

Pharmacy Policy Bulletin

Title: Onychomycosis agents

Policy #: Rx.01.168

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

▸ Intent:

The intent of this policy is to communicate the medical necessity criteria for efinaconazole (Jublia®), tavaborole (Kerydin®), ciclopirox (Ciclodan®, Penlac®) 8% topical solution and itraconazole (Onmel®) as provided under the member's prescription drug benefit.

▸ Description:

Efinaconazole (Jublia®) is an azole antifungal that inhibits fungal lanosterol 14 α -demethylase involved in the biosynthesis of ergosterol, a constituent of fungal cell membranes. Efinaconazole (Jublia®) is indicated for the topical treatment of onychomycosis of the toenails due to *Trichophyton rubrum* and *Trichophyton mentagophytes*.

Tavaborole (Kerydin®) is an oxaborole antifungal that inhibits fungal protein synthesis through the inhibition of an aminocyl-transfer ribonucleic acid (tRNA) synthetase (AARS). Tavaborole (Kerydin®) is indicated for the topical treatment of onychomycosis of the toenails due to *Trichophyton rubrum* and *Trichophyton mentagophytes*.

Ciclopirox (Cilodan®, Penlac®) is a hydroxypyridinone antifungal agent that inhibits the growth of pathogenic dermatophytes. The exact mechanism of action is unknown. Ciclopirox may inhibit transport of certain essential substrates into fungal cells, interfere with the synthesis of proteins, RNA and DNA, and alter cell permeability, osmotic fragility and endogenous respiration. Cilopirox (Ciclodan®, Penlac®) is indicated as a component of a comprehensive management program for topical treatment of immunocompetent patients with mild to moderate onychomycosis of fingernails and toenails, without lunula involvement, due to *Trichophyton rubrum*.

Itraconazole (Onmel®) is an azole antifungal that inhibits the cytochrome P450-dependent synthesis of ergosterol, which is a vital component of fungal cell membranes. Itraconazole (Onmel®) is indicated for the treatment of onychomycosis of the toenail caused by *Trichophyton rubrum* or *T. mentagophytes*.

Policy:

Efinaconazole (Jublia®), tavaborole (Kerydin®), ciclopirox (Ciclodan®, Penlac®) 8% topical solution or itraconazole (Onmel®), is approved when ALL of the following are present:

1. Diagnosis of onychomycosis confirmed by one of the following:
 - a. Positive potassium hydroxide (KOH) preparation; or
 - b. Culture; or
 - c. Histology
- and
2. Condition is causing debility or a disruption in their activities of daily living; and
 3. Inadequate response or inability to tolerate BOTH of the following:
 - a. oral generic terbinafine; and
 - b. oral generic itraconazole OR topical generic ciclopirox

Authorization duration: 1 year

Black Box Warning as shown in the drug Prescribing Information:

Itraconazole: CONGESTIVE HEART FAILURE, CARDIAC EFFECTS, AND DRUG INTERACTIONS

Do not administer itraconazole for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF. When itraconazole was administered intravenously to dogs and healthy human volunteers, negative inotropic effects were seen. If signs or symptoms of congestive heart failure occur during administration of itraconazole, discontinue administration.

Drug Interactions: Co-administration of cisapride, pimozide, quinidine, dofetilide, levacetylmethadol (levomethadyl), felodipine, oral midazolam, nisoldipine, triazolam, lovastatin, simvastatin, ergot alkaloids such as dihydroergotamine, ergometrine (ergonovine), ergotamine and methylergometrine (methylergonovine) or methadone with itraconazole is contraindicated. Itraconazole, a potent cytochrome P450 3A4 isoenzyme system (CYP3A4) inhibitor, may increase plasma concentrations of drugs metabolized by this pathway. Serious cardiovascular events, including QT prolongation, torsades de pointes, ventricular tachycardia, cardiac arrest, and/or sudden death have occurred in patients using cisapride, pimozide, levacetylmethadol (levomethadyl), methadone or quinidine concomitantly with itraconazole and/or other CYP3A4 inhibitors.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Ciclodan® (ciclopirox) [package insert]. Fairfield, NJ. Medimetriks Pharmaceuticals, Inc. November 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=246676e5-60a0-41dc-b665-30d5e670b426&type=display>. Accessed February 18, 2019.

Jublia® (efinaconazole) [package insert]. Bridgewater, NJ. Valeant Pharmaceuticals North America, LLC. September 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=922d4d25-c530-11e1-9b21-0800200c9a66&type=display>. Accessed February 18, 2019.

Kerydin® (tavaborole) [package insert]. Palo Alto, CA. Anacor Pharmaceuticals, Inc. August 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1ae61072-bca0-43f0-a741-07bda2d50c87&type=display>. Accessed February 18, 2019.

Onmel® (itraconazole) [package insert]. Greensboro, NC. Merz Pharmaceuticals, LLC. November 2012. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=fb8a2e5b-fd23-4977-81de-a95f4af168e2&type=display>. Accessed February 18, 2019.

Penlac® (ciclopirox) [package insert]. Bridgewater, NJ. Valeant Pharmaceuticals North America, LLC. June 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=9793245c-c3e0-4351-a2ab-b54b46aecb43&type=display>. Accessed February 18, 2019.

Applicable Drugs:

i Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Jublia®	Efinaconazole
Kerydin®	Tavaborole
Ciclodan®, Penlac®	Ciclopirox
Onmel®	Itraconazole

Cross References:

N/A

Policy Version Number:	6.00
P&T Approval Date:	January 10, 2019
Policy Effective Date:	April 01, 2019
Next Required Review Date:	January 10, 2020

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.