MATERIAL SAFETY DATA SHEET

Product Name: Tacrolimus Ointment, 0.1%

Revision Date: NA **Version No.**: 00

1. IDENTIFICATION

Product Name	**Tacrolimus Ointment 0.1%**
Manufacturer Name	**Encube Ethicals Pvt. Ltd.**
Address	Plot No.C-1, Madkaim Industrial Estate Madkaim, Post-Mardol, Ponda Goa – 403 404, India.
Recommended use	Human drug – treatment of dermatitis
Restrictions on use:	For topical use only. Use only as directed.

2. HAZARD(S) IDENTIFICATION

Classification:

Physical- Not hazardous

Health- A) Reproductive Toxicity Category 2
B) Aspiration Toxicity Category 1

Hazards statement-
May be fatal if swallowed and enters airways. Suspected of damaging fertility or the unborn child

Precautionary statement(s)
Obtain special instructions before use.
Do not handle until all safety precautions have been read and understood.
Wear protective clothing and gloves.
IF Swallowed: Immediately call a poison centre or doctor.
DoNOT induce vomiting.
IF exposed or concerned: Get medical attention.
Store locked up.

Dispose in accordance with local and national regulations

3. COMPOSITION / INFORMATION ON INGREDIENT

Chemical name	CAS No.	% w/w*
Tacrolimus	104987-11-3	0.1%
White Petrolatum	8009-03-8	--
Mineral Oil	8042-47-5	--
Paraffin	8002-74-2	--
Propylene Carbonate	108-32-7	--
White Wax	8012-89-3	--

*Formulation proprietary, we will make this information available to medical personal in the event of an emergency.

4. FIRST-AID MEASURES

If inhaled:	Remove person to fresh air. If irritation occurs or symptoms develop, get medical attention
In case of skin contact:	Remove contaminated clothing. Wash skin with soap and water If irritation develops and persists, get medical attention Launder clothing before reuse.
In case of eye contact:	Immediately flush eyes with water while lifting the upper. And lower lids. Get medical attention if irritation persists.
Ingestion:	Rinse mouth with water. Do NOT induce vomiting. Never give anything by mouth to a person who is unconscious or convulsing
Indication of immediate medical attention and special treatment, if necessary:	Immediate medical attention is required for ingestion.

5. FIRE-FIGHTING MEASURES

Extinguishing media:	Use water spray or fog, CO_2, dry chemical or foam. Do not use solid water jet as this may spread fire
Specific hazards during firefighting:	Product is not flammable or combustible but will burn in fire.
Special protective equipment for firefighters:	Firefighters should wear positive pressure self-contained breathing apparatus and full protective clothing for all fires involving chemicals. Cool fire exposed containers with water.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions:	Use personal protective equipment.
Environmental Precautions:	Prevent spill from entering sewers and water courses. Report releases as required by local and national authorities.
Methods and materials for containment And cleaning up:	Contain and collect with an inert absorbent material. Place in appropriate container for disposal. Clean area thorough

7. HANDLING AND STORAGE

Handling: Avoid the generation of mists.

Avoid contact with eyes, skin and clothing.

Wash thoroughly with soap and water after handling

Storage: Store as indicated on product packaging

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Appropriate engineering controls: Use with adequate general or local exhaust Ventilation to minimize exposures levels.

Individual protection measures:

Respiratory protection: None needed under normal use conditions. If exposure levels are excessive and irritation is experienced, a NIOSH approved organic vapor/particulate respirator is recommended. Selection of respiratory protection depends on the contaminant type, form and concentration. Select in accordance with OSHA 1910.134 and good Industrial Hygiene practice.

Skin protection: Impervious gloves recommended if contact with the drug product is possible.

