NEXUS
PHARMACEUTICALS

SAFETY DATA SHEET
for
Tacrolimus Injection, 5 mg (anhydrous tacrolimus)/mL

1. Identification

Product Identifier: Tacrolimus Injection, 5 mg (anhydrous tacrolimus)/mL
Synonyms: FK-506 and Fujimycin
Product Use: Indicated for the prophylaxis of organ rejection, in adult and pediatric patients receiving allogeneic kidney transplant, liver transplants and heart transplant, and in combination with other immunosuppressants.

Manufacturers: Nexus Pharmaceuticals, LLC
400 Knightsbridge Pkwy
Lincolnshire IL, 60069 USA

Emergency Telephone: 1-800-424-9300 – Chemtrec

General Use: Safety Data Sheets are designed to protect the health and safety of people in the workplace by providing information on the hazards of drug products and how they should be safely used, stored, transported, and disposed of.

2. Hazard Identification

Safety Data Sheet prepared in accordance with OSHA's Hazard Communication Standard (29 CFR 1910.1200); Regulation (EC) No 1272/2008 - Classification, Labelling and Packaging of Substances and Mixtures (CLP); and the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

GHS Classification:

Health	Environmental	Physical
Acute oral toxicity (Category 4), H302 Acute inhalation toxicity (Category 3), H331 Serious eye damage/eye irritation (Category 2A), H319 Specific target organ toxicity, repeated exposure (Category 1), H372 Reproductive toxicity (Category 2), H361	CNC	Flammable liquids (Category 2)

GHS Label:

Symbols:

Signal word: Danger

Hazard Statements	Precautionary Statements
Harmful if swallowed (Category 4), H302 Toxic if inhaled (Category 3), H331 Causes serious eye irritation (Category 2A), H319 Causes damage to organs (kidneys, thymus, lymph nodes, spleen, pancreas and lungs) through prolonged or repeated exposure, (Category 2), H372 Suspected of damaging fertility or the unborn child, (Category 2), H361	P203: Obtain, read, and follow all safety instructions before use. P210: Keep away from heat, hot surface, sparks, open flames, and other ignition sources. No smoking. P223: Do not allow contact with water. P240: Ground/bond container and receiving equipment. P241: Use explosion-proof equipment. P242: Use only non-sparking tools. P243: Take precautionary measures against static discharge. P260: Do not breathe dust, fume, gas, mist, vapors, and spray. P261: Avoid breathing dust, fume, gas, mist, vapors, spray. P264+P265: Wash hands thoroughly after handling. Do not touch eyes. P270: Do not eat, drink, or smoke when using this product. P271: Use only outdoors or in a well-ventilated area. P280: Wear protective gloves, protective clothing, eye protection, face protection, and hearing protection.

Other Hazards: No other hazards were identified. Personal protective equipment for the safe handling of this compound can be found in Section 8 – Exposure Controls/Personal Protection.

3. Composition / Information on Ingredients

Component	CAS Number	EINECS Number	Amount (%)	GHS Classification
Tacrolimus USP	109581-93-3	634-559-2	5 mg/mL[1]	Toxic if swallowed (Category 3), H302 Suspected of damaging fertility or the unborn child (Category 2), H361 Causes damage to organs (kidneys, thymus, lymph nodes, spleen, pancreas and lungs) through prolonged or repeated exposure, (Category 2), H372
Polyethyleneglycol 60 (PEG-60)/ Hydrogenated Castor Oil (HCO-60)	61788-85-0	500-147-5	200 mg/mL	Harmful if inhaled Category 4), H332
Dehydrated Alcohol USP	64-17-5	200-578-6	QS to 1 mL	Causes serious eye irritation (Category 2A), H319 Highly Flammable liquid and vapor (Category 2), H225

[1]Equivalent of 5 mg anhydrous tacrolimus USP per mL.

4. First Aid Measures

Description of First Aid Measures, Immediate Medical Attention, and Special Treatment, if Necessary:

Eye: If worn and easy to do, remove contact lenses. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Skin:	Wash exposed area with soap and water and remove contaminated clothing and/or shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation:	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion:	If swallowed in large amount, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Most Important Symptoms/Effects:	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.
Effects, Acute, and Delayed:	Known symptoms or effects (if any) are described in Section 11 – Toxicological Information.

