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: Sporanox (itraconazole)

Class: Antifungal

Formulary medication: Griseofulvin, ketoconazole, clotrimazole.

Effective Date: September 2004, updated January 2006

Policy/Criteria:

1. Terbinafine are considered medically necessary for treatment of the following conditions below (both required):

    a. Treatment of onychomycosis, associated with one of the following conditions (diagnosed and current on therapy)
        i. diabetic
        ii. immunocompromised
        iii. systemic dermatosis
        iv. onychomycosis on finger nails
        v. onychomycosis on toenail that impair movements

    b. Obtain appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) to confirm the diagnosis of onychomycosis.

2. Authorization of treatment is limited to 3 months. Continuation beyond three months therapy requires clinical justification, liver function test and other supportive documents.

Clinical Justification:

1. About 50% of patients empirically diagnosed with onychomycosis did not have a fungal infection.[3]

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.[4,5]

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, or when onychomycosis is part of a more serious pathology or results in a functional impairment.

Comparison of different antifungal agents:

TERBINAFINE

Treatment Duration: Prescribed in a continuous (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.[7]

Disadvantage: May cause hepatotoxicity.

Monitoring: Monitor for hepatotoxicity and leukopenia. Complete blood count and ALT and AST levels at baseline, then every 4 to 6 weeks during therapy.

Successful Rate: Mycological cure: 70%; Effective Treatment: 59%; Mycological Plus Clinical Cure: 38%.[8]

Relapse Rate: 85% of the 38% complete cure patients with no relapse, approximately 11-18% at up to 12 to 21 months after treatment.[8,9,10,11]

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: Much better compliance with daily medications

Disadvantage: May not take their medication at the correct time; Drug interaction 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%; Pulse 70.8%; Disease-free nail/Complete Cure Rate approximately 25% to 40%[12,13,14]

Relapse Rate: Recurrent nail dystrophy of 17% and mycological failure rate of 55% at 2 years after treatment.[15]

GRISEOFULVIN

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

Advantage: N/A

Disadvantage: Narrow spectrum, longer course of therapy and high relapse rate; Fungistatic rather than fungicidal.

Monitoring: Baseline LFTs, frequent repeat LFTs

Successful Rate: Mycological cure rate: 30-40%[16]

Relapse Rate: 50-85%[16]

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%[17]

Relapse Rate: 38%[17]

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, frequent repeat LFTs

Successful Rate: Complete cure rate: 28-36% after 6-7 months.[18,19]

Relapse Rate: 11%[18,19]

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%[20]

Relapse Rate: 20.7%[20]

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.[21,22]

Monitoring: None

Successful Rate: No established report.

Relapse Rate: Very high, but no established report.

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