Eye protection: Chemical safety goggles recommended if contact with the drug product is possible.
Other: None known.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state and form	A white to pale yellow, smooth, homogenous ointment
Odour:	Odourless
Odor threshold	NA
pH	NA
Flash point	200°F (> 93°C)

10. STABILITY AND REACTIVITY

Reactivity: Not reactive under normal conditions of use.
Chemical stability: Stable
Possibility of hazardous reactions: None known.
Conditions to avoid: None known.
Incompatible materials: Avoid oxidizing agents.
Hazardous decomposition products: Thermal decomposition may yield carbon oxides

11. TOXICOLOGICAL INFORMATION

Acute effects of exposure:

Inhalation: Inhalation of mists may cause minor irritation of the mucous membranes and upper respiratory tract.

Ingestion: Swallowing may cause gastrointestinal distress with nausea and diarrhea. Possible aspiration hazard. May enter the lungs during swallowing or vomiting and cause severe lung damage.

Skin contact: No adverse effects are expected. Minor irritation is possible. Therapeutic use has resulted in itching, stinging or burning of treated skin.

Eye contact: Contact may cause slight irritation with redness and tearing.

Chronic Effects: Prolonged systemic use of calcineurin inhibitors for sustained immunosuppression in animal studies and transplant patients following systemic administration has been associated with an increased risk of infections, lymphomas, and skin malignancies. These risks are associated with the intensity and duration of immunosuppression.

Sensitization: Components are not known to be sensitizers. Allergic reactions are possible in sensitive individuals.

Germ Cell Mutagenicity: 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.

Reproductive Toxicity: Reproductive toxicology studies were not performed with topical tacrolimus. In studies of oral tacrolimus no impairment of fertility was seen in male and female rats. Tacrolimus, given orally at 1.0 mg/kg to male and female rats, prior to and during mating, as well as to dams during gestation and lactation, was associated with embryolethality and with 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, 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. Reproduction studies were carried out with systemically administered tacrolimus in rats and rabbits. Adverse effects on the fetus were observed mainly at oral dose levels that were toxic to dams. Tacrolimus at oral doses of 0.32 and 1.0 mg/kg during organogenesis in rabbits was associated with maternal toxicity as well as an increase in incidence of abortions. At the higher dose only, an increased incidence of malformations and developmental variations was also seen. Tacrolimus, at oral doses of 3.2 mg/kg during organogenesis in rats, was associated with maternal toxicity and caused an increase in late resorptions, decreased numbers of live births, and decreased pup weight and viability. Tacrolimus, given orally at 1.0 and 3.2 mg/kg to pregnant rats after organogenesis and during lactation, was associated with reduced pup weights. No reduction in male or female fertility was evident

Carcinogenicity: None of the components are listed as carcinogens by IARC, NTP or OSHA. Oral (feed) carcinogenicity studies have been carried out with systemically administered tacrolimus 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 at daily doses up to 3 mg/kg and 5 mg/kg, respectively. 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/m /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.

12. ECOLOGICAL INFORMATION

Eco toxicity values: No data is available

Persistence and degradability: No data is available

Bio accumulative potential: No data is available

Mobility in soil: No data is available.

Other adverse effects: None known

13. DISPOSAL CONSIDERATIONS

Dispose in accordance with all local, state and federal regulations. No specific disposal method is recommended.

14. TRANSPORT INFORMATION

Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code): Not applicable – product is transported only in packaged form.

Special precautions: None known.

15. REGULATORY INFORMATION

Safety, health, and environmental regulations specific for the product in question.

CERCLA: This product is not subject to CERCLA release reporting. Many states have more stringent release reporting requirements. Report spills as required under federal, state and local regulations.

SARA Hazard Category (311/312): Chronic Health

EPA SARA 313: This product contains the following chemicals regulated under SARA Title III, section 313: None

EPA TSCA Inventory: This product is a drug and not subject to TSCA

CANADA:

Canadian CEPA: This product is a drug and not subject to CEPA regulations

16. OTHER INFORMATION

Distributed By

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End of Safety Data Sheet

Compiled by: Rahul Aumutkar 28.11.2023

Sumit Katariya **Approved by:** 28.11.2023