BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

JUBLIA® (efinaconazole) topical solution 10%
KERYDIN™ (tavaborole) topical solution 5%
Tavaborole topical solution 5%
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Julia (efinaconazole), Kerydin (tavaborole), generic tavaborole, and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 6 years of age or older

  2. Individual has a confirmed diagnosis of onychomycosis of toenail(s) due to **EITHER** *Trichophyton rubrum* or *Trichophyton mentagrophytes* as the causative organism

3. There is at least 20% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement

4. Individual's diagnosis is confirmed by using **BOTH** of the following:
   a. Positive potassium hydroxide (KOH) on microscopy
   b. Positive fungal culture

5. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following:
   a. Terbinafine
   b. Itraconazole
   c. Topical ciclopirox nail lacquer 8% solution

6. **Additional criteria for Kerydin (brand)**: Failure, contraindication per FDA label, intolerance, or is not a candidate for **generic tavaborole** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. **Additional criteria for Jublia (brand)**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Jublia (efinaconazole), Kerydin (tavaborole), generic tavaborole, and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual experienced a recurrent episode (a relapse or reinfection) of symptomatic confirmed diagnosis of onychomycosis of toenail(s) due to **EITHER** *Trichophyton rubrum* or *Trichophyton mentagrophytes* as the causative organism

2. Individual has been adherent with the medication

3. There is at least 20% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement

4. Individual's diagnosis is confirmed by using **BOTH** of the following:
   a. Positive potassium hydroxide (KOH) on microscopy
   b. Positive fungal culture

5. For continuation of **brand Kerydin**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **generic tavaborole** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. **Additional criteria for Jublia (brand)**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Jublia (efinaconazole) topical solution is an azole (triazole class) antifungal agent indicated for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*. Kerydin (tavaborole) topical solution is an oxaborole antifungal agent indicated for the treatment of onychomycosis of the toenails due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

Jublia (efinaconazole) inhibits fungal lanosterol 14-alpha demethylase that is involved in the biosynthesis of ergosterol, an integral component of fungal cell membrane. Safety and effectiveness in pediatric individuals has not been established.

Kerydin (tavaborole) inhibits fungal protein synthesis by inhibiting aminoacyl-transfer ribonucleic acid (tRNA) synthestase (AARS). Safety and effectiveness in pediatric individuals have not been established.

Coverage is dependent on individual member plan benefit.

Onychomycosis is a common dermatological condition. It is an infection of the nail apparatus caused by fungi that include dermatophytes, non-dermatophyte molds and yeasts (mostly Candida species). The toenails are affected in 80% of cases. Dermatophyte infection due to *Trichophyton rubrum* and/or *Trichophyton mentagrophytes* are the cause in over 90% of cases.

Onychomycosis is characterized by thickening of the distal end of the nail associated with some loosening or separation of the nail plate from the nail bed (onycholysis), and buildup of debris in the space created by the onycholysis (subungual hyperkeratosis). The nail plate turns yellow and vertical bands appear at the distal end of the nails. These foot infections are not life-threatening, but it may cause discomfort and pain.

Onychomycosis may be classified clinically as: distal and lateral subungual onychomycosis (DLSO) which accounts for the majority of cases and is almost always due to dermatophyte infection; superficial white onychomycosis (SWO) and is nearly always due to a dermatophyte infection, most commonly *Tricophyton mentagrophytes;* proximal subungual onychomycosis (PSO); candidal onychomycosis; and total dystrophic

onychomycosis. Any of these may eventually progress to total nail dystrophy where the nail plate is almost completely destroyed.

Only about 50% of nail dystrophy cases are caused by fungi making it important to establish the cause to rule out other conditions with similar presentations such as psoriasis and nail trauma. Despite this most onychomycosis is treated based on clinical presentation alone. Treatment should be initiated only with mycological confirmation of infection. Laboratory diagnosis consists of direct microscopy to visualize fungal elements in the nail sample and culture to identify the species.

The relative efficacy of different antifungal agents against different fungi is not completely understood and is poorly described due to use of different doses and dose scheduling, differing endpoints in the clinical studies, length of treatment, and lack of active comparisons. A common surrogate measure of efficacy is mycologic cure rate defined as having negative potassium hydroxide (KOH) on microscopy and negative fungal culture. Another measure used to assess efficacy is complete cure which is defined as no clinical involvement of the target nail or a mycologic cure defined as negative KOH and negative culture. Mycologic cure rates are numerically better than clinical cure rates and as a result may overemphasize efficacy of treatment. The goal of treatment is to eradicate the causative organism as demonstrated by microscopy and culture. All treatments for onychomycosis have relatively high failure rates. Recurrence rates range from approximately 20-50%

Topical and oral agents are available for the treatment of fungal nail infections. Treatment duration with these agents is usually months. There are no clinical trials that compare oral antifungal agents to topical agents. However, oral agents appear to achieve higher mycological cures than those seen with topical agents. A meta-analysis of onychomycosis treatments found the risk of severe liver injury or asymptomatic elevations of serum transaminases with all agents to be less than 2%. Topical antifungal preparations are available both as prescription only medicines and over-the-counter products. Topical therapy may be useful for the treatment of SWO and in very early cases of DLSO where the infection may be confined to the distal edge of the nail. Systemic therapy is more successful than topical treatment.

Oral terbinafine is the most effective agent and is considered first line treatment. When used continuously the mycologic cure rate is 76%. When used intermittently the mycologic cure rate is 59%. Oral Itraconazole is recommended when terbinafine cannot be used due to failure or intolerance. It has a mycologic cure rate of 63% with pulse dosing and 59% with continuous dosing. Oral Fluconazole is used for Candida species.

Topical Jublia (efinaconazole) has an absolute mycologic cure rate of 36.5-38.4% (Jublia package insert). Topical Kerydin (tavaborole) has an absolute mycologic cure rate of 23.7-23.9 (Kerydin package insert). Topical Ciclopirox nail lacquer has an absolute mycologic cure rate of 18-27% (package insert Penlac).

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Dermatophytoma:
A unique characteristic of onychomycosis:

It presents as a longitudinal yellow band; a round circumscribe yellow or a white patch in the nail plate

Lunula:
The crescent moon shape white area at the base of a fingernail or toenail where the cuticle and nail meet

Resources:

Jublia (efinaconazole) product information, revised by Bausch Health US LLC. 03-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Kerydin (tavaborole) product information, revised by PharmaDerm, A division of Fougera Pharmaceuticals Inc. 08-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 15, 2023. **Discontinued 2024-02-07.**

Tavaborole product information, revised by Alembic Pharmaceuticals Inc. 12-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Goldenstein AO, Bhatia N. Onychomycosis: Epidemiology, clinical features, and diagnosis. In: UpToDate, Dellavalle RP, Levy ML, Rosen T, Ofori AO (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated January 20, 2023. Accessed September 24, 2024.

Goldenstein AO, Bhatia N. Onychomycosis: Management. In: UpToDate, Dellavalle RP, Levy ML, Rosen T, Ofori AO (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated September 08, 2022. Accessed September 24, 2024.