## FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agent</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></td>
<td></td>
</tr>
<tr>
<td>topical solution</td>
<td></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></td>
<td></td>
</tr>
<tr>
<td>topical solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lamisil®</strong></td>
<td>Onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium)</td>
<td><strong>Onychomycosis</strong> - 250 mg daily</td>
</tr>
<tr>
<td>(terbinafine)</td>
<td></td>
<td><strong>Fingernail</strong> – treat 6 weeks</td>
</tr>
<tr>
<td>tablets,</td>
<td></td>
<td><strong>Toenail</strong> – treat 12 weeks</td>
</tr>
<tr>
<td>oral granules</td>
<td></td>
<td><strong>Tinea capitis</strong> – 125 mg -250 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(see table)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Dosage by body weight:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;25 kg 125 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25-35 kg 187.5 mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;35 kg 250 mg/day</td>
</tr>
<tr>
<td><strong>Onmel®</strong></td>
<td>Onychomycosis of the toenail caused by <em>Trichophyton rubrum</em> or <em>T. mentagrophytes</em></td>
<td><strong>Onychomycosis toenail</strong>-200 mg once daily for 12 weeks</td>
</tr>
<tr>
<td>(itraconazole)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tablets</td>
<td></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 <em>Trichophyton rubrum</em>)</td>
<td>Apply daily to affected area</td>
</tr>
<tr>
<td>(ciclopirox)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>topical solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agent</td>
<td>FDA Indication(s)</td>
<td>Dosing</td>
</tr>
<tr>
<td>---------------------------</td>
<td>------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sporanox® (itraconazole)</td>
<td>Blastomycosis, histoplasmosis, aspergillosis, onychomycosis of</td>
<td>Blastomycosis-200 mg daily (up to 400 mg daily if 200 mg not effective)</td>
</tr>
<tr>
<td>capsules, oral solution</td>
<td>the toenail or fingernail</td>
<td>Histoplasmosis-200 mg daily (up to 400 mg daily if 200 mg not effective)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aspergillosis-200-400 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Onychomycosis toenail-200 mg daily for 12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Onychomycosis fingernail-200 mg twice daily for 1 week, then 3 weeks off, then 200 mg twice daily for 1 more week</td>
</tr>
</tbody>
</table>

**CLINICAL RATIONALE**

**Esophageal candidiasis and candidemia**

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**

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)**

Onychomycosis typically causes no symptoms other than an undesirable appearance of the nail. 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.

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 and nail specimens for diagnosis before initiation of treatment.

The British Association of Dermatologists guidelines for the management of onychomycosis recommends both itraconazole and terbinafine as first line treatments for dermatophyte onychomycosis and generally prefer terbinafine over itraconazole. The American Academy of Family Physicians recommends terbinafine as first-line treatment for dermatophyte onychomycosis due to its tolerability, high cure rate, and low cost. A meta-analysis showed a mycotic cure rate of 76% for the use of terbinafine for systemic treatment of onychomycosis.
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).

Topical agents are recommended for patients who cannot take oral antifungals and in those with less than 50% of the distal nail affected and no lunular involvement.\textsuperscript{15} Ciclopirox is considered less effective than systemic therapy, but has no systemic side effects or drug interactions. Additionally, a comparative study showed combination of ciclopirox and oral terbinafine had a higher mycotic cure rate and complete cure rate compared to terbinafine alone.\textsuperscript{15} The prescribing information for Penlac indicates it is part of a comprehensive management program that 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}

**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 rates 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.\textsuperscript{13} A Cochrane review found that terbinafine for 4 weeks and griseofulvin for 8 weeks have demonstrated similar efficacy in three studies.\textsuperscript{14} Two comparative trials of terbinafine oral granules vs. griseofulvin in patients 4 to 12 years of age demonstrated superior rates of complete cure for terbinafine compared to griseofulvin.\textsuperscript{14,16}

A meta-analysis evaluated efficacy between griseofulvin and terbinafine in the treatment of tinea capitis infections. The review did not show a significant difference in the overall efficacy of the two drugs but specific efficacy differences were observed based on the infectious species. For tinea capitis caused by *Microsporum* spp., griseofulvin is superior ($p = 0.04$), whereas terbinafine is superior for *Trichophyton* spp. infection ($p = 0.04$). These results support species-specific differences in treatment efficacy between griseofulvin and terbinafine.

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**

Itraconazole, Terbinafine Prior Authorization with Quantity Limit

Quantity limits apply to all products. Prior authorization applies to brand name agents only.

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 a medication history with 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 AGENTS

- Lamisil® (terbinafine) - tablets, granules
- Onmel™ (itraconazole) - tablets
- Sporanox® (itraconazole) - capsules, oral solution

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)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>250 mg tablet</td>
<td>11000080100310</td>
<td>1 tablet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>125 mg granules</td>
<td>11000080103020</td>
<td>1 packet</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>187.5 mg granules</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 capsule</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>
</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), or Sporanox (itraconazole) 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 an FDA approved diagnosis other than onychomycosis (tinea unguium) for the requested agent OR
   b. The patient has a diagnosis of onychomycosis (tinea unguium) AND ALL of the following:
      i. The patient has not received treatment for onychomycosis with the requested agent in the past 12 months 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/terbinafine: 6 weeks for fingernail infection, 12 weeks for toenail infection
Sporanox/itraconazole: 2 weeks of pulse therapy for fingernail infection only, 12 weeks for toenail infection with or without fingernail involvement
Onmel/itraconazole: 12 weeks for toenail fungal infection

*Lamisil/Terbinex/terbinafine and Sporanox/Onmel/itraconazole are limited to one approval per 12 month period for onychomycosis (tinea unguium)

Length of approval for FDA approved diagnosis other than onychomycosis:
Lamisil or terbinafine: 6 weeks for tinea capitis or other FDA approved indications
Sporanox or itraconazole: 4 weeks for oropharyngeal or esophageal candidiasis or cutaneous fungal infections
Sporanox or itraconazole: 12 months for other FDA approved indications
Onmel/itraconazole: 12 months for other FDA approved indications
Ciclopirox, Efinaconazole, Tavaborole Prior Authorization with Quantity Limit

Quantity limits apply to all products. Prior authorization applies to brand name agents only.

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 AGENTS
- Jublia (efinaconazole 10% topical solution)
- Kerydin (tavaborole 5% topical solution)
- Penlac (ciclopirox 8% topical solution)\textsuperscript{a}
\textsuperscript{a} - available as a generic; generic only targeted for quantity limit

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)</td>
<td>901540370020</td>
<td>4 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>topical solution 10%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kerydin (tavaborole)</td>
<td>9015608002010</td>
<td>4 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>topical solution 5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penlac (ciclopirox)</td>
<td>9015003002020</td>
<td>6.6 mL / 30 days</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>topical solution 8%\textsuperscript{a}</td>
<td></td>
<td></td>
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</tbody>
</table>

\textsuperscript{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 \textbf{AND}
2. The patient has a diagnosis of onychomycosis (tinea unguium) \textbf{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 \textbf{AND}
4. Treatment of the patient’s onychomycosis (tinea unguium) is medically necessary and not entirely for cosmetic reasons \textbf{AND}
5. The fungal nail infection is confirmed by laboratory testing (KOH preparation, fungal culture or nail biopsy) \textbf{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 the requested agent is 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
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

**STEP THERAPY SUPPLEMENT**

**OBJECTIVE**
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

**CONDITIONS FOR APPROVAL**
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   **OR**
2. The patient's medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   **OR**
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   **OR**
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of Approval:** As per program specific criteria