Safety Data Sheet
Sirolimus Tablets

Strength: 0.5mg, 1mg & 2 mg. **Pack Size:** 30/90/100/500/1000 tablets per bottle for 0.5 mg
100/500/1000 tablets per bottle for 1 mg and 2 mg
Unit dose blisters of 10X10 for 0.5 mg, 1 mg, 2 mg

Revision No.: 02

EMERGENCY OVERVIEW

Each Sirolimus Tablets intended for oral administration contains Sirolimus and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

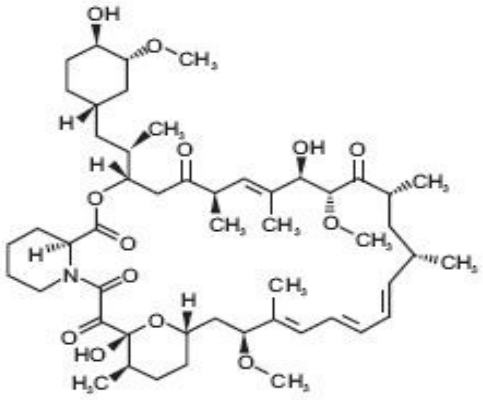
Section 1. Identification

Identification of the product

Product name: Sirolimus Tablet

Formula: $C_{51}H_{79}NO_{13}$

Chemical Name: (3S,6R,7E,9R,10R,12R,14S,15E,17E,19E,21S,23S,26R,27R,34aS)-9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34a-hexadecahydro-9,27-dihydroxy-3-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3H-pyrido[2,1-c][1,4] oxaazacyclohentriacontine-1,5,11,28,29 (4H,6H,31H)-pentone.



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

Address: Sarkhej – Bavla. N.H. 8A, Moraiya. Tal. Sanand.
Dist. Ahmedabad – 382210. State: Gujarat. India

Contact for information: Tel.: +91 79 6868100 Fax: +91 79 3750319

Emergency Telephone No. Tel.: +91 79 6868100

Recommended use / Therapeutic Category	Immunosuppressive agent.
Restriction on Use / Contraindications	Sirolimus is contraindicated in patients with a hypersensitivity to sirolimus

Section 2. Hazard(s) Information

Dose and Administration	Sirolimus tablets are to be administered orally once daily, consistently with or without food. Tablets should not be crushed, chewed or split.
Adverse Effects	The most common (> 30%) adverse reactions are: peripheral edema, hypertriglyceridemia, hypertension, hypercholesterolemia, creatinine increased, abdominal pain, diarrhea, headache, fever, urinary tract infection, anemia, nausea, arthralgia, pain, and thrombocytopenia.
Over Dose Effect	Reports of overdose with sirolimus have been received; however, experience has been limited. In general, the adverse effects of overdose are consistent with those listed in the adverse reactions section
Medical Conditions	Do not take sirolimus if you are allergic to sirolimus or any of the other ingredients in sirolimus. Before taking sirolimus, tells your doctor if you: have liver problems, have skin cancer or it runs in your family, have high cholesterol or triglycerides (fat in your blood), are pregnant or plan to become pregnant. You must use an effective method of birth control during treatment and for 12 weeks after you stop treatment with sirolimus. Tell your doctor right away if you become pregnant or think you are pregnant while taking sirolimus. It is not known whether sirolimus passes into breastmilk. You and your doctor should decide if you will take sirolimus or breastfeed. You should not do both. Tell your doctor about all the medicines you take, including prescription and non- prescription medicines, vitamins and herbal supplements. Using sirolimus with certain medicines may affect each other causing serious side effects. Sirolimus may affect the way other medicines work, and other medicines may affect how sirolimus works. Especially tell your doctor if you take: a medicine to lower your cholesterol or triglycerides ,cyclosporine (including Gengraf®^, Neoral®$, Sandimmune®#) or tacrolimus (Prograf®+) or other medicines that suppress the immune system, an antibiotic , an antifungal medicine , a medicine for high blood pressure or heart problems , an anti-seizure medicine , medicines used to treat stomach acid, ulcers, or other gastrointestinal problems , bromocriptine mesylate (Parlodel®*, Cycloset®~), danazol , medicines to treat HIV or hepatitis C , St. John's Wort .

Contraindications	Sirolimus is contraindicated in patients with a hypersensitivity to sirolimus
Pregnancy Comments	Use only if the potential benefit outweighs the potential risk to the embryo/fetus
Pregnancy Category	**C**

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component :		
Sirolimus	Not Found	53123-88-9
Inactive Ingredients :		
Citric acid monohydrate	Not Found	5949-29-1
Crospovidone	Not Found	9003-39-8
Glyceryl monooleate	Not Found	25496-72-4
Hypromellose	Not Found	9004-65-3
Lactose monohydrate	Not Found	5989-81-1
Microcrystalline cellulose	Not Found	9004-34-6
Poloxamer	Not Found	9003-11-6
Polyethylene glycol	Not Found	25322-68-3
Povidone	Not Found	9003-39-8
Sucrose	Not Found	57-50-1
Talc	Not Found	14807-96-6
Titanium dioxide	Not Found	13463-67-7
Vitamin E acetate	Not Found	7695-91-2
FD&C yellow(for 0.5 mg)	Not Found	Not Available
Aluminum Lake (for 0.5 mg)	Not Found	Not Available
Iron oxide yellow(for 0.5 mg)	Not Found	Not Available

Iron oxide black(for 2 mg)	Not Found	Not Available
Iron oxide red (for 2 mg)	Not Found	Not Available
Iron oxide yellow. (for 2 mg)	Not Found	Not Available

Section 4. First - aid measures

General

Inhalation

Remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen. Seek medical attention.

contact with skin

Immediately wash skin with soap and copious amounts of water for at least 15 minutes. If irritation persists, seek medical attention.

Ingestion

If swallowed, wash out mouth with water, provided person is concious. Seek medical advice

Remove and wash/dispose of contaminated clothing promptly.

Overdose Treatment

General supportive measures should be followed in all cases of overdose. Based on the low aqueous solubility and high erythrocyte and plasma protein binding of sirolimus, it is anticipated that sirolimus is not dialyzable to any significant extent.

Section 5. Fire - fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build-up of static electricity.

Fire Fighting Procedure	As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response	Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage	Store at 25°C (77°F), Protect from moisture. Use cartons to protect blister cards and strips from light. Dispense in a tight, light-resistant container as defined in the USP
Incompatibilities:	No data available.

Section 8. Exposure controls / personal protection

Respiratory Protection	Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.
Skin Protection	Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.
Eye protection	Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Engineering Control	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. Physical and chemical properties

Appearance	Sirolimus Tablets, 0.5 mg are yellow, round, biconvex, coated tablets imprinted with “1” in black ink on one side and plain on other side. Sirolimus Tablets, 1 mg are white to off-white, round, biconvex, film-coated tablets debossed with 11 on one side and plain on other side. Sirolimus Tablets, 2 mg are yellow, round, biconvex, coated tablets, debossed with 21 on one side and plain on other side.

Solubility in water	Freely soluble in chloroform, acetone, acetonitrile, insoluble in water.	**Odour**	Odourless
Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
% Volatile by volume	No Data Available	**Specific gravity**	No Data Available
		Vapour pressure	No Data Available

Other information Sirolimus is a white to off-white powder and is insoluble in water, but freely soluble in benzyl alcohol, chloroform, acetone, and acetonitrile.

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities:	No Data available.		

Section 11. Toxicological information

General Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ Eye contact, Skin contact and inhalation is not great risk as this product is capsules.

Other

In mice and rats, the acute oral LD_{50} was greater than 800 mg/kg.
Carcinogenicity studies were conducted in mice and rats. There was a statistically significant increase in malignant lymphoma at all dose levels compared with controls. Hepatocellular adenoma and carcinoma in males were considered sirolimus-related

Sirolimus was not genotoxic in the *in vitro* bacterial reverse mutation assay, the Chinese hamster ovary cell chromosomal aberration assay, the mouse lymphoma cell forward mutation assay, or the *in vivo* mouse micronucleus assay.

In male rats, atrophy of testes, epididymides, prostate, seminiferous tubules and/or reduction in sperm counts were observed. In female rats, reduced size of ovaries and uteri was observed. Reduction of sperm count in male rats was reversible upon cessation of dosing in one study. Testicular tubular degeneration was also seen in a 4 week intravenous study of sirolimus in monkeys at doses that were approximately equal to the clinical dose.

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 201676

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 01

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.