HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KERYDIN safely and effectively. See full prescribing information for KERYDIN.

KERYDIN® (tavaborole) topical solution, 5%
Initial U.S. Approval: 2014

INDICATIONS AND USAGE
KERYDIN is an oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes. (1)

Dosage and Administration
• Apply KERYDIN to affected toenails once daily for 48 weeks. (2)
• KERYDIN should be applied to the entire toenail surface and under the tip of each toenail being treated. (2)
• For topical use only. (2)
• Not for oral, ophthalmic, or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS
Solution, 5%. (3)

CONTRAINDICATIONS
None. (4)

ADVERSE REACTIONS
Common adverse reactions occurring in ≥1% in subjects treated with KERYDIN included application site exfoliation, ingrown toenail, application site erythema, and application site dermatitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Anacor Pharmaceuticals at 1-844-ANACOR [1-844-426-2267] or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

FULL PRESCRIBING INFORMATION: CONTENTS*
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Revised: 03/2015
Tavaborole is a white to off-white powder. It is slightly soluble in water and freely soluble in ethanol and propylene glycol.

Each mL of KERYDIN contains 43.5 mg of tavaborole. Inactive ingredients include alcohol, edetate calcium disodium, and propylene glycol.

12 CLINICAL PHARMACOLOGY

12.1 Pharmacokinetics

Tavaborole undergoes extensive metabolism. Renal excretion is the major route of elimination.

In a clinical pharmacology trial of six healthy adult male volunteers who received a single 200 μL topical application of KERYDIN to 1 toenail (following a single dose and a 2-week daily topical application of 200 μL of 5% tavaborole solution to 1 toenail) a mean absolute bioavailability of 10% was calculated based on AUC data (AUCso=105 ng·hr/mL, AUCinf=107 ng·hr/mL, AUC0-∞=108 ng·hr/mL, and the mean AUC0-4h=44.2 ± 29.5 ng·hr/mL). The mean AUC0-24h=28.1 ± 23.4 ng·hr/mL (n=24, range 15.1–28.8–24.8 ng·hr/mL).

12.2 Microbiology

The mechanism of action of tavaborole is inhibition of fungal protein synthesis. Tavaborole is a nonribosomal antibiotic that inhibits an aminoacyl-transfer RNA (farnesyl-AMP) (RNAfA) synthetase.

Activity in vitro and in vivo has been demonstrated.

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 from patients who did not demonstrate resistance following repeated exposure to tavaborole.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A dermal embryofetal development study was conducted in rabbits. Systemic embryofetal development studies were conducted in rats and rabbits and justifies the potential risk to the fetus.

13.2 Acute and Subchronic Toxicity

A dermal carcinogenicity study in CD-1 mice, topical doses of 5%, 10%, and 300 mg/kg/day tavaborole were administered during the period of organogenesis (gestational day 6-19). In the presence of an oral carcinogenic study in F344 rats topical doses of 5% and 10% tavaborole were administered (gestation day 6) through the end of lactation (lactation day 20). In the presence of animal Malaria F344 rat, no toxicologic effects or effects on postnatal development were noted at 100 μg/kg (20 times the MRHD based on AUC comparisons).

Nonteratogenic effects:

In a pre- and post-natal development study in rat, oral doses of 15, 50, and 150 mg/kg/day tavaborole were administered during the period of organogenesis. At term, no effects were observed in dams or litters in any of the treatment groups. No indication of delayed fetal development (defined as an increase in descending implantation at the treatment site was noted at 5% and 10% tavaborole solution. A decrease in fetal body weights was noted at 10% tavaborole solution. No drug related malformations were noted in rabbits at 10% tavaborole solution (20 times the MRHD based on AUC comparisons). No teratogenic effects were noted in rabbits at 5% tavaborole solution (20 times the MRHD based on AUC comparisons).

14 CLINICAL STUDIES

The efficacy and safety of KERYDIN was evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. KERYDIN was not applied once daily for the entire duration of the treatment period but for the first 28 days of the treatment period without dermatomycoses or onychomycosis (main) involvement.

A total of 1194 subjects (795 KERYDIN, 399 Vehicles) 10 to 88 years of age, 82% male, white, and Hispanic were included in these two trials. Efficacy assessments were made at 52 weeks after the first dose of treatment.

The Complete Cure endpoint included negative mycologic (negative KOH wet mount and negative culture) and negative dermatophyte or other fungal infection (both nail and skin lesions) as evidenced by a normal nail plate, no onychomycosis, and no subungual hyperkeratosis. Efficacy results from the two trials are summarized in Table 2.

