Safety Data Sheet
Tavaborole topical solution, 5%
Strength: 5 %

Pack Size: 10 mL **NDC** 72578-102-04 **Revision No.:** 00

Emergency Overview

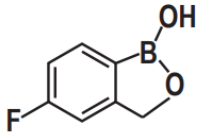
Tavaborole topical solution is an oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.

Section 1 : Identification

Product Name: **Tavaborole topical solution, 5%**

Formula: $C_7H_6BFO_2$

Chemical Name: 5-fluoro-1,3-dihydro-1-hydroxy-2,1-benzoxaborole.



Molecular Weight: 151.93 g/mol

Description: Tavaborole topical solution, 5% contains tavaborole, 5% (w/w) in a clear, colorless alcohol-based solution for topical use. The active ingredient, tavaborole, is an oxaborole antifungal with the chemical name of 5-fluoro-1,3-dihydro-1-hydroxy-2,1-benzoxaborole.

Dosage forms and strengths: Solution, 5%

Manufacturer / supplier identification

Company	Zydus Lifesciences Ltd. Changodar. Ahmedabad. India.
Address	Zydus Lifesciences Ltd. Changodar (Topical Formulation facility) Plot No. 254, Opp. Laxmi Narayan Petrol Pump, N. H 8A, Ahmedabad -382210 India
Contact for information	Tel.:+91 2717-616430 Fax: +91 2717-616430
Emergency Telephone No	Tel.:+91 2717-616401
US Customer Service	1 (877) 993 8779
Recommended use / Therapeutic Category	Tavaborole topical solution is an oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes.
Restriction on Use / Contraindications	None.

Section 2 : Hazard (s) Identification

Dose and Administration

Apply tavaborole topical solution to affected toenails once daily for 48 weeks.
Tavaborole topical solution should be applied to the entire toenail surface and under the tip of each toenail being treated.
Tavaborole topical solution is for topical use only and not for oral, ophthalmic, or intravaginal use.

Adverse effects

Common adverse reactions occurring in ≥1% in subjects treated with tavaborole included application site exfoliation, ingrown toenail, application site erythema, and application site dermatitis.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
In two clinical trials, 791 subjects were treated with tavaborole topical solution. The most commonly reported adverse reactions are listed below;

Adverse Reactions Occurring in ≥1% of Tavaborole Topical Solution, 5%-Treated Subjects and at a Greater Frequency than Observed with Vehicle

Preferred Term	Tavaborole N=791 n(%)	Vehicle N=395 n(%)
Application site exfoliation	21 (2.7%)	1 (0.3%)
Ingrown toenail	20 (2.5%)	1 (0.3%)
Application site erythema	13 (1.6%)	0 (0%)
Application site dermatitis	10 (1.3%)	0 (0%)

Post marketing Experience

The following adverse reactions have been identified during post marketing use of tavaborole topical solution. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug product exposure: Hypersensitivity; contact allergy.

Over Dose Effect

Overexposure may be irritating to the respiratory system.

Pregnancy Comments

Risk Summary

There are no available data on tavaborole topical solution use in pregnant women to inform a drug associated risk for major birth defects, miscarriage or adverse maternal or fetal outcomes. In oral animal reproductive studies, administration of tavaborole during the period of organogenesis resulted in embryofetal toxicity and malformations at 570 times the Maximum Recommended Human Dose (MRHD) based on Area Under the Curve (AUC) comparisons in rats and embryofetal toxicity at 155 times the MRHD based on AUC comparisons in rabbits. Embryofetal toxicity was noted following dermal administration in rabbits up to 36 times the MRHD based on AUC comparisons.
The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies carry some risk of birth defect, loss, or other adverse outcomes.
The background risk of major birth defects in the U.S. general population is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Pharmacokinteics

Tavaborole undergoes extensive metabolism. Renal excretion is the major route of elimination of the metabolites.
In a clinical pharmacology trial of six healthy adult male volunteers who received a single topical application of 5% 14C-tavaborole solution, tavaborole conjugates and metabolites were shown to be excreted primarily in the urine.
The pharmacokinetics (PK) of tavaborole was investigated in 24 adult subjects with distal subungual onychomycosis involving at least 4 toenails (including at least 1 great toenail) following a single dose and a 2-week daily topical application of 200 µL of a 5% solution of tavaborole to all ten toenails and 2 mm of skin surrounding each toenail. Steady state was achieved after 14 days of dosing. After a single dose, the mean (± standard deviation) peak concentration (Cmax) of tavaborole was 3.5 ± 2.3 ng/mL (n=21 with measurable concentrations, range 0.618 ng/mL to 10.2 ng/mL, LLOQ=0.5 ng/mL), and the mean AUClast ± SD was 44.4 ± 25.5 ng*hr/mL (n=21). After 2 weeks of daily dosing, the mean Cmax ± SD was 5.2 ± 3.5 ng/mL (n=24, range 1.5 ng/mL to 12.8 ng/mL), and the mean AUCτ ± SD was 75.8 ± 44.5 ng*hr/mL.
In another study PK of tavaborole was investigated in 22 subjects aged 12 years to less than 17 years with distal subungual onychomycosis involving at least 4 toenails (including at least 1 great toenail with at least 20% involvement) following once daily application of 5% solution of tavaborole to all ten toenails and 2 mm of skin surrounding each toenail for 29 days. On Day 29, the mean ± SD Cmax was 5.9 ± 4.9 ng/mL (n=21 with measurable concentrations, range 1.0 ng/mL to 16.4 ng/mL, LLOQ=0.5 ng/mL), and the mean ± SD AUC0-24 was 76.0 ± 62.5 ng*hr/mL.

Microbiology

Mechanism of Action
The mechanism of action of tavaborole is inhibition of fungal protein synthesis. Tavaborole inhibits protein synthesis by inhibition of an aminoacyl-transfer ribonucleic acid (tRNA) synthetase (AARS).
Activity in vitro and in clinical infections
Tavaborole has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections [see Indications and Usage (1)]:
Trichophyton rubrum
Trichophyton mentagrophytes
Mechanism of Resistance
Trichophyton mentagrophytes and Trichophyton rubrum strains from isolates collected in the clinical trials have not demonstrated resistance following repeated exposure to tavaborole.

Section 3: Composition / information on ingredients

Contains: Active: contains tavaborole, 5% (w/w)

Section 4: First -aid measures

4.1. Description of 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).
If exposed or concerned: Get medical advice/attention.
Inhalation: Remove to fresh air and keep at rest in a position comfortable for breathing.
Call a POISON CENTER/doctor/physician if you feel unwell.
Skin Contact: Remove contaminated clothing. Gently wash with plenty of soap and water followed by rinsing with water for at least 15 minutes. Call a POISON CENTER or doctor/physician if you feel unwell. Wash contaminated clothing before reuse.
Eye Contact: Rinse cautiously with water for at least 60 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention immediately.
Ingestion: Rinse mouth thoroughly with water. Do NOT induce vomiting. Seek medical attention immediately.

4.2. Most Important Symptoms and Effects Both Acute and Delayed

General: Causes serious eye damage.
Inhalation: Overexposure may be irritating to the respiratory system.
Skin Contact: Repeated or prolonged exposure is likely to cause irritation.
Eye Contact: Causes serious eye damage. Symptoms may include: Redness. Pain. Blurred vision. Severe burns.
Ingestion: Ingestion may cause nausea, vomiting and diarrhea.
Chronic Symptoms: None expected under normal conditions of use.

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: Dry chemical, alcohol foam, carbon dioxide.
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.
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.
Hazardous Combustion Products: Carbon monoxide, carbon dioxide, oxides of nitrogen and fluorine-bearing compounds.

Section 6: Accidental Release Measures

6.1. Personal Precautions, Protective Equipment and Emergency Procedures
General Measures: Avoid breathing (vapor, mist, spray). Avoid all contact with skin, eyes, or clothing. Eliminate every possible source of ignition.

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 Personnel
Protective Equipment: Equip cleanup crew with proper protection.
Emergency Procedures: Ventilate area. Stop leak if safe to do so. Eliminate ignition sources.

6.2. Environmental Precautions
Contain any spills with dikes or absorbents to prevent migration and entry into sewers or streams. Do not allow to enter drains or water courses. Contact competent authorities after a spill.

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.
Methods for Cleaning Up: Absorb and/or contain spill with inert material. Collect absorbed material and place into a sealed, labeled container for proper disposal. Do not take up in combustible material such as: saw dust or cellulosic material. Use only non-sparking tools.

6.4. Reference to Other Sections
For further information refer to section 13. See heading 8, Exposure Controls and Personal Protection

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.
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. Contaminated work clothing should not be allowed out of the workplace.

7.2. Conditions for Safe Storage, Including Any Incompatibilities
Technical Measures: Ground/bond container and receiving equipment. Use explosion-proof ventilating, lighting, electrical equipment.
Storage Conditions: Store in a cool, dry, well-ventilated place. Keep containers tightly closed.

Do not store near heat, flame, or other potential ignition sources. Do not store with oxidizers.
Do not store in unlabeled containers. Ground all equipment containing this material.
Incompatible Materials: Strong oxidizers.

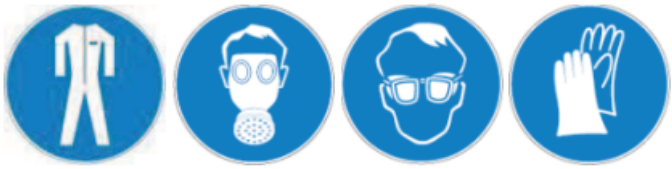
7.3. Specific End Use(s)

Bulk formulated pharmaceutical product/ formulated pharmaceutical product packaged in final form for patient use. Topical solution is an antifungal agent.

Section 8: Exposure controls/personal protection

8.1. Exposure Controls

Appropriate Engineering Controls: Gas detectors should be used when flammable gases/vapors may be released. Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Proper grounding procedures to avoid static electricity should be followed. Use explosion-proof equipment. Ensure adequate ventilation, especially in confined areas. Ensure all national/local regulations are observed.
Personal Protective Equipment: Protective clothing. Insufficient ventilation: wear respiratory protection. Protective goggles. Gloves.



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: Chemical resistant suit.
Respiratory Protection: Use a NIOSH-approved respirator or self-contained breathing apparatus whenever exposure may exceed established Occupational Exposure Limits.
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
Odor : Not available
Odor Threshold : Not available
pH : Not available
Evaporation Rate : Not available
Melting Point : Not available
Freezing Point : Not available
Boiling Point : ~78 °C (~172.40 °F) (100% ethanol)
Flash Point : 12 - 14 °C (53.6 - 57.2 °F) (100% ethanol)
Auto-ignition Temperature : Not available

Decomposition Temperature : Not available
Flammability (solid, gas) : Not Applicable
Lower Flammable Limit : 3.3 % (100% ethanol)
Upper Flammable Limit : 19 % (100% ethanol)
Vapor Pressure : ~ 59 mm Hg @ 20ºC (100% ethanol)
Relative Vapor Density at 20 °C : 1.59 (100% ethanol)
Relative Density : Not available
Specific gravity / density : 0.79 g/cm³ (100% ethanol)
Specific Gravity : Not available
Solubility : Not available
Partition Coefficient: N-Octanol/Water : ~0.32 (100% ethanol)
Viscosity : Not available
Explosion Data – Sensitivity to Mechanical Impact : Not expected to present an explosion hazard due to mechanical impact
Explosion Data – Sensitivity to Static Discharge : Not expected to present an explosion hazard due to static discharge

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. Pharmacological stability not guaranteed beyond expiration date imprinted on package.
10.3. Possibility of Hazardous Reactions: Hazardous polymerization will not occur.
10.4. Conditions to Avoid: Direct sunlight, extremely high or low temperatures, open flames, sources of ignition and incompatible materials.
10.5. Incompatible Materials: Strong oxidizers.
10.6. Hazardous Decomposition Products: Thermal decomposition generates: Fluorine compounds. Oxides of carbon.

Section 11: Toxicological information

11.1. Information on Toxicological Effects – Product

LD50 and LC50 Data: Not available
Skin Corrosion/Irritation: Not classified
Serious Eye Damage/Irritation: Causes serious eye damage.
Respiratory or Skin Sensitization: Not classified
Germ Cell Mutagenicity: Not classified
Teratogenicity: Not classified
Carcinogenicity: Not classified
Specific Target Organ Toxicity (Repeated Exposure): Not classified
Reproductive Toxicity: Not classified
Specific Target Organ Toxicity (Single Exposure): Not classified
Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: Overexposure may be irritating to the respiratory system.
Symptoms/Injuries After Skin Contact: Repeated or prolonged exposure is likely to cause irritation.
Symptoms/Injuries After Eye Contact: Causes serious eye damage. Symptoms may include: Redness. Pain. Blurred vision. Severe burns.
Symptoms/Injuries After Ingestion: Ingestion may cause nausea, vomiting and diarrhea.
Chronic Symptoms: None expected under normal conditions of use.

11.2. Information on Toxicological Effects - Ingredient(s)

LD50 and LC50 Data:
Tavaborole (174671-46-6)
ATE US (oral) 500.00 mg/kg body weight
ATE US (dermal) 1,100.00 mg/kg body weight
ATE US (dust, mist) 1.50 mg/l/4h
1,2-Propylene glycol (57-55-6)
LD50 Oral Rat 20000 mg/kg
LD50 Dermal Rabbit 20800 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
Ethyl alcohol (64-17-5)
OSHA Hazard Communication Carcinogen List In OSHA Hazard Communication Carcinogen list.

Section 12: Ecological information

12.1. Toxicity
1,2-Propylene glycol (57-55-6)
LC50 Fish 1 51600 mg/l (Exposure time: 96 h - Species: Oncorhynchus mykiss [static])
EC50 Daphnia 1 10000 mg/l (Exposure time: 24 h - Species: Daphnia magna)
Acute Toxicity: Not classified
EC50 Daphnia 2 1000 mg/l (Exposure time: 48 h - Species: Daphnia magna [Static])
Ethyl alcohol (64-17-5)
LC50 Fish 1 (Exposure time: 96 h - Species: Oncorhynchus mykiss [static])
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
Not available

12.3. Bioaccumulative Potential
1,2-Propylene glycol (57-55-6)
BCF Fish 1 < 1
Log Pow -0.92
Ethyl alcohol (64-17-5)
Log Pow -0.32
Bioaccumulative Potential Not established.

12.4. Mobility in Soil
Not available
12.5. Other Adverse Effects
Other Information: Avoid release to the environment.

Section 13: Disposal consideration

13.1. Waste treatment methods
Sewage Disposal Recommendations: Do not dispose of waste into sewer. Do not empty into drains; dispose of this material and its container in a safe way.
Waste Disposal Recommendations: Dispose of waste material in accordance with all local, regional, national, provincial, territorial and international regulations.

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
MFAG Number : 130
14.3. In Accordance with IATA
Proper Shipping Name : ETHYL ALCOHOL SOLUTION
Packing Group : II
Identification Number : UN1170
Hazard Class : 3
Label Codes : 3
ERG Code (IATA) : 3L
14.4. In Accordance with TDG
Proper Shipping Name : ETHYL ALCOHOL SOLUTION
Packing Group : II
Hazard Class : 3
Identification Number : UN1170
Label Codes : 3

Section 15: Regulatory information

Generic Medicine. NDC no- 72578-102-04 (10 mL).

Section 16: Other information

None

The information contained herein is based on the state of our knowledge. It characterizes the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.

Date of issue: 13/04/2023 **Supersedes edition:** N/A