TACROLIMUS CAPSULES
Material Safety Data Sheet

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product name: Tacrolimus Capsules USP

Material Name: Tacrolimus

Chemical formula of active ingredient: $C_{44}H_{69}NO_{12}.H_2O$

CAS number: 109581-93-3

Chemical name of active ingredient:

[3*S*[3*R**[*E*(1*S**,3*S**,4*S**)],4*S**,5*R**,8*S**,9*E*,12*R**,14*R**,15*S**,16*R**,18*S**,19*S**,-26a*R**]] 5,6,8, 11,12, 13,14, 15, 16, 17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3 methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl) -15,19epoxy-3H-pyrido[2,1-*c*][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone,monohydrate

Use: Clinical

Supplier of Data: **Strides Arcolab Ltd**
Opposite to IIMB, Bilekahalli
Bangalore – 560076
India

For emergency or
Product information, call 1 877 244 9825

2. COMPOSITION/INFORMATION ON INGREDIENTS

Specific chemical identity:

[3*S*[3*R**[*E*(1*S**,3*S**,4*S**)], 4*S**,5*R**,8*S**,9*E*,12*R**,14*R**,15*S**,16*R**,18*S**,19*S**,-26a*R**]]5,6,8, 11, 12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy 3 methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10, 12,18-tetramethyl-8-(2-propenyl)-15,19epoxy-3H-pyrido[2,1-*c*][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone,monohydrate

OSHA PEL: No data available.

ACGIH TLV: No data available.

Product also contains excipients (lactose, hydroxypropyl methylcellulose,croscarmellose sodium, and magnesium stearate; the 0.5 mg capsule shell contains gelatin, titanium dioxide, F D & C blue 1 and F D & C red 40, the 1 mg capsule shell contains gelatin, titanium dioxide, F D & C blue 1 and ferric oxide yellow and the 5 mg capsule shell contains gelatin, titanium dioxide, F D & C blue 1, D & C red 28 and D & C yellow 10.

3. HAZARDS IDENTIFICATION

Emergency Overview: EXERCISE CARE TO PREVENT CONTACT OR EXPOSURE.

See sections 4 and 11 for effects in animals.

Routes of Absorption: Inhalation, ingestion, eye and skin absorption.

Acute effects: See section 11.

Target Organs/Systemic toxicity: See section 11.

Reproductive/developmental toxicity: See section 11.

Mutagenicity and Carcinogenicity: See section 11.

Occupational exposure limit: No data available.

Medical conditions aggravated by exposure: No data available.

Symptoms of Exposure: Irritant. Causes irritation on contact with eyes, skin, mucous membranes, and upper respiratory tract. In addition, headache, nausea and vomiting may occur upon exposure.

4. FIRST AID MEASURES

Eye contact

Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a physician for treatment advice.

Skin contact

Remove contaminated clothing immediately. Rinse skin immediately with plenty of water for 15-20 minutes. Call a physician for treatment advice.

Inhalation

Move person to fresh air immediately. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth to mouth, if possible. Call a physician for further treatment advice.

Ingestion

Do not induce vomiting unless told to do so by a poison control center or physician. Do not give any liquid to an unconscious person. Do not give anything by mouth to an unconscious person.

Have the product container or label with you when calling a poison control center or physician, or going for treatment.

For Adverse Reaction Reporting, call 1 877 244 9825 or email: Drugsaftey@stridesarco.com

5. FIRE-FIGHTING MEASURES

Extinguishing media:

Water spray, dry chemical, carbon dioxide or foam as appropriate.

Special fire-fighting procedures:

When heated to decomposition it emits toxic fumes. Burns with an almost nonluminous flame which is difficult to detect in strong light.

6. ACCIDENTAL RELEASE MEASURES

In case of spill or release: Wear gloves, safety glasses or goggles, and lab coat or coveralls to prevent contact. Wipe working surfaces to dryness, then wash with soap and water.

Confine and contain small spills using inert material (e.g. paper towels moistened with water, spill control pillows, absorbents). In the event of a large spill, dike the area to prevent runoff. Clean the spill area with soap and water. Discard spill cleanup materials in accordance with local regulation.

7. HANDLING AND STORAGE

Special precautions- Storage

Wear appropriate protective clothing, suitable eye protection, suitable gloves, and an approved respirator. Do not permit eating, drinking, or smoking near material. Wash thoroughly after handling. Avoid contact with eyes, skin, or clothing.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15°C to 30°C (59° to 86°F).

Label precautionary statement: Material intended for clinical uses only.

8. EXPOSURE CONTROL / PERSONAL PROTECTION

Occupational exposure band / handling category: No data available.

Protective clothing and equipment:

Wear gloves to prevent skin contact. Wash hands with soap and water whenever gloves are removed. Wear safety glasses with side shields or goggles when handling this material to prevent

eye contact. Air hood, lab coat, apron, boots or other impermeable clothing may be worn when handling large amounts of Tacrolimus.

Respiratory protection: Under indicated use, air line mask is recommended.

Skin protection: Wear gloves to prevent skin contact. Wash hands with soap and water whenever gloves are removed.

Ventilation: Use local exhaust ventilation when necessary.

Comments: None

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state: Crystals or crystalline powder

Color: White

Odor: Odorless

Boiling point: No data available.

Melting point: Approximately 126 - 130°C (decomposition)

Freezing point: No data available.

Percent volatility: No data available.

Specific gravity (H_2o=1): No data available.

Molecular weight of active ingredient: 822.03

Solubility of active ingredient: Insoluble in water, freely soluble in ethanol, and very soluble in methanol, DMSO and chloroform.

Vapor pressure (mmHg): No data available.

9. PHYSICAL AND CHEMICAL PROPERTIES (CONTINUED)

Vapor density (Air = 1): No data available.

Evaporation rate (Butyl acetate = 1): No data available.

pH: None

10. STABILITY AND REACTIVITY

Stability: Tacrolimus capsule is stable if stored as directed.

Incompatibility: Reactive with oxidizing agents, acids and alkalis.

11. TOXICOLOGICAL INFORMATION

Acute toxicity: No data available.

Repeated dose toxicity: No data available.

Carcinogenicity:

Carcinogenicity studies were carried out in male and female rats and mice. In the 80-week mouse study and in the 104-week rat study no relationship of tumor incidence to tacrolimus dosage was found. The highest doses used in the mouse and rat studies were 0.8 – 2.5 times (mice) and 3.5 – 7.1 times (rats) the recommended clinical dose range of 0.1 – 0.2 mg/kg/day when corrected for body surface area.

Genotoxicity:

No evidence of genotoxicity was seen in bacterial (*Salmonella* and *E. coli*) or mammalian (Chinese hamster lung-derived cells) in vitro assays of mutagenicity, the in vitro CHO/HGPRT assay of mutagenicity, or in vivo clastogenicity assays performed in mice; tacrolimus did not cause unscheduled DNA synthesis in rodent hepatocytes.

Teratogenicity/Reprotoxicity:

No impairment of fertility was demonstrated in studies of male and female rats. Tacrolimus, given orally at 1.0 mg/kg (0.7 – 1.4X the recommended clinical dose range of 0.1 – 0.2 mg/kg/ day based on body surface area corrections) to male and female rats, prior to and during mating, as well as to dams during gestation and lactation, was associated with embryolethality and with adverse effects on female reproduction. Effects on female reproductive function (parturition) and embryolethal effects were indicated by a higher rate of preimplantation loss and increased numbers of undelivered and nonviable pups. When given at 3.2 mg/kg (2.3 – 4.6X the recommended clinical dose range based on body surface area correction), tacrolimus was associated with maternal and paternal toxicity as well as reproductive toxicity including marked adverse effects on estrus cycles, parturition, pup viability and pup malformations.

In reproduction studies in rats and rabbits, adverse effects on the fetus were observed mainly at dose levels that were toxic to dams. Tacrolimus at oral doses of 0.32 and 1.0 mg/kg during organogenesis in rabbits was associated with maternal toxicity as well as an increase in incidence of abortions; these doses are equivalent to 0.5 – 1X and 1.6 – 3.3X the recommended clinical dose range (0.1 – 0.2 mg/kg) based on body surface area corrections. At the higher dose only, an increased incidence of malformations and developmental variations was also seen. Tacrolimus,

at oral doses of 3.2 mg/kg during organogenesis in rats, was associated with maternal toxicity and caused an increase in late resorptions, decreased numbers of live births and decreased pup weight and viability. Tacrolimus, given orally at 1.0 and 3.2 mg/kg (equivalent to 0.7 – 1.4X and 2.3 – 4.6X the recommended clinical dose range based on body surface area corrections) to pregnant rats after organogenesis and during lactation, was associated with reduced pup weights. No reduction in male or female fertility was evident.

Local irritation: No data available.

12. ECOLOGICAL INFORMATION

No data available.

13. DISPOSAL CONSIDERATIONS

Spills: Wash contaminated area with water and dispose in waste water treatment

System in accordance with state and local regulatory requirements.

Waste disposal: Dispose waste in accordance with state and local regulatory requirements.

14. TRANSPORTATION INFORMATION

DOT shipping name: Not regulated.

DOT hazard class/ division: Not regulated.

DOT #: Not regulated.

Packaging authorization: Not regulated.

Non-bulk packaging: Not regulated.

Quantity limits: Not regulated.

DOT packaging group: Not regulated.

DOT labels: Not regulated.

Vessel stowage: Not regulated.

IATA / ICAO – Non Hazardous - Not Regulated

IATA Proper shipping name: N/A

IATA UN / ID No: N/A

IATA Hazard Class: N/A

IATA Packing Group: N/A

IATA Label: N/A

IMDG – Non Hazardous - Not Regulated

IMDG Proper shipping name: N/A

IMDG UN / ID No: N/A

IMDG Hazard Class: N/A

IMDG Flash Point: N/A

IMDG Label: N/A

DOT – Non Hazardous - Not Regulated

DOT Proper shipping name: N/A

DOT UN / ID No: N/A

DOT Hazard Class: N/A

DOT Flash Point: N/A

DOT Packing Group: N/A

DOT Label: N/A

15. REGULATORY INFORMATION

US TSCA: No data available.

SARA: No data available.

EU risk and safety phrases: No data available.

16. OTHER INFORMATION

None

ABREVIATIONS

CAS: Chemical Abstract Service

DOT: Department of Transportation

DMSO: Dimethyl Sulfoxide

N/A: Not Applicable

OEL: Occupational Exposure Limit

SARA: Superfund Amendments and Reauthorization Act

TLV: Threshold Limit Value

TSCA: Toxic Substance Control Act