



SAFETY DATA SHEET

Revision date: 31-Mar-2014

Version: 2.0

Page 1 of 11

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Sirolimus Oral Solution

Trade Name: RAPAMUNE
Chemical Family: Macrocyclic lactone

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product used as immunosuppressive agent

Details of the Supplier of the Safety Data Sheet

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2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Reproductive Toxicity: Category 1B
Acute aquatic toxicity: Category 1
Chronic aquatic toxicity: Category 1

EU Classification:

EU Indication of danger: Toxic to Reproduction: Category 2
Dangerous for the Environment

EU Risk Phrases:

R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Label Elements

Signal Word: Danger
Hazard Statements: H360FD - May damage fertility. May damage the unborn child.
H400 - Very toxic to aquatic life
H410 - Very toxic to aquatic life with long lasting effects

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 2 of 11
Version: 2.0

Precautionary Statements:

- P201 - Obtain special instructions before use
- P281 - Use personal protective equipment as required
- P308 + P313 - IF exposed or concerned: Get medical attention/advice
- P405 - Store locked up
- P273 - Avoid release to the environment
- P391 - Collect spillage
- P501 - Dispose of contents/container in accordance with all local and national regulations



Other Hazards

Australian Hazard Classification (NOHSC):

Hazardous Substance. Non-Dangerous Goods.

Note: This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Sirolimus	53123-88-9	Not Listed	Repr. Cat.2;R60-61; N,R50/53	Repr. 1B,H360FD; Aquatic Acute 1,H400; Aquatic Chronic 1,H410	1
Ethanol	64-17-5	200-578-6	F; R11	Flam. Liq. 2 (H225)	1.5-2.5

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	GHS Classification	%
Soy fatty acids	68308-53-2	269-657-0	Not Listed	Not Listed	*
Ascorbyl palmitate	137-66-6	205-305-4	Not Listed	Not Listed	*
Glycerides, unsatd. mono- and di-	67701-32-0	266-951-0	Not Listed	Not Listed	*
Propylene glycol	57-55-6	200-338-0	Not Listed	Not Listed	*
Polysorbate 80	9005-65-6	Not Listed	Not Listed	Not Listed	*
Lecithin	8002-43-5	232-307-2	Not Listed	Not Listed	*

Additional Information:

* Proprietary
 Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.
 In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the R phrases and CLP/GHS abbreviations mentioned in this Section, see Section 16

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 3 of 11
Version: 2.0

4. FIRST AID MEASURES

Description of First Aid Measures

- Eye Contact:** Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
- Skin Contact:** Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
- Ingestion:** Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
- Inhalation:** Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed

- Symptoms and Effects of Exposure:** For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
- Medical Conditions Aggravated by Exposure:** None known

Indication of the Immediate Medical Attention and Special Treatment Needed

- Notes to Physician:** None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture

- Hazardous Combustion Products:** Formation of toxic gases is possible during heating or fire.
- Fire / Explosion Hazards:** Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters

During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up

- Measures for Cleaning / Collecting:** Contain the source of the spill or leak. Absorb spills with non-combustible absorbent material and transfer into a labeled container for disposal. Clean spill area thoroughly. Prevent discharge to
- Additional Consideration for Large Spills:** Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 4 of 11
Version: 2.0

7. HANDLING AND STORAGE

Restrict access to work area. Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. It is recommended that all operations be fully enclosed and no air recirculated.

Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.
Specific end use(s): No data available

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

Refer to available public information for specific member state Occupational Exposure Limits.

