Prograf® (Tacrolimus) Capsules

Safety Data Sheet

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SECTION 1: IDENTIFICATION

1.1. Product Identifier

Product Form: Mixture

Product Name: Prograf® (Tacrolimus) Capsules

Material Name: Tacrolimus, FK506

CAS No: 109581-93-3

Chemical Name of Active Ingredient: [3S-[3R*[E(1S*,3S*,4S*)], 4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]] 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)-15,19-epoxy-3H-pyrido[2,1-c][1,4] oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, monohydrate

Chemical Formula of Active Ingredient: $C_{44}H_{69}NO_{12}•H_2O$

1.2. Intended Use of the Product

Use of the substance/mixture: Prophylaxis of organ rejection in patients receiving allogeneic liver, kidney or heart transplants. For professional use only.

1.3. Name, Address, and Telephone of the Responsible Party

Company

Astellas US LLC
1 Astellas Way
Northbrook, IL 60062
Tel.: 800-888-7704
www.us.astellas.com

1.4. Emergency Telephone Number

Emergency Number : 800-727-7003 Medical Communications

SECTION 2: HAZARDS IDENTIFICATION

This product is a drug, as defined by the US Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) It is in solid, final form for direct administration to the patient. Therefore, is it exempt from the US 2012 Hazard Communication Standard, as defined in the 29 CFR 1910.1200(b)(5)(iii).

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

This product is a drug, as defined by the US Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) It is in solid, final form for direct administration to the patient. Therefore, is it exempt from the US 2012 Hazard Communication Standard, as defined in the 29 CFR 1910.1200(b)(5)(iii).

SECTION 4: FIRST AID MEASURES

4.1. Description of First Aid Measures

First-aid Measures General: Never give anything by mouth to an unconscious person. If you feel unwell, seek medical advice (show the label if possible).

First-aid Measures After Inhalation: Remove to fresh air and keep at rest in a position comfortable for breathing. Obtain medical attention if breathing difficulty persists.

First-aid Measures After Skin Contact: Gently wash with plenty of soap and water. Obtain medical attention if irritation develops or persists.

First-aid Measures After Eye Contact: Rinse cautiously with water for at least 5 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention if pain, blinking, or redness persist.

First-aid Measures After Ingestion: Do not induce vomiting. Rinse mouth. Immediately call a POISON CENTER or doctor/physician.

4.2. Most important symptoms and effects, both acute and delayed

Symptoms/Injuries: Harmful if swallowed. Suspected of damaging the unborn child. Causes damage to organs through prolonged or repeated exposure.

Symptoms/Injuries After Inhalation: Exposure to capsule contents: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Exposure to capsule contents: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Exposure to capsule contents: May cause eye irritation.

Symptoms/Injuries After Ingestion: Nausea. Headache. Vomiting.

Chronic Symptoms: Suspected of damaging the unborn child. Causes damage to organs through prolonged or repeated exposure (pancreas, thymus, lymph nodes, spleen, kidneys).

4.3. Indication of Any Immediate Medical Attention and Special Treatment Needed

If you feel unwell, seek medical advice (show the label where possible).

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Water spray, fog, carbon dioxide (CO_2), alcohol-resistant foam, or dry chemical.

Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

5.2. Special Hazards Arising From the Substance or Mixture

Fire Hazard: Not considered flammable but may burn at high temperatures.

Explosion Hazard: Product is not explosive.

Reactivity: Hazardous reactions will not occur under normal conditions.

5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire.

Firefighting Instructions: Use water spray or fog for cooling exposed containers.

Protection During Firefighting: Do not enter fire area without proper protective equipment, including respiratory protection.

Other Information: Refer to Section 9 for flammability properties.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Use only as directed.

6.1.1. For Non-emergency Personnel

Protective Equipment: Use appropriate personal protection equipment (PPE).

Emergency Procedures: Evacuate unnecessary personnel.

6.1.2. For Emergency Responders

Protective Equipment: Equip cleanup crew with proper protection.

Emergency Procedures: Upon arrival at the scene, a first responder is expected to recognize the presence of dangerous goods, protect oneself and the public, secure the area, and call for the assistance of trained personnel as soon as conditions permit.

6.2. Environmental Precautions

Prevent entry to sewers and public waters. Notify authorities if product enters sewers or public waters.