5. Fire Fighting Measures

Suitable Extinguishing Media:	Use water spray (fog), foam, dry powder, or carbon dioxide as appropriate for surrounding fire and materials.
Special Hazards Arising from the Chemical:	No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen, and other nitrogen-containing compounds.
Fire and Explosion Hazards:	No information identified. High concentrations of finely divided organic particles can explode if ignited.
Special Protective Measures for Firefighters:	In case of fire in the surroundings, use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

6. Accidental Release Measures

Personal Precautions, Protective Equipment, and Emergency Procedures:	Wear appropriate protective clothing to avoid exposure. Avoid dust formation and breathing dust. Ensure adequate ventilation.

Environmental Precautions:	Do not empty into drains. Avoid release to the environment.
Methods and Materials for Containment:	Prevent further leakage or spillage if safe to do so. Do not let product enter drains. Discharge into the environment must be avoided.
Cleaning Up:	Clean spill area thoroughly using HEPA filtered vacuum to sweep up dry solids, wet-brushing, or by absorbing spilled liquids.
Other Information:	See Sections 8 and 13 for more information.

7. Handling and Storage

Precautions for Safe Handling:	Avoid contact with skin and eyes. Use appropriate personal protective equipment when handling. Generation of dust or volatile vapors should be minimized.
Storage Conditions:	When not in use, store in a tightly sealed container inside a sealed secondary container containing desiccant at 2°C to 8°C.

8. Exposure Controls / Personal Protection

Control Parameters/Occupational Exposure Limits:

Exposure Limits Component Name	OSHA PEL (TWA)	ACGIH TLV (TWA)	NIOSH REL (TWA)
Tacrolimus USP	N.E.	N.E.	N.E.
Polyethyleneglycol 60 (PEG-60)/ Hydrogenated Castor Oil (HCO-60)	N.E.	N.E.	N.E.
Dehydrated Alcohol USP	1000 ppm (1900 mg/m^3)	N.E.	1000 ppm (1900 mg/m^3)

N.E. = Not established

Appropriate Engineering Controls:	Use a laboratory fume hood or local exhaust ventilation to minimize airborne dust or volatile vapors when handling.

Respiratory Protection:	Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. At a minimum, a tight-fitting full-face respirator with HEPA filter is required when performing dust-generating operations and for spill cleanup.
Hand Protection:	Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.
Eye Protection:	Wear safety glasses with side shields, chemical splash goggles, or full-face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Skin and Body Protection:	Wear proper gowning appropriate to the task. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (such as cafeterias) or out-of-doors. Employees must be trained in proper gowning and degowning practices.
Other Protective Measures:	Wash hands in the event of contact with this substance, especially before eating, drinking, or smoking. Protective equipment is not to be worn outside the work area (such as in common areas or out-of-doors).
Environmental Exposure Control:	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedure.

9. Physical and Chemical Properties

Physical Form/Appearance:	Clear, colorless to yellow solution
Formula:	Mixture
Molecular Mass:	No data available
Odor:	No data available
Odor Threshold:	No data available

pH:	No data available
Melting Point:	No data available
Freezing Point:	No data available
Boiling Point:	No data available
Flash Point:	No data available
Relative Evaporation Rate (butyl acetate = 1):	No data available
Vapor Pressure:	No data available
Relative Vapor Density:	No data available
Relative Density:	No data available
Solubility:	No data available
Partition Coefficient (n-octanol/water):	No data available
Auto-Ignition Temperature:	No data available
Decomposition Temperature:	No data available
Viscosity, Kinematic:	No data available
Viscosity, Dynamic:	No data available
Explosion Limits:	No data available
Explosive Properties:	No data available
Oxidizing Properties:	No data available

10. Stability and Reactivity

Reactivity:	Contact with incompatible materials and exposure to heat.
Chemical Stability:	Stable under normal storage conditions.
Possibility of Hazardous Reactions:	None known.
Conditions to Avoid:	Contact with incompatible materials and exposure to heat.
Incompatible Materials:	Acids, bases, and oxidizers.
Hazardous Decomposition Products:	Not available.

11. Toxicology Information

Signs and Symptoms of Overexposure: No information is available for this compound.

Likely Routes of Exposure: All the formulation components may be absorbed by inhalation, ingestion, and skin and eye contact.

Acute Toxicity:

Tacrolimus Injection: Oral ATE_{mix}: ≈ 850 mg/kg
Inhalation ATE_{mix}: ≈ 9.66 mg/L

Tacrolimus USP: Rat – oral LD_{50} of 134 mg/kg, rat (juvenile) – oral of 32 mg/kg to 100 mg/kg, and baboons – oral LD_{50} of 5 mg/kg.

Polyethylene glycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): Rat – oral LD_{50} of > 2000 mg/kg and rat – inhalation LC_{50} of > 2.06 mg/L (OECD Test Guideline 403).

Dehydrated Alcohol USP: Rat – oral LD_{50} of 10470 mg/kg and rat – inhalation LC_{50} of 124.4 mg/L (4 hours – vapor).

Skin Corrosion/Irritation: Based on the available data the criteria not met.

Serious Eye Damage/Irritation:

Dehydrated Alcohol USP: Causes serious eye irritation.

Skin Sensitization:

Tacrolimus USP: Could not be classified.

Germ Cell Mutagenicity: Based on the available data the criteria not met.

Carcinogenicity:

Dehydrated Alcohol USP: Could not be classified.

Reproductive/Developmental Effects:

Tacrolimus USP: Rat – oral NOAEL of 0.32 mg/kg/day (reproductive and embryofetal effects).

Polyethylene glycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): Rat – oral NOAEL of 1000 mg/kg/day (reproductive and developmental effects).

Specific target organ toxicity – single exposure: No information is available for this compound.

Specific Target Organ Toxicity – Repeated Exposure:

Tacrolimus USP: Rat – oral NOAEL of 0.15 mg/kg/day (52 weeks), rat – oral NOAEL of 1 mg/kg/day (13 weeks), rat – oral NOAEL of 0.32 mg/kg/day (13 weeks), baboon – oral NOAEL of 1 mg/kg/day (52 weeks), and baboon – oral NOAEL of 1 mg/kg/day (13 weeks). The kidneys, thymus, lymph nodes, spleen, pancreas, and lungs were the primary organs affected in toxicity studies.

Repeated dose exposure:

Tacrolimus USP: Dog – oral NOAEL of 600 mg/kg/day (39-weeks) and rats – oral NOAEL of 750 mg/kg/day (9 months).

Polyethylene glycol 60 (PEG-60)/ Hydrogenated Castor Oil (HCO-60): Rat- Oral NOAEL of 1000 mg/kg (2 weeks - systemic toxicity).

Dehydrated Alcohol USP: Rat – Oral NOAEL of 1.730 mg/kg, and rat - oral LOAEL of 3200 mg/kg.

12. Ecological Information

Toxicity:	Tacrolimus USP: No data available. Polyethyleneglycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): *Oryzias latipes* LC_{50} of > 10.000 mg/L (48 hours); *Daphnia magna* EC_{50} of > 100 mg/L (48 hours); *Desmodesmus subspicatus* EC_{50} of > 100 mg/L (72 hours). Dehydrated Alcohol USP: *Pimephales promelas* (fathead minnow) LC_{50} of 15300 mg/L (96 hours); *Ceriodaphnia dubia* (water flea) static test LC_{50} of 5012 mg/L (48 hours); *Chlorella vulgaris* (fresh water algae) static test ErC_{50} of 275 mg/L (72 hours); Activated sludge static test IC_{50} of > 1000 mg/L (3 hours); *Danio rerio* (zebra fish) semi-static test NOEC of 250 mg/L (120 hours); *Daphnia magna* (water flea) semi-static test NOEC of 9.6 mg/L (9 days).
Persistence and Degradability:	Tacrolimus USP: No data available. Polyethyleneglycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): No data available. Dehydrated Alcohol USP: Readily biodegradable.

Bioaccumulative Potential:	Tacrolimus USP: No data available. Polyethyleneglycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): No data available. Dehydrated Alcohol USP: Due to the distribution coefficient n-octanol/water, accumulation in organisms is not expected.
Mobility in Soil:	Tacrolimus USP: No data available. Polyethyleneglycol 60 (PEG-60)/Hydrogenated Castor Oil (HCO-60): No data available. Dehydrated Alcohol USP: No data available.
Results of PBT and vPvB Assessment:	This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.
Other Adverse Effects:	No data available.

13. Disposal Considerations

Waste Treatment Methods: Dispose of any cleanup materials and waste residue according to prescribed federal, state, and local regulations.

14. Transportation Information

Transport:	Based on the available data, dehydrated alcohol USP is classified as classified as hazardous/dangerous ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN Number:	UN 1170
UN Proper Shipping Name:	UN 1170 - Ethanol or Ethyl alcohol or Ethanol solution
DOT Hazard Class:	3 (Flammable liquid)
Packing Group:	II

Marine Pollutant:	Based on the available data, this substance is not regulated as an environmental hazard or a marine pollutant.
Special Transport Precautions:	Avoid release to the environment.
Transport in Bulk According to Annex II of Marpol and the IBC Code:	Not applicable.

15. Regulatory Information

Safety, Health, and Environmental Regulations/Legislation Specific for the Substance or Mixture:	This SDS generally complies with the requirements listed under current guidelines in the US, EU, and Canada. Consult your local or regional authorities for more information.
Chemical Safety Assessment:	No chemical safety assessment has been carried out.
TSCA:	Dehydrated Alcohol USP is listed under the TSCA.
Canada DSL/NDSL:	Dehydrated Alcohol USP is listed under Domestic Substances List.
SARA Section 313:	This substance is not known to contain a toxic chemical or chemicals in excess of the applicable *de minimis* concentration as specified in 40 CFR §372.38(a) subject to the reporting requirements of section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR Part 372.
California Proposition 65:	This product contains the following Proposition 65 chemicals. Ethyl alcohol is only considered a Proposition 65 developmental hazard when it is ingested as an alcoholic beverage, developmental and/or reproductive harm.
Additional Information:	No additional information available.

16. Other Information

Full Text of H Phrases and GHS Classification:

Acute oral toxicity, Harmful if swallowed, (Category 4), H302

Acute inhalation toxicity, Toxic if inhaled, (Category 3), H331

Serious eye damage/eye irritation, Causes serious eye irritation, (Category 2A), H319

Specific target organ toxicity, repeated exposure, Causes damage to organs (kidneys, thymus, lymph nodes, spleen, pancreas and lungs) through prolonged or repeated exposure, (Category 1), H372

Reproductive toxicity, Suspected of damaging fertility or the unborn child, (Category 2), H361

Flammable liquids, Highly Flammable liquid and vapor, (Category 2)

Abbreviations and Acronyms:

ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; ATEmix - Acute Toxicity Estimate for mixture; API - Active Pharmaceutical Ingredient; CAS# - Chemical Abstract Services Number; CHO - Chinese Hamster Ovary Cells; CHO-K1 - CHO K1 Line Cells; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; CNC - Could Not Classify; DNEL - Derived No Effect Level; DOT - Department of Transportation; DPRA - Direct Peptide Reactivity Assay; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European

Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; HEPA - High Efficiency Particulate Air; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IARC - International Agency for Research on Cancer; IBC - Institutional Biosafety Committee; IMDG - International Maritime Dangerous Goods; IP – Intraperitoneal (IP); IV - Intravenous; LD_{50} - Median Lethal Dose; LD_{Lo} - Lowest Lethal Dose; LC_{50} - Median Lethal Concentration; EC_{50} - Median Effective Concentration; EL50 - Median Effective Loading Rate; LL_{50} - Median Lethal Loading Rate; NC - Not Classified; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PEL - Permissible Exposure Limit; PNEC - Predicted No Effect Concentration; REL - Recommended Exposure Limit; SAR - Structure-Activity Relationship; SARA - Superfund Amendments and Reauthorization Act; SC – Subcutaneous; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TLV - Threshold Limit Value; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; UN - United Nations; US WEELs - United Sates Workplace Environmental Exposure Levels; US - United States; and WHMIS - Workplace Hazardous Materials Information System.

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