Prograf® (Tacrolimus) Granules

Safety Data Sheet

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SECTION 1: IDENTIFICATION

1.1. Product Identifier

Product Form: Mixture

Product Name: Prograf® (Tacrolimus) Granules

Synonyms: FK506

1.2. Intended Use of the Product

Use of the substance/mixture: Prograf (tacrolimus) granules is a medicinal product for oral use intended for prophylaxis of transplant in adult and pediatric kidney, liver or heart allograft recipients. 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

2.1. Classification of the Substance or Mixture

GHS-US classification

Repr. 2	H361
STOT RE 1	H372
Comb. Dust	

Full text of hazard classes and H-statements : see section 16

2.2. Label Elements

GHS-US Labeling

Hazard Pictograms (GHS-US) :

GHS08

Signal Word (GHS-US) : Danger

Hazard Statements (GHS-US) : May form combustible dust concentrations in air.
H361 - Suspected of damaging fertility or the unborn child.
H372 - Causes damage to organs (immune system, kidneys) through prolonged or repeated exposure.

Precautionary Statements (GHS-US) : P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P260 - Do not breathe vapors, mist, or spray.
P264 - Wash hands, forearms, and other exposed areas thoroughly after handling.
P270 - Do not eat, drink or smoke when using this product.
P280 - Wear protective gloves, protective clothing, and eye protection.
P308+P313 - If exposed or concerned: Get medical advice/attention.
P314 - Get medical advice/attention if you feel unwell.
P405 - Store locked up.
P501 - Dispose of contents/container in accordance with local, regional, national, and international regulations.

2.3. Other Hazards

Exposure may aggravate pre-existing eye, skin, or respiratory conditions.

2.4. Unknown Acute Toxicity (GHS-US)

No data available

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substances

Not applicable

3.2. Mixture

Name	Product Identifier	%	GHS-US classification
Lactose, monohydrate	(CAS-No.) 64044-51-5	> 95	Comb. Dust
Tacrolimus	(CAS-No.) 109581-93-3	< 5	Acute Tox. 3 (Oral), H301 Skin Irrit. 2, H315 Eye Irrit. 2A, H319 Repr. 2, H361 STOT SE 3, H335 STOT RE 1, H372

Full text of H-phrases: see section 16

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 where possible).

First-aid Measures After Inhalation: Using proper respiratory protection, move the exposed person to fresh air at once. Encourage exposed person to cough, spit out, and blow nose to remove dust. Immediately call a poison center, physician, or emergency medical service.

First-aid Measures After Skin Contact: Remove contaminated clothing. Drench affected area with water for at least 15 minutes. Obtain medical attention if irritation develops or persists.

First-aid Measures After Eye Contact: Rinse cautiously with water for at least 15 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention.

First-aid Measures After Ingestion: Rinse mouth. Do NOT induce vomiting. Obtain medical attention.

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

Symptoms/Injuries: Pharmaceutical. When handling in workplace settings, in quantities that are most likely above the therapeutic dose, this product may be harmful if absorbed through the eyes, skin, or respiratory tract. Potential adverse reactions from prescribed doses and overdoses are: tremor, darrhoea, nausea, and renal dysfunction. These occur with oral and intravenous administration, and may respond to a reduction in dosing. At higher doses Modigraf acts as an immunosuppressant. Diarrhoea was sometimes associated with other gastrointestinal complaints such as nausea and vomiting. Occupational exposure has not been fully investigated. Delayed effects after long-lasting, repeated exposure may include nephrotoxicity and neurotoxicity. Medical conditions generally recognized as being aggravated by accidental exposure are: pre-existing skin and respiratory conditions, and renal insufficiency. Hypertension is a common adverse effect of therapeutic administration and antihypertensive therapy may be required. While calcium channel blocking agents can be effective in treating Modigraf-related hypertension, care should be taken since interference with tacrolimus metabolism may require a larger dosage reduction.

Symptoms/Injuries After Inhalation: Dust may be harmful or cause irritation.

Symptoms/Injuries After Skin Contact: Prolonged exposure may cause skin irritation.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Ingestion may cause adverse effects.

Chronic Symptoms: Suspected of damaging fertility or the unborn child. Causes damage to organs (immune system, kidneys) through prolonged or repeated exposure.

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

If exposed or concerned, get medical advice and attention. If medical advice is needed, have product container or label at hand. Modigraf is used for prophylaxis of transplant rejection in adult and pediatric kidney or liver allograph recipients. Tacrolimus is a highly potent and immunosuppressive agent. In particular, tacrolimus inhibits the formation of cytotoxic lymphocytes, which are mainly responsible for graft rejection. Tacrolimus suppresses T-cell activation and T-helper-cell dependent B-cell proliferation, as well as the formation of lymphkines (such as interleukins-2, -3, and y-interferon) and the expression of the interleukin-2 receptor. Treatment should follow standard procedure for the therapeutic group.

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Use extinguishing media appropriate for surrounding fire.

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: Combustible Dust.

Explosion Hazard: Dust explosion hazard in air.

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: Risk of dust explosion.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Do not get in eyes, on skin, or on clothing. Do not breathe dust. Avoid generating dust. Remove ignition sources. Keep away from heat, hot surfaces, sparks, open flames, and other ignition sources. No smoking.

6.1.1. For Non-emergency Personnel

Protective Equipment: Use appropriate personal protective 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. Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters.

6.3. Methods and Material for Containment and Cleaning Up

For Containment: Contain solid spills with appropriate barriers and prevent migration and entry into sewers or streams. Avoid generation of dust during clean-up of spills.

Methods for Cleaning Up: Clean up spills immediately and dispose of waste safely. Contact competent authorities after a spill. Use explosion proof vacuum during cleanup, with appropriate filter. Do not mix with other materials. Vacuum clean-up is preferred. If sweeping is required use a dust suppressant. Use only non-sparking tools.

6.4. Reference to Other Sections

See Section 8 for exposure controls and personal protection and Section 13 for disposal considerations.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Additional Hazards When Processed: Accumulation and dispersion of dust with an ignition source can cause a combustible dust explosion. Keep dust levels to a minimum and follow applicable regulations.

Precautions for Safe Handling: Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work. Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not breathe dust. Avoid contact with eyes, skin and clothing. Avoid creating or spreading dust. Keep away from heat, sparks, open flames, hot surfaces. – No smoking.

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations. Avoid creating or spreading dust. Use explosion-proof electrical, ventilating, lighting equipment. Proper grounding procedures to avoid static electricity should be followed.

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

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

Storage Temperature: < 25 °C (72 °F)

7.3. Specific End Use(s)

Prograf (tacrolimus) granules is a medicinal product for oral use intended for prophylaxis of transplant in adult and pediatric kidney, liver or heart allograft recipients. For professional use only.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

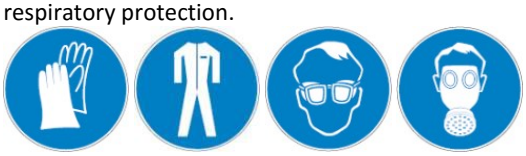
8.1. Control Parameters

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), AIHA (WEEL), NIOSH (REL), or OSHA (PEL).

8.2. Exposure Controls

Appropriate Engineering Controls : Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Ensure adequate ventilation, especially in confined areas. Ensure all national/local regulations are observed. Proper grounding procedures to avoid static electricity should be followed. Use explosion-proof equipment. Use local exhaust or general dilution ventilation or other suppression methods to maintain dust levels below exposure limits. Power equipment should be equipped with proper dust collection devices. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment.

Personal Protective Equipment : Gloves. Protective clothing. Protective goggles. Insufficient ventilation: wear respiratory protection.



Materials for Protective Clothing : Chemically resistant materials and fabrics.

Hand Protection : Wear protective gloves.

Eye Protection : Chemical safety goggles.

Skin and Body Protection : Wear suitable protective clothing.

Respiratory Protection : If exposure limits are exceeded or irritation is experienced, approved respiratory protection should be worn. In case of inadequate ventilation, oxygen deficient atmosphere, or where exposure levels are not known wear approved respiratory protection.

Other Information : When using, do not eat, drink or smoke.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State	: Solid
Appearance	: Sachets containing white colored granules
Odor	: No data available
Odor Threshold	: No data available
pH	: No data available
Evaporation Rate	: No data available
Melting Point	: No data available
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	: No data available
Partition Coefficient: N-Octanol/Water	: No data available
Viscosity	: No data available

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, and incompatible materials. Sparks, heat, open flame and other sources of ignition. Dust accumulation (to minimize explosion hazard).

10.5. Incompatible Materials: Strong acids, strong bases, strong oxidizers.

10.6. Hazardous Decomposition Products: The nature of the decomposition products are unknown.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information On Toxicological Effects

Acute Toxicity: Not classified

Tacrolimus (109581-93-3)	
LD50 Oral Rat	134 - 194 mg/kg

Skin Corrosion/Irritation: Not classified

Serious Eye Damage/Irritation: Not classified

Respiratory or Skin Sensitization: Not classified (No indications for sensitization).

Germ Cell Mutagenicity: Not classified (No indication of genetic toxicity).

Carcinogenicity: Not classified (There are no indications for a carcinogenic potential).

Reproductive Toxicity: Suspected of damaging fertility or the unborn child. (Animal studies have revealed that tacrolimus may impair fertility and that it may cause harm to the foetus. Tacrolimus is excreted in breastmilk. Based on the characteristics of the drug compound, suspicion of reproductive activity is warranted. Therefore, it is advised to avoid contact during pregnancy/while nursing).

Specific Target Organ Toxicity (Single Exposure): Not classified

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

Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: Dust may be harmful or cause irritation.

Symptoms/Injuries After Skin Contact: Prolonged exposure may cause skin irritation.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Ingestion may cause adverse effects.

Chronic Symptoms: Suspected of damaging fertility or the unborn child. Causes damage to organs through prolonged or repeated exposure.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

Ecology - General : Not classified.

12.2. Persistence and Degradability

Prograf® (Tacrolimus) Granules	
Persistence and Degradability	Not established.

12.3. Bioaccumulative Potential

Prograf® (Tacrolimus) Granules	
Bioaccumulative Potential	Not established.

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/container in accordance with local, regional, national, and international regulations.

Additional Information: Container may remain hazardous when empty. Continue to observe all precautions.

Ecology – Waste Materials: Avoid release to the environment.

SECTION 14: TRANSPORT INFORMATION

The shipping description(s) stated herein were prepared in accordance with certain assumptions at the time the SDS was authored, and can vary based on a number of variables that may or may not have been known at the time the SDS was issued.

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

Prograf® (Tacrolimus) Granules	
SARA Section 311/312 Hazard Classes	Delayed (chronic) health hazard Fire hazard Sudden release of pressure hazard

15.2 US State Regulations Neither this product nor its chemical components appear on any US state lists, or its chemical components are not required to be disclosed

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

Date of Preparation or Latest Revision : 04/03/2018

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

GHS Full Text Phrases:

Acute Tox. 3 (Oral)	Acute toxicity (oral) Category 3
Comb. Dust	Combustible Dust
Eye Irrit. 2A	Serious eye damage/eye irritation Category 2A
Repr. 2	Reproductive toxicity Category 2
Skin Irrit. 2	Skin corrosion/irritation Category 2
STOT RE 1	Specific target organ toxicity (repeated exposure) Category 1
STOT SE 3	Specific target organ toxicity (single exposure) Category 3
H301	Toxic if swallowed
H315	Causes skin irritation
H319	Causes serious eye irritation
H335	May cause respiratory irritation
H361	Suspected of damaging fertility or the unborn child
H372	Causes damage to organs through prolonged or repeated exposure

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.

Astellas US GHS SDS