6.3. Methods and Material for Containment and Cleaning Up

For Containment: Contain and collect as any solid.

Methods for Cleaning Up: Clean up spills immediately and dispose of waste safely. Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting. Contact competent authorities after a spill.

6.4. Reference to Other Sections

See Heading 8. Exposure controls and personal protection. For further information refer to section 13.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Additional Hazards When Processed: Avoid breaking or crushing capsules.

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures. Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations.

Storage Conditions: Store in a dry, cool and well-ventilated place. Keep container closed when not in use. Keep/Store away from direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Products: Strong acids, strong bases, strong oxidizers.

Storage Temperature: 25 °C (77 °F); excursions permitted to 15 °C - 30 °C (59 °F - 86 °F).

7.3. Specific End Use(s)

Prophylaxis of organ rejection in patients receiving allogeneic liver, kidney or heart transplants. For professional use only.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameters

For substances listed in section 3 that are not listed here, there are no established exposure limits from the manufacturer, supplier, importer, or the appropriate advisory agency including: ACGIH (TLV), NIOSH (REL), or OSHA (PEL).

8.2. Exposure Controls

Appropriate Engineering Controls	: Ensure adequate ventilation, especially in confined areas. Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Ensure all national/local regulations are observed.
Personal Protective Equipment	: Not generally required. The use of personal protective equipment may be necessary as conditions warrant.
Materials for Protective Clothing	: Chemically resistant materials and fabrics.
Hand Protection	: Wear chemically resistant protective gloves.

Eye Protection	: Chemical goggles or safety glasses.
Skin and Body Protection	: Wear suitable protective clothing.
Respiratory Protection	: None required under normal product handling conditions. Use NIOSH-approved dust mask if dust has the potential to become airborne.
Environmental Exposure Controls	: Do not allow the product to be released into the environment.
Consumer Exposure Controls	: Do not eat, drink or smoke during use.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State	: Solid
Appearance	: **0.5 mg:** hard gelatin light yellow capsule branded with "607" on the capsule body and "0.5 mg" on the capsule cap. **1 mg**: hard gelatin white capsule branded with "617" on the capsule body and "1 mg" on the capsule cap. **5 mg:** hard gelatin grayish red capsule branded with "657" on the capsule body and "5 mg" on the capsule cap.
Odor	: Odorless
Odor Threshold	: No data available
pH	: No data available
Evaporation Rate	: No data available
Melting Point	: 126 - 130 °C (258.8 - 266 °F) (decomposition)
Freezing Point	: No data available
Boiling Point	: No data available
Flash Point	: No data available
Auto-ignition Temperature	: No data available
Decomposition Temperature	: No data available
Flammability (solid, gas)	: No data available
Vapor Pressure	: No data available
Relative Vapor Density at 20 °C	: No data available
Relative Density	: No data available
Solubility	: Insoluble in water, freely soluble in ethanol, and very soluble in methanol, DMSO and chloroform
Partition Coefficient: N-Octanol/Water	: No data available
Viscosity	: No data available
Molecular Weight Of Active Ingredient	: 822.03

9.2. Other Information No additional information available.

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity: Hazardous reactions will not occur under normal conditions.

10.2. Chemical Stability: Stable under recommended handling and storage conditions (see section 7).

10.3. Possibility of Hazardous Reactions: Hazardous polymerization will not occur.

10.4. Conditions to Avoid: Direct sunlight. Extremely high or low temperatures. Ignition sources. Incompatible materials.

10.5. Incompatible Materials: Strong acids, strong bases and strong oxidants.

10.6. Hazardous Decomposition Products: Carbon oxides (CO, CO_2). Nitrogen oxides. Thermal decomposition generates toxic vapors.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information On Toxicological Effects

Acute Toxicity: Oral: Harmful if swallowed.

Prograf® (Tacrolimus) Capsules	
ATE (Oral)	1,340.00 mg/kg body weight

Tacrolimus (109581-93-3)	
LD50 Oral Rat	134 - 194 mg/kg
LD50 I.V. Rat	23.6 - 57 mg/kg

Cellulose hydroxypropyl methyl ether (9004-65-3)	
LD50 Oral Rat	>= 4000 mg/kg

Magnesium stearate (557-04-0)	
LD50 Oral Rat	> 2000 mg/kg

Skin Corrosion/Irritation: Not classified

Serious Eye Damage/Irritation: Not classified

Respiratory or Skin Sensitization: Not classified

Germ Cell Mutagenicity: Not classified

Tacrolimus (109581-93-3)	
Additional information	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.