Ethanol

ACGIH Threshold Limit Value (STEL)	1000 ppm
Australia TWA	1000 ppm
	1880 mg/m ³
Austria OEL - MAKs	1000 ppm
	1900 mg/m ³
Belgium OEL - TWA	1000 ppm
	1907 mg/m ³
Bulgaria OEL - TWA	1000.0 mg/m ³
Czech Republic OEL - TWA	1000 mg/m ³
Denmark OEL - TWA	1000 ppm
	1900 mg/m ³
Estonia OEL - TWA	500 ppm
	1000 mg/m ³
Finland OEL - TWA	1000 ppm
	1900 mg/m ³
France OEL - TWA	1000 ppm
	1900 mg/m ³
Germany - TRGS 900 - TWAs	500 ppm
	960 mg/m ³
Germany (DFG) - MAK	500 ppm
	960 mg/m ³
Greece OEL - TWA	1000 ppm
	1900 mg/m ³
Hungary OEL - TWA	1900 mg/m ³
Latvia OEL - TWA	1000 mg/m ³
Lithuania OEL - TWA	500 ppm
	1000 mg/m ³
Netherlands OEL - TWA	260 mg/m ³
OSHA - Final PELs - TWAs:	1000 ppm
	1900 mg/m ³
Poland OEL - TWA	1900 mg/m ³
Portugal OEL - TWA	1000 ppm
Romania OEL - TWA	1000 ppm
	1900 mg/m ³
Russia OEL - TWA	1000 mg/m ³

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 5 of 11
Version: 2.0

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Slovakia OEL - TWA	500 ppm 960 mg/m ³
Slovenia OEL - TWA	1000 ppm 1900 mg/m ³
Spain OEL - TWA	1000 ppm 1910 mg/m ³
Sweden OEL - TWAs	500 ppm 1000 mg/m ³
Switzerland OEL -TWAs	500 ppm 960 mg/m ³
Vietnam OEL - TWAs	1000 mg/m ³
Propylene glycol	
Australia TWA	150 ppm 474 mg/m ³ 10 mg/m ³
Ireland OEL - TWAs	150 ppm 470 mg/m ³ 10 mg/m ³
Latvia OEL - TWA	7 mg/m ³
Lithuania OEL - TWA	7 mg/m ³

The purpose of the Occupational Exposure Band (OEB) classification system is to separate substances into different Hazard categories when the available data are sufficient to do so, but inadequate to establish an Occupational Exposure Limit (OEL). The OEB given is based upon an analysis of all currently available data; as such, this value may be subject to revision when new information becomes available.

Sirolimus

Pfizer Occupational Exposure Band (OEB): OEB 5 (control exposure to <1ug/m³)

Exposure Controls

Engineering Controls:

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.

Personal Protective Equipment:

Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands:

Impervious, disposable gloves (double suggested) are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes:

Wear safety glasses or goggles if eye contact is possible.

Skin:

Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection:

If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Liquid	Color:	Yellow
Odor:	No data available.	Odor Threshold:	No data available.
Molecular Formula:	Mixture	Molecular Weight:	Mixture
Solvent Solubility:	No data available		

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 6 of 11
Version: 2.0

9. PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility: No data available
pH: No data available.
Melting/Freezing Point (°C): No data available
Boiling Point (°C): No data available.
Partition Coefficient: (Method, pH, Endpoint, Value)

Sirolimus

Measured Log P >4.63

Propylene glycol

No data available

Ascorbyl palmitate

No data available

Lecithin

No data available

Glycerides, unsatd. mono- and di-

No data available

Ethanol

No data available

Polysorbate 80

No data available

Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available

Vapor Pressure (kPa): No data available

Vapor Density (g/ml): No data available

Relative Density: No data available

Viscosity: No data available

Flammability:

Autoignition Temperature (Solid) (°C): No data available

Flammability (Solids): No data available

Flash Point (Liquid) (°C): No data available

Upper Explosive Limits (Liquid) (% by Vol.): No data available

Lower Explosive Limits (Liquid) (% by Vol.): No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available

Chemical Stability: Stable under normal conditions of use.

Possibility of Hazardous Reactions

Oxidizing Properties: No data available

Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions.

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Known Clinical Effects: Adverse effects associated with therapeutic use include hypersensitivity reactions, nausea, weakness, skin rash, weight loss, inflammation of the mouth (stomatitis), itching sensation (pruritus), decreased red blood cell count (anemia), decreased white blood cells (leukopenia).

