

MTF Formulary Management for Topical Antifungals for Onychomycosis Subclass

Defense Health Agency Pharmacy Operations Division

Bottom Line

- The recent entrants efinaconazole (Jublia) and tavaborole (Kerydin) are now designated with nonformulary status; generically available ciclopirox (Penlac) remains Uniform Formulary.
- Manual prior authorization applies to Jublia and Kerydin.
- While the newer agents offer an additional topical option, modest efficacy and high cost should limit their use.
- For the majority of Military Health System (MHS) beneficiaries, oral agents, such as terbinafine (Lamisil), are significantly more effective when comparing complete cure rates, as well as ease of use.

Uniform Formulary Decision: The Director, DHA, approved recommendations from the February 2016 DoD P&T Committee meeting on May 5, 2016, with an implementation date of August 10, 2016.

Topical Antifungals Uniform Formulary (UF) drugs		
	MTFs <u>may</u> have on formulary*	MTFs <u>must not</u> have on formulary
None*	<ul style="list-style-type: none"> • ciclopirox generic (Penlac) 	<ul style="list-style-type: none"> • efinaconazole (Jublia)** • tavaborole (Kerydin)**
<p>* Note that generic topical clotrimazole is on the BCF as part of the Antifungal Drug Class. **Prior Authorization applies (see below)</p>		

Clinical Summary

- While there are no head-to-head trials of the available topical antifungals, they all have similar efficacy endpoints in the studies that led to FDA approval. Endpoints include a mycological component with negative fungal culture and potassium hydroxide prep, as well as a subjectively “clear” toenail.
- While the extent of nail involvement studied with the recent entrants differed, both had failure rates exceeding 80% in the complete cure metric. Accounting for the higher percentage of nail involvement treated with the generically available ciclopirox, efficacy is likely similar with the newer agents.
- Effectiveness for all agents by degree of nail involvement is not available in the published literature, but it is notable that no nail with greater than 60% involvement was studied by the recent entrants. The maximum percentage of nail involvement ranged from up to 50% with efinaconazole, to up to 60% with tavaborole, to up to 65% with ciclopirox.
- The complete cure rates at one year with efinaconazole (Jublia) in the two pivotal trials were 17.8% and 15.2% for the active arms, versus 3.3% and 5.5% in the vehicle arms, respectively. In comparison, complete cure rates at one year in the two pivotal trials with tavaborole (Kerydin) were 6.5% and 9.1% for the active arms, versus 0.5% and 1.5% in the vehicles, respectively. Efficacy data with ciclopirox supports complete cure rates ranging from 5.5% to 8.5%.
- Depending on the number and which toe is involved, the amount of topical product required will vary. For example, the great toe requires 2 drops of efinaconazole instead of one drop.
- Although not part of the class as a direct comparator, oral terbinafine efficacy data was reviewed. Terbinafine was able to achieve 38% complete cure rate in the FDA pivotal trial leading to approval, and is considered the gold standard for treatment of onychomycosis. It also requires a shorter 12-week course when used for toenail onychomycosis.
- While relapse rates are not delineated for the newer agents, ciclopirox has a reported 40% 3-month relapse rate, and terbinafine has a five-year relapse rate of 20%.
- All the topical agents require 48 weeks of daily topical application. There are slight differences in application method. Efinaconazole uses a brush applicator, while tavaborole has a dropper. The ciclopirox is lacquer-based, creating a tacky effect after application and requires weekly removal, as well as debridement of the nail per the FDA label.

- Prescribers of treatments for onychomycosis are encouraged to try ciclopirox generic and oral terbinafine, if clinically indicated, before using the more recent entrants tavaborole and efinaconazole, which require manual prior authorization. (See below.)

Safety & Tolerability

- Adverse events were similar to the vehicle-only groups in trials examining the topical agents.
- Safety issues are rare overall and the safety profile for the topical agents is similar. The adverse event rates for the topicals centered on application site reactions. These included exfoliation, ingrown toenail, dermatitis, vesicle, and site pain.
- Aside from hypersensitivity issues and ensuring topical use as directed, there are no significant drug-drug interactions, and no warnings or precautions for the newer topical agents.

Prior Authorization

- Manual prior authorization applies to new and current users of both Jublia and Kerydin.
- Jublia or Kerydin are approved if the patient has diagnostically confirmed onychomycosis.
- Additionally, the patient must have tried generic ciclopirox and had a therapeutic failure, and also must have tried itraconazole or terbinafine and had a therapeutic failure, unless there are contraindications or previous history of adverse effects.
- Treatment is not approved for cosmetic reasons; the patient must be immunocompromised or have a history of cellulitis, history of diabetes, or significant pain or disruption of their daily activities.
- Only one 48-week treatment course will be approved in a 2-year period.
- Treatment gaps of more than 30 days will require submittal of a new prior authorization form.

References

- DoD P&T Committee minutes: <http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee: <http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee>
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil

Topical Antifungals Onychomycosis Price Comparison at MTF	
Drug	MTF Cost/Month (February 2016)
Basic Core Formulary	
None	
Uniform Formulary	
Ciclopirox generic (Penlac)	\$ Most Cost-Effective
Nonformulary	
Tavaborole (Kerydin)	\$\$\$\$ Least Cost-Effective
Efinaconazole (Jublia)	\$\$\$\$ Least Cost-Effective
Legend:	
\$ = "Most Cost-Effective" represents Rx's with the <u>lowest cost</u> and best clinical efficacy	
\$\$ = "Less Cost-Effective" represents <u>higher cost</u> Rx's with similar clinical efficacy	
\$\$\$ = "Less Cost-Effective" represents <u>next higher cost</u> Rx's with similar clinical efficacy	
\$\$\$\$ = "Least Cost-Effective" represents Rx's with the <u>highest cost</u> with similar clinical efficacy	