

SECTION 1: IDENTIFICATION

1.1. Product Identifier

Product Form: Mixture

Product Name: Prograf® (Tacrolimus) Injection

Material Name: Tacrolimus, FK506

Formula: C₄₄H₆₉NO₁₂•H₂O

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-3methoxycyclohexyl)-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

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.

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

Classification (GHS-US)

Flam. Liq. 2 H225

Eye Irrit. 2A H319

Repr. 2 H361

Full text of H-phrases: see section 16

2.2. Label Elements

GHS-US Labeling

Hazard Pictograms (GHS-US)



Signal Word (GHS-US)

: Danger

Hazard Statements (GHS-US)

: H225 - Highly flammable liquid and vapor.

H319 - Causes serious eye irritation.

H361 - Suspected of damaging the unborn child.

Precautionary Statements (GHS-US)

: P201 - Obtain special instructions before use.

P202 - Do not handle until all safety precautions have been read and understood.

P210 - Keep away from heat, hot surfaces, open flames, sparks. - No smoking.

P233 - Keep container tightly closed.

P240 - Ground/bond container and receiving equipment.

P241 - Use explosion-proof electrical, lighting, ventilating equipment.

P242 - Use only non-sparking tools.

P243 - Take precautionary measures against static discharge.

P264 - Wash hands, forearms, and exposed areas thoroughly after handling.

P273 - Avoid release to the environment.

P280 - Wear eye protection, protective clothing, protective gloves.

P303+P361+P353 - IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower.

P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P308+P313 - If exposed or concerned: Get medical advice/attention.

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P337+P313 - If eye irritation persists: Get medical advice/attention.
P370+P378 - In case of fire: Use alcohol resistant foam, carbon dioxide (CO₂), dry extinguishing powder, water to extinguish.
P403+P235 - Store in a well-ventilated place. Keep cool.
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 those with pre-existing eye, skin, or respiratory conditions. Accidental exposure may cause headaches, nausea, or vomiting. May cause a warm sensation upon inhalation or skin contact.

2.4. Unknown Acute Toxicity (GHS-US)

No data available

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substance

Not applicable

3.2. Mixture

| Name | Product Identifier | % | Classification (GHS-US) |
|---------------------------------------|----------------------|-----|--|
| Ethyl alcohol | (CAS No) 64-17-5 | 80 | Flam. Liq. 2, H225 Eye Irrit. 2A, H319 |
| Castor oil, hydrogenated, ethoxylated | (CAS No) 61788-85-0 | 20 | Not classified |
| Tacrolimus | (CAS No) 104987-11-3 | 0.5 | Acute Tox. 3 (Oral), H301 Repr. 2, H361 |

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 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: Rinse immediately with plenty of water. 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: 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: Causes serious eye irritation. Suspected of damaging the unborn child.

Symptoms/Injuries After Inhalation: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Stinging, tearing, redness, and swelling of eyes.

Symptoms/Injuries After Ingestion: Ingestion is likely to be harmful or have adverse effects.

Chronic Symptoms: May damage the unborn child.

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, alcohol-resistant foam, carbon dioxide (CO₂), dry chemical powder.

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: Highly flammable liquid and vapor.

Explosion Hazard: May form flammable/explosive vapor-air mixture.

Reactivity: Hazardous reactions will not occur under normal conditions.

5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire. Under fire conditions, hazardous fumes will be present.

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Firefighting Instructions: Use water spray or fog for cooling exposed containers. In case of major fire and large quantities: Evacuate area. Fight fire remotely due to the risk of explosion.

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: Avoid all contact with skin, eyes, or clothing. Avoid breathing (vapor, mist, spray). Keep away from heat/sparks/open flames/hot surfaces. – No smoking.

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: Stop leak if safe to do so. Eliminate ignition sources. Ventilate area.

6.2. Environmental Precautions

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

6.3. Methods and Material for Containment and Cleaning Up

For Containment: Contain any spills with dikes or absorbents to prevent migration and entry into sewers or streams. Do not take up in combustible material such as saw dust or cellulosic material.

Methods for Cleaning Up: Clear up spills immediately and dispose of waste safely. Spills should be contained with mechanical barriers. Transfer spilled material to a suitable container for disposal. Use only non-sparking tools. 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: Any proposed use of this product in elevated-temperature processes should be thoroughly evaluated to assure that safe operating conditions are established and maintained. Proper grounding procedures to avoid static electricity should be followed. Handle empty containers with care because residual vapors are flammable.

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. Ground/bond container and receiving equipment. Use explosion-proof electrical, ventilating, and lighting equipment.

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. Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.

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

Storage Temperature: 5 - 25 °C (41 - 77 °F)

7.3. Specific End Use(s)

Prophylaxis of organ rejection in patients receiving allogeneic liver, kidney or heart transplants.

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).

| Ethyl alcohol (64-17-5) | | |
|-------------------------|--------------------------------------|------------------------|
| USA ACGIH | ACGIH STEL (ppm) | 1000 ppm |
| USA NIOSH | NIOSH REL (TWA) (mg/m ³) | 1900 mg/m ³ |
| USA NIOSH | NIOSH REL (TWA) (ppm) | 1000 ppm |
| USA IDLH | US IDLH (ppm) | 3300 ppm (10% LEL) |
| USA OSHA | OSHA PEL (TWA) (mg/m ³) | 1900 mg/m ³ |
| USA OSHA | OSHA PEL (TWA) (ppm) | 1000 ppm |

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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. Gas detectors should be used when flammable gases/vapors may be released. Use explosion-proof equipment. Ensure all national/local regulations are observed.

