This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

**Drug:** Lamisil (terbinafine)  
**Class:** Antifungal  
**Effective Date:** November 2013  
**Renewal Date:** November 2014

**Policy/Criteria:**

1. Terbinafine is a formulary agent limited to 3 months of treatment without prior authorization.  
2. Continuation beyond three months therapy requires clinical justification (e.g. zero nail growth, severe immunosuppression, and high dermatophyte resistance), liver function tests, and a time-out period of 12 weeks.

**Clinical Justification:**

1. About 50% of patients empirically diagnosed with onychomycosis did not have a fungal infection.¹  
2. Onychomycosis may present clinically in a manner that is similar to other nail disorders. Some of the nail diseases that mimic onychomycosis include yellow-nail syndrome, idiopathic onycholysis, psoriasis, traumatic onychodystrophies, nail bed tumors, and contact dermatitis.²,³  
3. Patients with asymptomatic onychomycosis who are not at significant risk for amputation should be given topical therapy or no therapy at all. Treatment may be considered of potential clinical benefit when the condition is associated with co-morbid conditions, when onychomycosis is part of a more serious pathology, or results in a functional impairment.⁴,⁵  
4. Patients should be advised that due to binding of the antimycotic drug to keratin in the nail and continued exposure to fungus to medication, improvement will continue after oral therapy has stopped. It may take 48-72 weeks to fully assess cure.⁵  
5. In cases of treatment failure at 3 months, it is recommended to consider an alternative drug or nail removal in combination with a further course of therapy to cover the period of regrowth.⁵
Comparison of different antifungal agents:

**TERBINAFINE**

Treatment Duration: Prescribed (daily) fashion for the treatment of fingernail (generally a 6-week course) and toenail (generally a 12-week course).

Advantage: Metabolized by multiple CYP450 enzymes; 1A2, 2B6, 2C8, 2C9, 2C19, 3A4, 3A5, thus, the chances of a drug interaction is minimal.\(^8\)

Disadvantage: May cause hepatotoxicity.

Monitoring: Monitor for hepatotoxicity, taste or smell disturbances, depression, leucopenia, and SJS. Complete CBC, ALT and AST levels at baseline, then every 4 to 6 weeks during therapy.

Successful Rate: Mycological cure: 70%; Effective Treatment: 59%; Mycological AND Clinical Cure: 38%.\(^9\)

Relapse Rate: 85% of the 38% complete cure patients with no relapse, approximately 11-18% at up to 12 to 21 months after treatment.\(^9,10,11,12\)

**ITRACONAZOLE**

Treatment Duration: Can be used in either a "pulse" dosage (i.e., patient receives medication daily for one week, followed by three weeks off medication) or continuous (daily) dosage for the treatment of tinea unguium. Treatment duration is generally 2-3 months for fingernails and 3-4 months for toenails.

Advantage: Daily dosing resulting in better compliance.

Disadvantage: Several drug interactions with medications metabolized by the cytochrome p-450 system

Monitoring: May cause hepatotoxicity. ALT and AST levels at baseline, then every 4 to 6 weeks during therapy.

Successful Rate: Continuous 66.3% and Pulse 70.8% in toenails; Disease-free nail/Complete Cure Rate approximately 25% to 40%.\(^13,14,15\)

Relapse Rate: Recurrent toenail dystrophy of 17% and mycological failure rate of 55% at 2 years after treatment.\(^15\)

**GRISEOFULVIN**

Treatment Duration: 500mg daily for 6-9 months for fingernail and 12-18 months in toenail infections.

Advantage: FDA-approved for children with onychomycosis (rare).
Disadvantage: Narrow spectrum, longer course of therapy and high relapse rate, fungistatic rather than fungicidal

Monitoring: Baseline LFTs, repeat LFTs.

Successful Rate: Mycological cure rate: 30-40% in toenails and 70% in fingernails.\textsuperscript{17}

Relapse Rate: 50-85%.\textsuperscript{17}

**KETOCONAZOLE**

Treatment Duration: 200-400mg once daily for 6-12 months.

Advantage: N/A

Disadvantage: Narrow spectrum, longer course of therapy and high relapse rate; hepatotoxicity; extensive drug interaction.

Monitoring: Baseline CBC and LFTs, frequent repeat LFTs

Successful Rate: Complete cure rate: 20%.\textsuperscript{18}

Relapse Rate: 38%.\textsuperscript{18}

**FLUCONAZOLE**

Treatment Duration: 300-450 mg taken once weekly, 3-6 months for finger nail infection; 6-12 months for toenail infection.

Advantage: First-line therapy for candidal infections but also active against dermatophytes; once weekly dosing increase compliance

Disadvantage: Not FDA-approved for onychomycosis

Monitoring: Baseline LFTs, repeat LFTs

Successful Rate: Complete cure rate: 28-36% after 6-7 months.\textsuperscript{19,20}

Relapse Rate: 11\%\textsuperscript{19,20}

**POSACONAZOLE**

Treatment Duration: 200-400mg daily for 6 months for toenail infection

Advantage: Fewer adverse effects than itraconazole

Disadvantage: Not FDA-approved for onychomycosis, several drug-drug interactions
Monitoring: Baseline LFTs, repeat LFTs

Successful Rate: Complete cure rate: 46-54% after 6 months.\textsuperscript{21}

Relapse Rate: Non-studied

**CICLOPIROX**

Treatment Duration: 48 weeks of application

Advantage: The ability of the drug to penetrate the keratin of the nail compared to non-prescription topical; minimal side effect and drug interaction.

Disadvantage: Limited to toenails with <50% involvement, no proximal plate involvement;

Monitoring: None

Successful Rate: Mycological cure rate: 36\%\textsuperscript{22}

Relapse Rate: 20.7\%\textsuperscript{22}

**OTHER TOPICAL AGENTS:**

Agent: Naftifine, miconazole, clotrimazole and other AF cream

Advantage: Over-the-counter, very inexpensive.

Disadvantage: None of them are FDA-approved. Poor efficacy. May only benefit for mild onychomycosis and children who have thinner nail for easier penetration.\textsuperscript{23,24}

Monitoring: None

Successful Rate: No established report.

Relapse Rate: Very high, but no established report.
REFERENCES: