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 1-844-4ANACOR [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.

Revised: 02/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
16.2 Storage and Handling
17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

KERYDIN (tavaborole) topical solution, 5% is an oxaborole antifungal indicated for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*.

2 DOSAGE AND ADMINISTRATION

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

3 DOSAGE FORMS AND STRENGTHS

KERYDIN topical solution, 5% is a clear, colorless alcohol-based solution. Each milliliter of solution contains 43.5 mg (5% w/w) of tavaborole.

4 CONTRAINDICATIONS

None.

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 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 KERYDIN. The most commonly reported adverse reactions are listed below (Table 1).

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

Preferred Term	KERYDIN 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%)

A cumulative irritancy study revealed the potential for KERYDIN to cause skin irritation. There was no evidence that KERYDIN causes contact sensitization.

7 DRUG INTERACTIONS

In vitro studies have shown that tavaborole, at therapeutic concentrations, neither inhibits nor induces cytochrome P450 (CYP450) enzymes.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies with KERYDIN in pregnant women. KERYDIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Systemic embryofetal development studies were conducted in rats and rabbits and a dermal embryofetal development study was conducted in rabbits.

Oral administration:
In an oral embryofetal development study in rats, oral doses of 30, 100, and 300 mg/kg/day tavaborole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rats. In the presence of maternal toxicity, embryofetal toxicity (increased embryofetal resorption and/or deaths) and drug-related skeletal malformations and variations suggestive of delayed development (i.e., a delay in ossification) were noted in fetuses at 300 mg/kg/day tavaborole [570 times the Maximum Recommended Human Dose (MRHD) based on Area Under the Curve (AUC) comparisons]. No developmental toxicity was noted in rats at 100 mg/kg/day tavaborole (26 times the MRHD based on AUC comparisons).

In an oral embryofetal development study in rabbits, oral doses of 15, 50, and 150 mg/kg/day tavaborole were administered during the period of organogenesis (gestational days 7-19) to pregnant female rabbits. In the presence of maternal toxicity, excessive embryofetal mortality due to post-implantation loss was noted at 150 mg/kg/day tavaborole. No drug related malformations were noted in rabbits at 150 mg/kg/day tavaborole (155 times the MRHD based on AUC comparisons). No embryofetal mortality was noted in rabbits at 50 mg/kg/day tavaborole (16 times the MRHD based on AUC comparisons).

Topical administration:
In a dermal embryofetal development study in rabbits, topical doses of 1%, 5%, and 10% tavaborole solution were administered during the period of organogenesis (gestational days 6-28) to pregnant female rabbits. A dose dependent increase in dermal irritation at the treatment site was noted at 5% and 10% tavaborole solution. A decrease in fetal bodyweight was noted at 10% tavaborole solution. No drug related malformations were noted in rabbits at 10% tavaborole solution (36 times the MRHD based on AUC comparisons). No embryofetal toxicity was noted in rabbits at 5% tavaborole solution (26 times the MRHD based on AUC comparisons).

Nonteratogenic effects:
In an oral pre- and post-natal development study in rats, oral doses of 15, 60, and 100 mg/kg/day tavaborole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of minimal maternal toxicity, no embryofetal toxicity or effects on postnatal development were noted at 100 mg/kg/day (29 times the MRHD based on AUC comparisons).

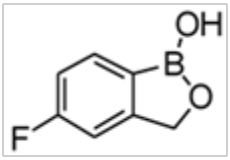
8.3 Nursing Mothers
It is not known whether tavaborole is excreted in human milk following topical application of KERYDIN. Because many drugs are excreted in human milk, caution should be exercised when KERYDIN is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
In clinical trials of 791 subjects who were exposed to KERYDIN, 19% were 65 years of age and over, while 4% were 75 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

KERYDIN (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. The chemical formula is $C_7H_6BFO_2$, the molecular weight is 151.93 and the structural formula is:



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 Mechanism of Action

KERYDIN is an oxaborole antifungal [see *Clinical Pharmacology (12.4)*].

12.2 Pharmacodynamics

At therapeutic doses, KERYDIN is not expected to prolong QTc to any clinically relevant extent.

12.3 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 topical application of 5% ^{14}C-tavaborole solution, tavaborole conjugates and metabolites were shown to be excreted primarily in the urine.

The pharmacokinetics of tavaborole was investigated in 24 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 (C_{max}) of tavaborole was 3.54 ± 2.26 ng/mL (n=21 with measurable concentrations, range 0.618-10.2 ng/mL, LLOQ=0.5 ng/mL), and the mean AUC_{last} was 44.4 ± 25.5 ng*hr/mL (n=21). After 2 weeks of daily dosing, the mean C_{max} was 5.17 ± 3.47 ng/mL (n=24, range 1.51-12.8 ng/mL), and the mean AUC_{τ} was 75.8 ± 44.5 ng*hr/mL.

12.4 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.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In an oral carcinogenicity study in Sprague-Dawley rats, oral doses of 12.5, 25, and 50 mg/kg/day tavaborole were administered to rats once daily for 104 weeks. No drug related neoplastic findings were noted at oral doses up to 50 mg/kg/day tavaborole (14 times the MRHD based on AUC comparisons).

In a dermal carcinogenicity study in CD-1 mice, topical doses of 5%, 10%, and 15% tavaborole solution were administered to mice once daily for 104 weeks. No drug related neoplastic findings were noted at topical doses up to 15% tavaborole solution (89 times the MRHD based on AUC comparisons).

Tavaborole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Human lymphocyte chromosomal aberration assay) and one in vivo genotoxicity test (rat micronucleus assay).

No effects on fertility were observed in male and female rats that were administered oral doses up to 300 mg/kg/day tavaborole (107 times the MRHD based on AUC comparisons) prior to and during early pregnancy.

14 CLINICAL STUDIES

The efficacy and safety of KERYDIN was evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. KERYDIN or vehicle was applied once daily for 48 weeks in subjects with 20% to 60% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement.

A total of 1194 subjects (795 KERYDIN, 399 Vehicle) 18 to 88 years of age, 82% male, 84% white, participated in these two trials. Efficacy assessments were made at 52 weeks following a 48-week treatment period.

The Complete Cure efficacy endpoint included negative mycology (negative KOH wet mount and negative fungal culture) and Completely Clear Nail (no clinical evidence of onychomycosis as evidenced by a normal toenail plate, no onycholysis, and no subungual hyperkeratosis). Efficacy results from the two trials are summarized in Table 2.

Table 2: Efficacy Outcomes

	Trial 1		Trial 2	
Efficacy Variable	**KERYDIN N=399 n(%)**	**Vehicle N=194 n(%)**	**KERYDIN N=396 n(%)**	**Vehicle N=205 n(%)**
Complete Cure[a]	26 (6.5%)	1 (0.5%)	36 (9.1%)	3 (1.5%)
Complete or Almost Complete Cure[b]	61 (15.3%)	3 (1.5%)	71 (17.9%)	8 (3.9%)
Mycologic Cure[c]	124 (31.1%)	14 (7.2%)	142 (35.9%)	25 (12.2%)

a. Complete cure defined as 0% clinical involvement of the target toenail plus negative KOH and negative culture.

b. Complete or almost complete cure defined as ≤10% affected target toenail area involved and negative KOH and culture.

c. Mycologic cure defined as negative KOH and negative culture.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

KERYDIN (tavaborole) topical solution, 5% is a clear, colorless solution supplied in an amber glass bottle with a screw cap. At initial use, the screw cap is replaced with the dropper assembly.

KERYDIN (tavaborole) topical solution, 5% is supplied in the following presentations:

NDC 55724-111-11: One 12 mL bottle containing 10 mL of solution with one glass pointed-tip dropper
NDC 55724-111-21: One 10 mL bottle containing 4 mL of solution with one glass pointed-tip dropper

16.2 Storage and Handling

Store at 20–25°C (68–77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature].
CAUTION: Flammable. Keep away from heat and flame.
Discard product within 3 months after insertion of the dropper.
Keep bottle tightly closed. Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use)

The patient should be told the following:

- Use KERYDIN as directed by a health care professional.
- KERYDIN is for external use only. Avoid contact with eyes, mouth, or vagina. Avoid contact with skin other than skin immediately surrounding the treated nail(s). Wipe away excess solution from surrounding skin.
- Clean and dry nails prior to KERYDIN use. KERYDIN should be applied to completely cover the nail surface and also applied under the tip of each nail being treated. Allow solution to dry following application.
- The impact of nail polish or other cosmetic nail products on the efficacy of KERYDIN has not been evaluated.
- Inform a health care professional if the area of application shows signs of persistent irritation (for example, redness, itching, swelling).
- Forty-eight (48) weeks of daily application with tavaborole is considered the full treatment for toenail onychomycosis.
- Do not use KERYDIN for any disorder other than that for which it is prescribed.
- Product is flammable. Avoid use near heat or open flame.

Manufactured for:
Anacor Pharmaceuticals, Inc.
1020 East Meadow Circle
Palo Alto, CA 94303

Issued: 02/2015

U.S. Patent Nos. 7,767,657 and 7,582,621

PATIENT INFORMATION
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.