Carcinogenicity: Not classified

Tacrolimus (109581-93-3)	
Additional information	The highest dose used in the mouse was 3.0 mg/kg/day (0.9 to 2.2 times the AUC at clinical doses of 0.075 to 0.2 mg/kg/day) and in the rat was 5.0 mg/kg/day (0.265 to 0.65 times the AUC at clinical doses of 0.075 to 0.2 mg/kg/day). A 104-week dermal carcinogenicity study was performed in mice with tacrolimus ointment (0.03% - 3%), equivalent to tacrolimus doses of 1.1-118 mg/kg/day or 3.3-354 mg/m2/day. In the study, the incidence of skin tumors was minimal and the topical application of tacrolimus was not associated with skin tumor formation under ambient room lighting. However, a statistically significant elevation in the incidence of pleomorphic lymphoma in high dose male (25/50) and female animals (27/50) and in the incidence of undifferentiated lymphoma in high dose female animals (13/50) was noted in the mouse dermal carcinogenicity study. Lymphomas were noted in the mouse dermal carcinogenicity study at a daily dose of 3.5 mg/kg (0.1% tacrolimus ointment). No drug-related tumors were noted in the mouse dermal carcinogenicity study at a daily dose of 1.1 mg/kg (0.03% tacrolimus ointment). The relevance of topical administration of tacrolimus in the setting of systemic tacrolimus use is unknown.

Reproductive Toxicity: Suspected of damaging the unborn child.

Tacrolimus (109581-93-3)	
Additional information	Tacrolimus given orally at 1.0 mg/kg (0.8 to 2.2 times the clinical dose range of 0.075 to 0.2 mg/kg/day based on body surface area) to male and female rats, prior to and during mating, as well as to dams during gestation and lactation, was associated with embryolethality and adverse effects on female reproduction. Effects on female reproductive function (parturition) and embryolethal effects were indicated by a higher rate of pre-implantation loss and increased numbers of undelivered and nonviable pups. When given at 3.2 mg/kg (2.6 to 6.9 times the clinical dose range based on body surface area), 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.

Specific Target Organ Toxicity (Single Exposure): Not classified

Specific Target Organ Toxicity (Repeated Exposure): Causes damage to organs through prolonged or repeated exposure.

Tacrolimus (109581-93-3)	
Additional information	The primary target organs of tacrolimus toxicity in rats and baboons were the pancreas, thymus, lymph nodes and spleen; in rats, the kidneys were also affected. In 52-week repeated dose oral toxicity studies, the NOAEL for rats was 0.15 mg/kg/day, while for baboons the NOAEL was 1.0

	mg/kg/day.

Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: Exposure to capsule contents: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Exposure to capsule contents: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Exposure to capsule contents: May cause eye irritation.

Symptoms/Injuries After Ingestion: Nausea. Headache. Vomiting.

Chronic Symptoms: Suspected of damaging the unborn child. Causes damage to organs through prolonged or repeated exposure (pancreas, thymus, lymph nodes, spleen, kidneys).

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity No additional information available.

12.2. Persistence and Degradability No additional information available.

12.3. Bioaccumulative Potential No additional information available.

12.4. Mobility in Soil No additional information available.

12.5. Other Adverse Effects

Other Information : Avoid release to the environment.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Waste Disposal Recommendations: Dispose of contents and container according to local, regional, national, and international regulations.

Ecology – Waste Materials: Avoid release to the environment.

SECTION 14: TRANSPORT INFORMATION

14.1. In Accordance with DOT Not regulated for transport.

14.2. In Accordance with IMDG Not regulated for transport.

14.3. In Accordance with IATA Not regulated for transport.

SECTION 15: REGULATORY INFORMATION

15.1 US Federal Regulations Not applicable

15.2 US State Regulations Not applicable

SECTION 16: OTHER INFORMATION, INCLUDING DATE OF PREPARATION OR LAST REVISION

Revision Date : 05/27/2015

Other Information : This document has been prepared in accordance with the SDS requirements of the OSHA Hazard Communication Standard 29 CFR 1910.1200.

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.

SDS US (GHS HazCom)