Medication Policy Manual

Policy No: dru384

Topic: Branded topical antifungal nail solutions:
   - Jublia®, efinaconazole 10%
   - Kerydin®, tavaborole 5%

Date of Origin: January 19, 2015

Committee Approval Date: January 13, 2017

Next Review Date: January 2018

Effective Date: February 1, 2017

IMPORTANT REMINDER
This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Jublia and Kerydin are self-administered topical antifungal solutions indicated for the treatment of fungal infection of the toenails (i.e. onychomycosis) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*. 
Policy/Criteria

I. Most contracts require prior authorization approval of efinaconazole (Jublia) and tavaborole (Kerydin) prior to coverage. Efinaconazole and tavaborole may be considered medically necessary in patients with onychomycosis when criteria A and B are met

A. Treatment with terbinafine or itraconazole has been inadequate in achieving complete mycological cure after 12 weeks of continuous therapy, unless both are contraindicated or not tolerated.

AND

B. Onychomycosis is associated with one or more of the following conditions and supported by clinical documentation:

1. Diabetes
2. Immunocompromised host (e.g., HIV)
3. Peripheral neuropathy
4. Peripheral circulatory disorders
5. History of significant cellulitis (requiring systemic antibiotic therapy)
6. Recurring ingrown toenails (secondary to onychomycosis) requiring surgical repair or removal
7. Functional impairment from onychomycosis, such as bleeding or pain, which affects performing normal daily activities

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers efinaconazole and tavaborole to be self-administered medications.

B. When prior authorization is approved, efinaconazole and tavaborole may be authorized for a duration of up to 48 weeks.

III. Efinaconazole and tavaborole are considered not medically necessary when used for a treatment duration beyond 48 weeks.

Position Statement

- There is insufficient evidence to support the use of one antifungal over another in the treatment of toenail onychomycosis due to the lack of direct comparative evidence; however, systemic therapy is typically preferred over topical therapies according to clinical guidelines. [1]

- Generic oral antifungals (i.e. terbinafine and itraconazole) offer the best value in the treatment of onychomycosis of the toenails and are dosed for 12 consecutive weeks for this indication. [2]

- Topical antifungals may be clinically appropriate in patients who are at increased risk for hepatotoxicity or drug-drug interactions associated with systemic antifungal therapy.
Although onychomycosis is generally a cosmetic concern for patients, treatment may be of potential clinical benefit in patients with an increased risk of complications or relapse (e.g. diabetics, peripheral vascular disease, immunocompromised), or in patients with significant pain leading to functional impairment (e.g. difficulty walking or standing). [1,3]

Treatment duration in clinical studies evaluating the safety and efficacy of efinaconazole and tavaborole was 48 weeks [4,5]

Background

- Onychomycosis of the toenail is a relatively common and relapsing condition in the adult population.[6]
- Toenail onychomycosis is most commonly caused by dermatophytes, including Trichophyton rubrum and Trichophyton mentagrophytes. [7]
- Current FDA approved treatment options for toenail onychomycosis include systemic antifungals (terbinafine, itraconazole, and griseofulvin) and topical antifungal nail lacquers (ciclopirox, efinaconazole, and tavaborole). Although fluconazole has been used in clinical practice for toenail onychomycosis, it is not FDA approved for this indication.
- Oral treatments are more commonly prescribed for onychomycosis and appear to have the benefit of shorter treatment times and better cure rates than topical preparations. [3,8]

Clinical Efficacy

- Although efinaconazole and tavaborole have been shown to be effective in achieving a modest chance of complete cure in patients with onychomycosis relative to placebo, there is insufficient evidence to conclude that either medication is more effective or safer than less costly generic oral alternatives such as terbinafine and itraconazole.[5,9-11]
  * Efinaconazole was evaluated in two randomized, placebo-controlled trials in patients with onychomycosis. Placebo-adjusted rates for complete cure were 9.7% in one study, and 14.5% in another after 48 weeks of treatment. One of the studies was considered low-confidence due to moderate overall attrition and high differential attrition, potentially leading to erosion of randomization.
  * Tavaborole was evaluated in two fair-confidence, randomized, placebo controlled trials in patients with onychomycosis. Placebo-adjusted complete cure ranged from 6% to 7.6% after 48 weeks of treatment.
  * Complete cure was defined as complete resolution of signs and symptoms, as well as mycological cure (negative potassium hydroxide examination and negative fungal culture). Assessment of signs and symptoms of infection may be subjective and potentially bias trial results.

- There is no evidence that assesses long-term treatment outcomes with any of the antifungals for toenail onychomycosis in relation to improvement in functional impairment, such as pain or ability to walk or stand.

- Treatment guidelines, which were written before the availability of tavaborole, efinaconazole and other newer topical antifungals for use in the treatment of onychomycosis, largely favor systemic therapy for most nail infections. [12]
- Griseofulvin is no longer considered a drug of choice due to its low cure rates, high relapse rates, and relatively long duration of therapy (up to 1 year may be necessary).[13]
- Ciclopirox nail lacquer is generally not recommended due to the low likelihood of treatment success. Based on the combined results of two randomized controlled trials, 15 patients would need to be treated for 48 weeks for one patient to achieve mycological cure.[14,15]

**Safety**
- Adverse reactions associated with topical antifungal nail lacquers are generally mild, and are limited to superficial reactions such as redness, irritation, and application site exfoliation.
- All systemic antifungals, including terbinafine, itraconazole, and fluconazole inhibit hepatic enzymes (CYP2D6 and CYP3A4 respectively) and may potentially interact with other medications metabolized by these enzymes.
- All systemic antifungals may cause hepatotoxicity and liver enzyme (aminotransferase) elevations. Rates of discontinuation due to liver enzyme elevations are low for all the systemic antifungals. Discontinuation rates range from 0.11% to 1.22% for continuous therapy, and 0.24% to 0.85% for intermittent therapy. Discontinuation rates were higher for fluconazole than terbinafine and itraconazole when taken continuously or intermittently. [16]

### Cross References

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<thead>
<tr>
<th>Codes</th>
<th>Number</th>
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<tr>
<td>ICD-10</td>
<td>B35.1</td>
<td>A fungal infection of the nail, usually caused by dermatophytes; yeasts; or nondermatophyte molds.</td>
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References


Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
<tr>
<td>01/13/2017</td>
<td>No criteria changes with this annual update</td>
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<tr>
<td>01/08/2016</td>
<td>Addition of ICD-10 code</td>
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