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 7 of 11
Version: 2.0

11. TOXICOLOGICAL INFORMATION

Acute Toxicity: (Species, Route, End Point, Dose)

Sirolimus

Mouse Oral LD50 > 2500 mg/kg
Rat Oral LD50 > 800mg/kg

Lecithin

Rat Oral LD50 > 8 ml/kg

Ethanol

Mouse Oral LD50 3,450 g/m³
Rat Oral LD50 7,060mg/kg
Mouse Inhalation LC50 4h 39g/m³
Rat Inhalation LC50 10h 20,000ppm

Polysorbate 80

Rat Oral LD50 25 g/kg

Acute Toxicity Comments:

A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Propylene glycol

Skin Irritation Rabbit Mild
Eye Irritation Rabbit Mild

Ethanol

Eye Irritation Rabbit Severe

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Sirolimus Monkey No route specified 0.05 mg/kg/day NOAEL Lymphoid tissue, Spleen, Thymus, Gastrointestinal System

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Sirolimus

Reproductive & Fertility Rat No route specified 0.1 mg/kg/day NOAEL Embryotoxicity, Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Sirolimus

In Vitro Bacterial Mutagenicity (Ames) *Salmonella*, *E. coli* Negative
In Vitro Chromosome Aberration Chinese Hamster Ovary (CHO) cells Negative
In Vitro Forward Mutation Assay Mouse Lymphoma Negative
In Vivo Micronucleus Mouse Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Sirolimus

86 Week(s) Mouse No route specified 6 mg/kg/day LOAEL Tumors, Lymphatic system
104 Week(s) Rat No route specified 0.2 mg/kg/day LOAEL Male reproductive system, Tumors

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 8 of 11
Version: 2.0

11. TOXICOLOGICAL INFORMATION

Carcinogen Status: Carcinogenicity of the mixture has not been determined. Alcohol is listed as a carcinogen by IARC. The IARC monograph examining the carcinogenic potential of ethanol examined only alcoholic beverages. No other components are listed as carcinogens by IARC, US OSHA or NTP.

Ethanol
IARC: Group 1 (Carcinogenic to Humans)
OSHA: Listed

12. ECOLOGICAL INFORMATION

Environmental Overview: See aquatic toxicity data, below:

Toxicity:
Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Sirolimus
Pseudokirchneriella subcapitata (Green Alga) OECD EC50 72 Hours 0.063 mg/L

Ethanol
Fingerling Trout NPDES LC50 24 Hours 11,200 mg/L
Oncorhynchus mykiss (Rainbow Trout) NPDES LC50 96 Hours 12,900 mg/L
Pimephales promelas (Fathead Minnow) NPDES LC50 96 Hours 14,200 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)

Sirolimus
Measured Log P >4.63

Mobility in Soil: No data available

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 9 of 11
Version: 2.0

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Canada - WHMIS: Classifications

WHMIS hazard class:

Class D, Division 2, Subdivision A



Soy fatty acids

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	269-657-0

Sirolimus

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	Not Listed

Ethanol

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	carcinogen initial date 4/29/11 in alcoholic beverages developmental toxicity initial date 10/1/87 in alcoholic beverages
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-578-6

Ascorbyl palmitate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	205-305-4

Glycerides, unsatd. mono- and di-

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 10 of 11
Version: 2.0

15. REGULATORY INFORMATION

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	266-951-0
Propylene glycol	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	200-338-0
Polysorbate 80	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	Not Listed
Lecithin	
CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	232-307-2

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Reproductive toxicity-Cat.1B; H360FD - May damage fertility. May damage the unborn child.
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life
Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Toxic to Reproduction: Category 2
N - Dangerous for the environment

R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients.

Revision date: 31-Mar-2014

Prepared by: Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

SAFETY DATA SHEET

Material Name: Sirolimus Oral Solution
Revision date: 31-Mar-2014

Page 11 of 11
Version: 2.0

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet