## FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Indication(s)</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Jublia</strong></td>
<td>Onychomycosis of the toenails due to Trichophyton rubrum and Trichophyton mentagrophytes</td>
<td>Apply to affected toenail once daily for 48 weeks</td>
</tr>
<tr>
<td>(efinaconazole)</td>
<td>Topical solution</td>
<td></td>
</tr>
<tr>
<td><strong>Kerydin™</strong></td>
<td>Onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes</td>
<td>Apply to affected toenail once daily for 48 weeks</td>
</tr>
<tr>
<td>(tavaborole)</td>
<td>Topical solution</td>
<td></td>
</tr>
<tr>
<td><strong>Lamisil</strong></td>
<td>Onychomycosis of the toenail or fingernail</td>
<td><strong>Onychomycosis</strong> - 250 mg daily</td>
</tr>
<tr>
<td>(terbinafine)</td>
<td>Fingernail – treat 6 weeks</td>
<td><strong>Toenail</strong> - treat 12 weeks</td>
</tr>
<tr>
<td>Tablets,</td>
<td>Tinea capitis</td>
<td><strong>Tinea capitis</strong> - 125 mg -250 mg daily for 6 weeks (see table)</td>
</tr>
<tr>
<td>Oral granules</td>
<td></td>
<td><strong>Dosage by body weight:</strong></td>
</tr>
<tr>
<td><strong>Onmel</strong></td>
<td>Onychomycosis of the toenail due to Trichophyton rubrum or T. mentagrophytes in non-immunocompromised patients</td>
<td><strong>Onychomycosis toenail</strong> -200 mg once daily for 12 weeks</td>
</tr>
<tr>
<td>(itraconazole)</td>
<td>Topical solution</td>
<td></td>
</tr>
<tr>
<td><strong>Penlac</strong></td>
<td>Onychomycosis of the toenail or fingernail (topical treatment in immunocompetent patients with mild to moderate onychomycosis without lunula involvement, due to Trichophyton rubrum)</td>
<td>Apply daily to affected area</td>
</tr>
<tr>
<td>(ciclopirox)</td>
<td>Topical solution</td>
<td></td>
</tr>
<tr>
<td><strong>Sporanox</strong></td>
<td>Blastomycosis, histoplasmosis, aspergillosis, onychomycosis of the toenail or fingernail</td>
<td><strong>Blastomycosis</strong> -200 mg daily (up to 400 mg daily if 200 mg not effective)</td>
</tr>
<tr>
<td>(itraconazole)</td>
<td>Capsules, Oral solution</td>
<td><strong>Histoplasmosis</strong> -200 mg daily (up to 400 mg daily if 200 mg not effective)</td>
</tr>
<tr>
<td><strong>Terbinex Kit</strong></td>
<td>Onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium)</td>
<td><strong>Aspergillosis</strong> -200-400 mg daily</td>
</tr>
<tr>
<td>(terbinafine)</td>
<td>Tablets</td>
<td><strong>Onychomycosis toenail</strong> -200 mg daily for 12 weeks</td>
</tr>
<tr>
<td><strong>Sporanox</strong></td>
<td></td>
<td><strong>Onychomycosis fingernail</strong> -200 mg twice daily for 1 week, then 3 weeks off, then 200 mg twice daily for 1 more week</td>
</tr>
<tr>
<td>(itraconazole)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Tinea capitis** - 125 mg -250 mg daily for 6 weeks (see table)
CLINICAL RATIONALE

Esophageal candidiasis and candidemia\textsuperscript{4}
Infectious Diseases Society of America (IDSA) guidelines recommend oral fluconazole as the first line therapy for candidemia in non neutropenic patients and for esophageal candidiasis. Fluconazole is also recommended for prophylaxis against esophageal candidiasis in at risk patients. For patients with fluconazole-refractory disease, guidelines recommend itraconazole or voriconazole. Up to 80% of patients with fluconazole refractory esophageal candidiasis will respond to itraconazole.

Blastomycosis and histoplasmosis\textsuperscript{5,6}
Itraconazole is the recommended therapy for the treatment of chronic cavity pulmonary histoplasmosis. Other forms of histoplasmosis are generally treated with amphotericin B. IDSA guidelines recommend itraconazole as the first line oral agent for the treatment of mild to moderate blastomycosis. Itraconazole is also recommended in patients as a step down from amphotericin B for more severe cases of blastomycosis. Fluconazole and voriconazole are considered alternatives for the treatment of blastomycosis.

Onychomycosis (Tinea unguium)
Guidelines (Medical Letter, 2012) recommend oral terbinafine or oral itraconazole as first line therapy for onychomycosis.\textsuperscript{12} The British Association of Dermatologists guidelines for the management of onychomycosis recommended both itraconazole and terbinafine as first line treatments for dermatophyte onychomycosis and generally prefer terbinafine over itraconazole.\textsuperscript{24} Several meta-analyses have found oral terbinafine more effective than oral itraconazole for onychomycosis.\textsuperscript{8-11} The guidelines consider oral fluconazole as an alternative (off-label use). Nail specimens are recommended prior to any drug therapy to confirm diagnosis of onychomycosis. Ciclopirox is considered less effective than systemic therapy, but has no systemic side effects or drug interactions.\textsuperscript{12}

Prescribing information for Penlac states that the drug is indicated as a topical component of a comprehensive management program in immunocompetent patients with mild to moderate onychomycosis of fingernails and toenails without lunula involvement, due to \textit{Trichophyton rubrum}. The comprehensive management program includes removal of the unattached, infected nails as frequently as monthly, by a health care professional who has special competence in the diagnosis and treatment of nail disorders, including minor nail procedures.\textsuperscript{3}

Onychomycosis typically causes no symptoms other than an undesirable appearance of the nail.\textsuperscript{16,17} Guidelines recommend consideration of treatment if walking is uncomfortable, abnormal looking nails are causing significant psychological distress, or if the patient has diabetes, vascular disease, or a connective tissue disorder. Treatment may be necessary if the nail infection is the source of a fungal skin infection or if the person is, or may become, severely immunocompromised.\textsuperscript{16}

Onychomycosis can be difficult to distinguish from other causes of nail dystrophy and because of slow nail growth (six months for fingernails and twelve months for toenails) evidence of treatment failure may not be apparent for several months or more. If the diagnosis is not confirmed and improvement does not occur, it is impossible to ascertain if treatment failure has occurred or if the initial diagnosis was incorrect. Guidelines on the treatment of fungal and candidal infections of the nail recommend laboratory confirmation of the diagnosis before initiation of treatment.\textsuperscript{16,17} An FDA public health advisory concerning the association of congestive heart failure and hepatic adverse events with the administration of Lamisil and Sporanox recommends that healthcare providers obtain nail specimens for laboratory testing prior to prescribing the medications for onychomycosis to confirm the diagnosis.\textsuperscript{18}
**Tinea capitis**

The guidelines for the management of tinea capitis in children from the European Society for Pediatric Dermatology note that terbinafine, itraconazole, and fluconazole appear to have efficacy rate and potential adverse effects similar to those of griseofulvin in children with tinea capitis caused by the *Trichophyton* species. Griseofulvin is the treatment of choice for cases caused by *Microsporum* species.¹³ A Cochrane review found that terbinafine for 4 weeks and griseofulvin for 8 weeks have demonstrated similar efficacy in three studies.¹⁴ Two comparative trials of terbinafine oral granules vs. griseofulvin in patients 4-12 years of age demonstrated superior rates of complete cure for terbinafine compared to griseofulvin.¹⁵,¹⁹

For additional clinical information see the Prime Therapeutics Formulary Chapter 1.9A: Antifungal Agents, Imidazole and Triazole Agents and Formulary Chapter 14.5E Topical Antifungals, Non-imidazoles.

**REFERENCES**

18. FDA Public Health Advisory: The safety of Sporanox® capsules and Lamisil® tablets for the treatment of onychomycosis. Available at:
Itraconazole, Terbinafine
Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Itraconazole, Terbinafine Prior Authorization (PA) Criteria is to assure appropriate selection of patients for treatment according to product labeling and/or clinical trials and/or guidelines and to discourage cosmetic utilization. The PA defines appropriate use for the treatment of onychomycosis as a confirmed fungal nail infection that is considered medically necessary to treat. Brand products are included in this program and generics targeting to be determined by client. Topical terbinafine products are not included. For brand agents, the program requires the trial of a generic antifungal onychomycosis agent or that the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one generic antifungal onychomycosis agent. Approval will not be granted to patients who have any FDA labeled contraindication(s) to the requested agent. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET DRUGS
- Lamisil® (terbinafine) – tablets, granules
- Onmel™ (itraconazole) - tablets
- Sporanox® (itraconazole) – capsules, oral solution
- Terbinex™ (terbinafine) - tablets
  a - Lamisil cream and spray are not included in the program
  b - available as a generic; designated target as determined by client

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMITS

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Quantity Per Day (Or As Noted)</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamisil (terbinafine)a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>250 mg tabletb</td>
<td>11000080100310</td>
<td>1 tablet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>125 mg granules packet</td>
<td>11000080103020</td>
<td>1 packet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>187.5 mg granules packet</td>
<td>11000080103030</td>
<td>1 packet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Onmel (itraconazole)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mg tablet</td>
<td>11407035000330</td>
<td>1 tablet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Sporanox (itraconazole)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mg capsuleb</td>
<td>11407035000120</td>
<td>4 capsule</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>10 mg/mL oral solution</td>
<td>11407035002020</td>
<td>40 mL</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Terbinex (terbinafine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>250 mg tablet</td>
<td>11000080506420</td>
<td>1 tablet</td>
<td>M, N, O, or Y</td>
</tr>
</tbody>
</table>

a - Lamisil cream and spray not included in the program
b - available as a generic; designated target as determined by client

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Lamisil (terbinafine), Onmel (itraconazole), Sporanox (itraconazole), or Terbinex (terbinafine) will be approved when ALL of the following are met:
1. The patient does not have any FDA labeled contraindication(s) to the requested agent
   AND
2. ONE of the following:
   a. The patient has a diagnosis for fungal infection other than onychomycosis (tinea unguium)
   OR
   b. The patient has a diagnosis of onychomycosis (tinea unguium) AND ALL of the following:
i. No evidence of prior authorization for the requested drug is seen in the past 12 months of claims history
   **AND**

ii. The patient has one of the following: diabetes mellitus, peripheral vascular insufficiency, immune deficiency due to medical condition or treatment (e.g. cancer chemotherapy, HIV/AIDS, anti-rejection therapy post organ transplant), pain limiting normal activity, or secondary bacterial infection in the surrounding skin or systemic dermatosis with impaired skin integrity
   **AND**

iii. Treatment of the patient’s onychomycosis (tinea unguium) is medically necessary and not entirely for cosmetic reasons
   **AND**

iv. Fungal nail infection is confirmed by laboratory testing (KOH preparation, fungal culture or nail biopsy)
   **AND**

v. If the requested agent is a brand agent, ONE of the following:
   1. The patient’s medication history includes use of a generic antifungal onychomycosis agent (e.g. itraconazole, terbinafine, ciclopirox) in the past 90 days
   **OR**
   2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one generic antifungal onychomycosis agent
   **AND**

3. One of the following:
   a. The requested quantity (dose) is **NOT** greater than the program quantity limit
   **OR**
   b. All of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      **AND**
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
      **AND**
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
   **OR**
   c. All of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      **AND**
      ii. The requested quantity (dose) is greater than the FDA labeled dose
      **AND**
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

**Length of approval for onychomycosis***
Lamisil/Terbinex/terbinafine: 6 weeks for fingernail infection, 12 weeks for toenail infection
Sporanox/Onmel/itraconazole: 2 weeks of pulse therapy for fingernail infection only, 12 weeks for toenail infection with or without fingernail involvement

* Lamisil/Terbinex/terbinafine and Sporanox/Onmel/itraconazole are limited to one approval per 12 month period for onychomycosis (tinea unguium)
Length of approval for diagnosis other than onychomycosis:
Lamisil or terbinafine for 6 weeks for tinea capitis or other fungal infections
Sporanox or itraconazole for 4 weeks for oropharyngeal or esophageal candidiasis or cutaneous fungal infections;
Sporanox or itraconazole for 12 months for other fungal infections
Ciclopirox, Efinaconazole, Tavaborole Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Ciclopirox, Efinaconazole, tavaborole Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical trials and to discourage cosmetic utilization. The PA defines appropriate use as confirmed fungal nail infections that are considered medically necessary to treat and cannot be treated with an oral antifungal agent. The program requires the trial of a generic antifungal onychomycosis agent or that the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one generic antifungal onychomycosis agent. Approval will not be granted to patients who have any FDA labeled contraindication(s) to the requested agent. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET DRUG
- **Jublia** (efinaconazole 10% topical solution)
- **Kerydin** (tavaborole 5% topical solution)
- **Penlac** (ciclopirox 8% topical solution)\(^a\)

\(^a\) available as a generic; designated target as determined by client

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMITS

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Quantity Per Day (Or As Noted)</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jublia (efinaconazole) topical solution 10%</td>
<td>90154037002020</td>
<td>4 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Kerydin (tavaborole) topical solution 5%</td>
<td>90156080002010</td>
<td>4 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>Penlac (ciclopirox) topical solution 8%(^a)</td>
<td>90150030002020</td>
<td>6.6 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
</tbody>
</table>

\(^a\) available as a generic; designated target as determined by client

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
*Jublia* (efinaconazole), *Kerydin* (tavaborole), or *Penlac* (ciclopirox) will be approved when ALL of the following are met:

1. The patient does not have any FDA labeled contraindication(s) to the requested agent
   **AND**
2. The patient has a diagnosis of onychomycosis (tinea unguium)
   **AND**
3. The patient has one of the following: diabetes mellitus, peripheral vascular insufficiency, immune deficiency due to medical condition or treatment (e.g. cancer chemotherapy, HIV/AIDS, anti-rejection therapy post organ transplant), pain limiting normal activity, or secondary bacterial infection in the surrounding skin or systemic dermatosis with impaired skin integrity
   **AND**
4. Treatment of the patient’s onychomycosis (tinea unguium) is medically necessary and not entirely for cosmetic reasons
   **AND**
5. The fungal nail infection is confirmed by laboratory testing (KOH preparation, fungal culture or nail biopsy)
   **AND**
6. The patient has a treatment failure with, a contraindication to an oral antifungal agent, or the prescriber has provided documentation that an oral antifungal agent is not clinically appropriate 

**AND**

7. If treating with Penlac, ciclopirox 8% topical solution; treatment will include removal of the unattached, infected nail(s) by an appropriate health care professional 

**AND**

8. If the requested agent is a brand agent, ONE of the following:
   a. The patient’s medication history includes use of a generic antifungal onychomycosis agent (e.g. itraconazole, terbinafine, ciclopirox) in the past 90 days
   
   OR
   
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one generic antifungal onychomycosis agent

**AND**

9. ONE Of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
   
   OR
   
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         
         **AND**
         
         ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
         
         **AND**
         
         iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
   
   OR
   
   c. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         
         **AND**
         
         ii. The requested quantity (dose) is greater than the FDA labeled dose
         
         **AND**
         
         iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

**Length of approval:** 12 months