Table 2: Efficacy Outcomes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Moniliales Cure</th>
<th>Moniliales Curea</th>
<th>Moniliales Cureb</th>
<th>Trichophyton Cure</th>
<th>Trichophyton Curea</th>
<th>Trichophyton Cureb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>N=791</td>
<td>n(%=17)</td>
<td>n(%=10)</td>
<td>n(%=14)</td>
<td>n(%=18)</td>
<td>n(%=17)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>N=396</td>
<td>n(%=18)</td>
<td>n(%=12)</td>
<td>n(%=14)</td>
<td>n(%=19)</td>
<td>n(%=13)</td>
</tr>
</tbody>
</table>

Clinical studies in vocal and subclinical infections [see Indications and Usage (1)] prior to and during early pregnancy.

6 ADVERSE REACTIONS

6.1 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 the rates in clinical trials of another drug and may not reflect the rates observed in practice.

In two clinical trials, 791 subjects were treated with KERYDIN. The commonly reported adverse reactions are listed below (Table 1).

Table 1: Adverse Reactions Occurring in ≥1% of KERYDIN Topical Solution, Reportable Adverse Reactions

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Treatment</th>
<th>n(%=1%)</th>
<th>n(%=1%)</th>
<th>n(%=1%)</th>
<th>n(%=1%)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Trial 1</td>
<td>n(%=1%)</td>
<td>n(%=1%)</td>
<td>n(%=1%)</td>
<td>n(%=1%)</td>
<td>n(%=1%)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>n(%=1%)</td>
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</table>

6.2 Post-Marketing Surveillance

In safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of older individuals cannot be ruled out.

7 CLINICAL PHARMACOLOGY

7.1 Absorption

Each mL of KERYDIN contains 43.5 mg of tavaborole. Inactive ingredients include alcohol, edetate calcium disodium, and propylene glycol.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies with KERYDIN in pregnant women. Use of this drug during pregnancy should be avoided if possible. Potential benefits of potential benefits to the fetus justifies the potential risk to the fetus.

8.2 Lactation

A dermal embryofetal development study was conducted in rabbits. In the presence of an oral embryofetal development study was conducted in rabbits. Systemic embryofetal development studies were conducted in rats and rabbits and justifies the potential risk to the fetus.

8.3 Nursing Mothers

It is not known whether tavaborole is excreted in human milk following topical application of KERYDIN. Because many drugs are excreted in human milk, caution should be exercised when KERYDIN is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

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 the rates in clinical trials of another drug and may not reflect the rates observed in practice.

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9 ADVERSE REACTIONS

9.1 General Information

Common side effects include: skin peeling, ingrown toenail, painful toenail, and difficulty cleaning toenail.
General information about the safe and effective use of KERYDIN

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about KERYDIN that is written for health professionals. Do not use KERYDIN for a condition for which it was not prescribed. Do not give KERYDIN to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in KERYDIN?

Active ingredient: tavaborole
Inactive ingredients: alcohol, propylene glycol, and edetate calcium disodium

Instructions for Use

KERYDIN® (ker’ i din)
(tavaborole) Topical Solution, 5%

Important information: KERYDIN is for use on toenails only. Do not use KERYDIN in your mouth, eyes, or vagina.

Read the Instructions for Use that comes with KERYDIN before you start using it. Talk to your healthcare provider if you have any questions.

How to apply KERYDIN:

Your toenails should be clean and dry before you apply KERYDIN.

Step 1: Before you apply KERYDIN to your affected toenail for the first time, remove the cap from the KERYDIN bottle. (See Figure A) Throw away the cap.

Step 2: Remove the wrapping from the dropper that comes with KERYDIN. Insert the dropper into the KERYDIN bottle. (See Figure B)

Step 3: With the dropper inserted into the KERYDIN, squeeze the bulb and then release the bulb to draw KERYDIN into the dropper.

Step 4: Remove the dropper from the bottle and hold the dropper tip over your affected toenail.

Step 5: Slowly squeeze the bulb to apply KERYDIN to your toenail. Apply enough solution to completely cover your toenail. You may need to use more than one drop. (See Figure C)

Step 6: Use the dropper tip to gently spread KERYDIN to cover the entire toenail up to the edges of the toenail. (See Figure D)

Step 7: In addition to the top of the toenail, also apply KERYDIN under the tip of the toenail. Use the dropper tip to gently spread KERYDIN under the entire tip of the toenail. (See Figures E and F)

Step 8: Repeat Steps 3 to 7 to apply KERYDIN to each affected toenail.

Step 9: Let the KERYDIN dry completely. This may take a couple of minutes.

If KERYDIN comes in contact with surrounding skin, use a tissue to wipe any excess solution from the surrounding skin. Do not wipe KERYDIN off of your toenails.

Step 10: After applying KERYDIN to your toenails, insert the dropper back into the bottle and screw it on tightly.

Step 11: Wash your hands with soap and water after applying KERYDIN.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

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