 °C. Protect from weather action. Transport up to 25 kg usually in one packing (PE drum), up to 5 kg (canister) or samples up to 100 g (tabular foil) -this is outside packing only, inside packing is PE foil always.</p> <p>14.2 Classification of material/preparation for individual Mode of transport: material is not classified as dangerous for transport</p>	
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<p>Transport over land (ADR/RID): UN Number: not determined Class of dangerous: not determined Label: not determined Package: not determined Classification codes: not determined Note: not determined</p> <p>Carriage by sea (IMDG): UN Number: not determined Class of dangerous: not determined Label: not determined Package: not determined Classification codes: not determined Note: not determined</p> <p>Air transport (ICAO/IATA): UN Number: not determined Class of dangerous: not determined Label: not determined Package: not determined Classification codes: not determined Note: not determined</p> <p>15 Regulatory information Classification of product according to the laws and regulations valid in the Czech Republic (consistent with EU regulations): product is classified as toxic</p> <p>15.1 Information at package of substance: Hazard identification symbol: T toxic</p> <p>Risk phrases: R 20/21/22 R 45 R 64</p> <p>Safety phrases: S 22 Do not breathe dust. S 36/37 Wear suitable protective clothing and gloves. S 53 Avoid exposure - obtain special instructions before use</p> <p>15.2 Specifications of EU: relate to the market and application is not restricted</p> <p>15.3 Specifications for protection of people and environment: relate to the market and application is not restricted</p> <p>16 Additional information</p> <p>16.1 Full version of R phrases: R 20/21/22 Harmful by inhalation, in contact with skin and if swallowed R 45 May cause cancer R 64 May cause harm to breastfed babies</p>	
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