What is KERYDIN?

KERYDIN is a prescription medicine used to treat fungal infections of the toenails.
It is not known if KERYDIN is safe and effective in children.

What should I tell my healthcare provider before using KERYDIN?

Before using KERYDIN, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if KERYDIN can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if KERYDIN passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use KERYDIN?

See the "Instructions for Use" at the end of this Patient Information for detailed information about the right way to use KERYDIN.

- Use KERYDIN exactly as your healthcare provider tells you to use it.
- Apply KERYDIN to your affected toenails 1 time each day.
- KERYDIN is used for 48 weeks.
- It is not known if the use of nail polish or other cosmetic nail products (such as gel nails or acrylic nails) will affect how KERYDIN works.

What should I avoid while using KERYDIN?

- Avoid getting KERYDIN on skin that is not surrounding the treated toenail.
- KERYDIN is flammable. Avoid heat and flame while applying KERYDIN to your toenail.

What are the possible side effects of KERYDIN?

KERYDIN may cause irritation at the treated site. The most common side effects include: skin peeling, ingrown toenail, redness, itching, and swelling. Tell your healthcare provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects of KERYDIN.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store KERYDIN?

- Store KERYDIN at room temperature, between 68°F to 77°F (20°C to 25°C).
- KERYDIN is flammable. Keep away from heat and flame.
- Keep the bottle tightly closed.
- Safely throw away KERYDIN after 3 months of inserting the dropper.

Keep KERYDIN and all medicines out of the reach of children.

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

Manufactured for: Anacor Pharmaceuticals, Inc., 1020 East Meadow Circle, Palo Alto, CA, 94303
For more information, call 1-844-4ANACOR [1-844-426-2267] or go to www.kerydin.com.

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: 02/2015

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)**

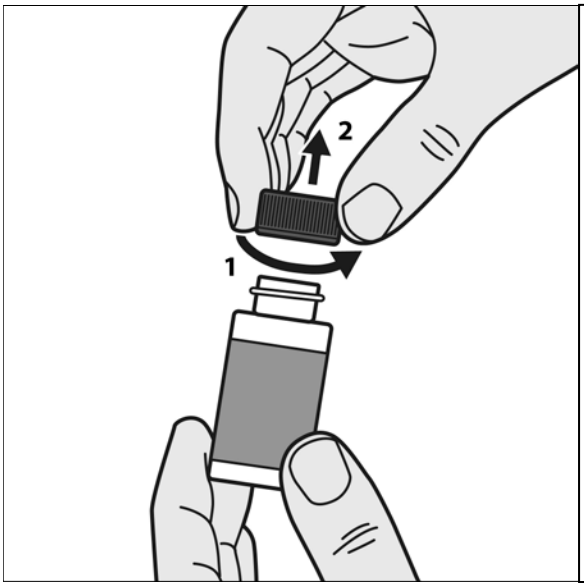


Figure A

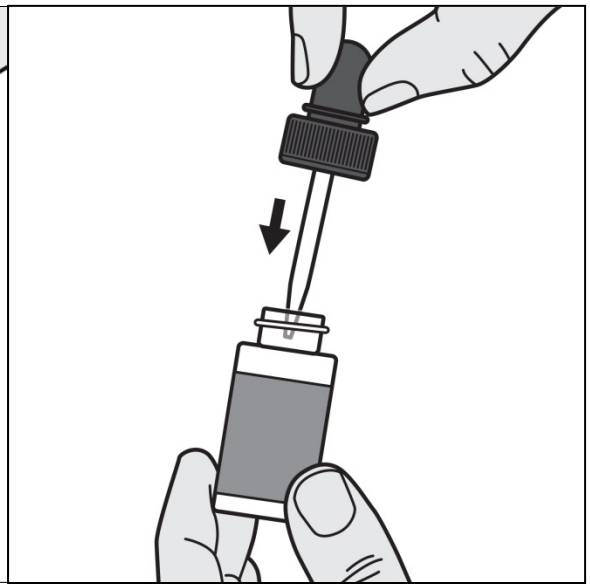


Figure B

Only apply KERYDIN using the provided dropper. Do not use the dropper for any other purpose.