Personal Protective Equipment

: Protective goggles. Gloves. Protective clothing.



Materials for Protective Clothing

: Chemically resistant materials and fabrics.

Hand Protection

: Wear chemically resistant protective gloves.

Eye Protection

: Chemical safety goggles.

Skin and Body Protection

: Wear suitable protective clothing.

Respiratory Protection

: In case of insufficient ventilation, wear suitable respiratory equipment.

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 | : Liquid |
| Appearance | : Clear solution |
| 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 | : 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 | : 822.03 (Tacrolimus) |

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:** Highly flammable liquid and vapor. May form flammable or explosive vapor-air mixture.
- 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. Strong oxidizers.
- 10.6. Hazardous Decomposition Products:** Thermal decomposition generates: Carbon oxides (CO, CO₂), toxic fumes.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information On Toxicological Effects

Acute Toxicity: Not classified

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| | |
|---------------------------------|---------------|
| Tacrolimus (104987-11-3) | |
| LD50 Oral Rat | 134 mg/kg |
| Ethyl alcohol (64-17-5) | |
| LD50 Oral Rat | 10470 mg/kg |
| LD50 Dermal Rat | 20 ml/kg |
| LC50 Inhalation Rat | 124.7 mg/l/4h |

Skin Corrosion/Irritation: Not classified

Serious Eye Damage/Irritation: Causes serious eye irritation.

Respiratory or Skin Sensitization: Not classified

Germ Cell Mutagenicity: Not classified (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 (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.)

Reproductive Toxicity: Suspected of damaging the unborn child. (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 embryoletality and with adverse effects on female reproduction. Effects on female reproductive function [parturition] and embryoletal 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.)

Specific Target Organ Toxicity (Single Exposure): Not classified

Specific Target Organ Toxicity (Repeated Exposure): Not classified

Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Stinging, tearing, redness, and swelling of eyes.

Symptoms/Injuries After Ingestion: Ingestion is likely to be harmful or have adverse effects.

Chronic Symptoms: May damage the unborn child.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

| | |
|--------------------------------|--|
| Ethyl alcohol (64-17-5) | |
| EC50 Daphnia 1 | 9268 - 14221 mg/l (Exposure time: 48 h - Species: Daphnia magna) |
| LC 50 Fish 2 | > 100 mg/l (Exposure time: 96 h - Species: Pimephales promelas [static]) |

12.2. Persistence and Degradability No additional information available.

12.3. Bioaccumulative Potential

| | |
|--------------------------------|-------|
| Ethyl alcohol (64-17-5) | |
| Log Pow | -0.32 |

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 waste material in accordance with all local, regional, national, and international regulations.

Additional Information: Handle empty containers with care because residual product is flammable.

Ecology – Waste Materials: Avoid release to the environment.

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SECTION 14: TRANSPORT INFORMATION

14.1. In Accordance with DOT

Proper Shipping Name : ETHYL ALCOHOL SOLUTIONS
Hazard Class : 3
Identification Number : UN1170
Label Codes : 3
Packing Group : II
ERG Number : 127



14.2. In Accordance with IMDG

Proper Shipping Name : ETHANOL SOLUTION (ETHYL ALCOHOL SOLUTION)
Hazard Class : 3
Identification Number : UN1170
Packing Group : II
Label Codes : 3
EmS-No. (Fire) : F-E
EmS-No. (Spillage) : S-D



14.3. In Accordance with IATA

Proper Shipping Name : Ethanol solution
Packing Group : II
Identification Number : UN1170
Hazard Class : 3
Label Codes : 3
ERG Code (IATA) : 3L



SECTION 15: REGULATORY INFORMATION

15.1 US Federal Regulations

| | |
|---|---|
| Prograf® (Tacrolimus) Injection | |
| SARA Section 311/312 Hazard Classes | Fire hazard Delayed (chronic) health hazard Immediate (acute) health hazard |
| Castor oil, hydrogenated, ethoxylated (61788-85-0) | |
| Listed on the United States TSCA (Toxic Substances Control Act) inventory | |
| Ethyl alcohol (64-17-5) | |
| Listed on the United States TSCA (Toxic Substances Control Act) inventory | |

15.2 US State Regulations

| | |
|---|---|
| Ethyl alcohol (64-17-5) | |
| U.S. - California - Proposition 65 - Carcinogens List | WARNING: This product contains chemicals known to the State of California to cause cancer. |
| U.S. - California - Proposition 65 - Developmental Toxicity | WARNING: This product contains chemicals known to the State of California to cause birth defects. |
| Ethyl alcohol (64-17-5) | |
| U.S. - Massachusetts - Right To Know List | |
| U.S. - New Jersey - Right to Know Hazardous Substance List | |
| U.S. - Pennsylvania - RTK (Right to Know) List | |

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

Revision Date : 01/19/2015
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 |
| Eye Irrit. 2A | Serious eye damage/eye irritation Category 2A |
| Flam. Liq. 2 | Flammable liquids Category 2 |
| Repr. 2 | Reproductive toxicity Category 2 |

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| | |
|------|---|
| H225 | Highly flammable liquid and vapor |
| H301 | Toxic if swallowed |
| H319 | Causes serious eye irritation |
| H361 | Suspected of damaging fertility or the unborn child |

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)