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)**

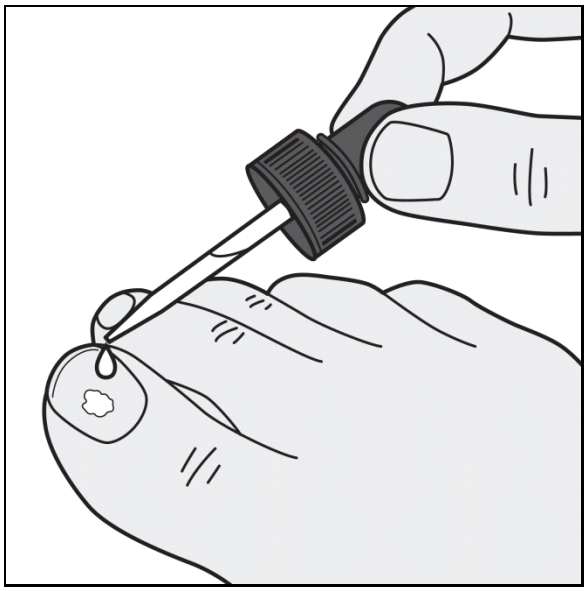


Figure C

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)**

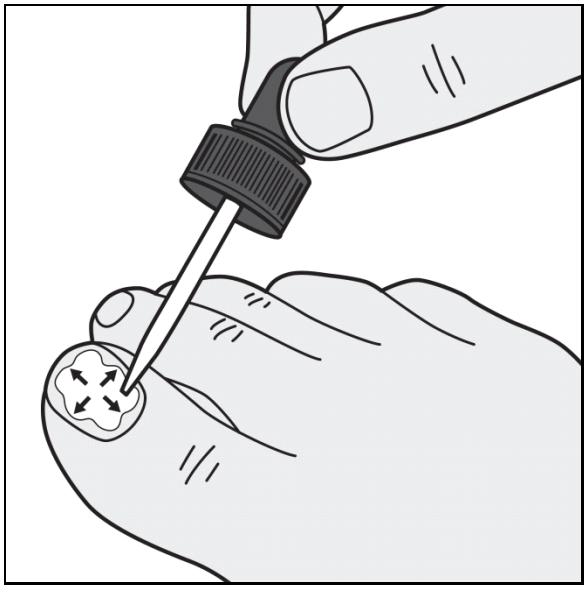


Figure D

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)**

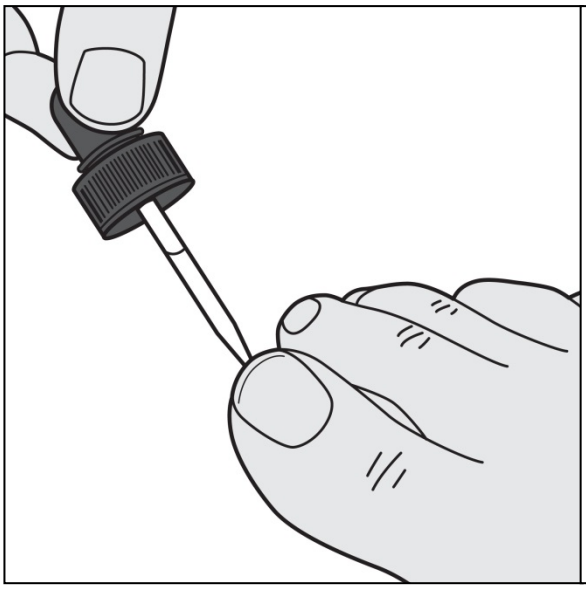


Figure E

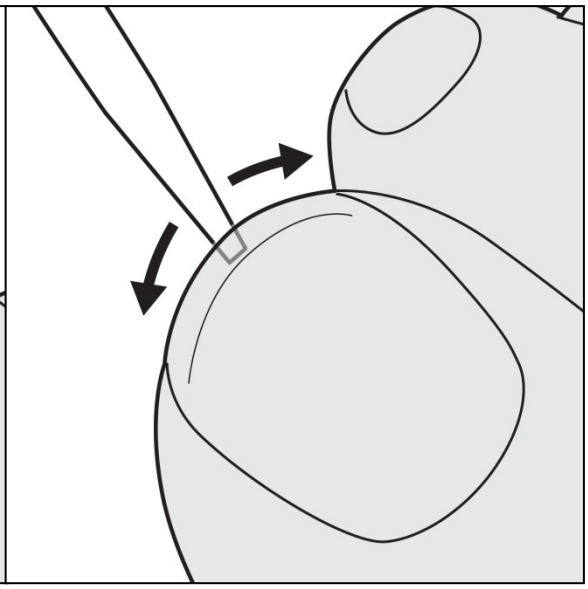


Figure F

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.

Manufactured for: Anacor Pharmaceuticals, Inc., 1020 East Meadow Circle, Palo Alto, CA, 94303

Issued: 02/2015