

Which oral antifungal is best for toenail onychomycosis?

Evidence-based answer

Terbinafine, 250 mg taken daily for 12 weeks, is the best regimen for toenail onychomycosis due to better clinical and

mycologic cure rates, tolerability, and cost effectiveness (strength of recommendation [SOR]: **A**, meta-analyses).

Clinical commentary

This expensive treatment is not always a high priority

In my practice of mostly uninsured patients, onychomycosis treatment is not a high priority. The recommended drug, terbinafine, is costly and not available as a generic. Since this is primarily a cosmetic problem, we usually don't treat it in my population. In the rare case that

someone is willing to pay out of pocket, however, I will now use terbinafine, based on this review. At one of my practices, itraconazole was available at a reduced price, but that discount is outweighed by the superior safety profile of terbinafine.

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Evidence summary

Fungal infections of the nail (onychomycosis) are often treated for relief of local symptoms and cosmetic reasons. Griseofulvin, fluconazole, itraconazole, and terbinafine have all been used orally.

A meta-analysis comparing the efficacy of terbinafine (Lamisil), pulse-dosed and continuous-dosed itraconazole (Sporanox), fluconazole (Diflucan), and griseofulvin showed mycological cure rates of varying degrees for each treatment (**TABLE**).¹ Another meta-analysis of 6 studies comparing terbinafine with itraconazole reported odds ratios ranging from 1.8 (95% confidence interval [CI], 1.1–2.8) to 2.9 (95% CI, 1.9–4.1), indicating an 80% to 190% increased likelihood of clinical cure with terbinafine compared with itraconazole.²

Lower relapse rates with terbinafine

Longer-term mycologic cure and clinical relapse rates have also been reported. A 5-year blinded prospective study found long-term mycologic cures of 46% for terbinafine vs 13% for itraconazole (number needed to treat [NNT]=4.3). This study also showed a lower clinical relapse for terbinafine (21% vs 48%; NNT=3.7).³ A cost-efficacy analysis of terbinafine, itraconazole, and griseofulvin found terbinafine to be the most cost-effective (**TABLE**).⁴

A randomized, double-blind, controlled trial compared daily terbinafine with pulse-dose terbinafine.⁵ Daily terbinafine (250 mg for 3 months) had a 70.9% mycologic cure, while pulse-dose terbinafine (500 mg daily for 1 week per

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Terbinafine has the best rates of long-term cure

TABLE

Efficacy and cost of treating toenail onychomycosis^{1,4}

TREATMENT	MYCOLOGICAL CURE RATES	COST PER CURE*
Terbinafine (continuous)	76% (± 3%)	\$ 645
Itraconazole (pulse-dose)	63% (± 7%)	\$ 856
Itraconazole (continuous)	59% (± 5%)	\$ 1845
Griseofulvin	60% (± 6%)	\$ 2722
Fluconazole	48% (± 5%)	Not reported

* Cost includes drug, monitoring, and office visits (in 1996 dollars).

month for 3 months) had only a 58.7% mycologic cure (relative risk [RR]=1.21 [95% CI, 1.02–1.43]; NNT=8.2). There was no significant difference in tolerability of the regimens.

Terbinafine is well-tolerated by most patients. A telephone survey after treatment with daily terbinafine or pulse-dose itraconazole reported greater ease and convenience, and higher overall satisfaction with continuous terbinafine vs pulse-dose itraconazole.⁶

A multicenter trial of diabetic patients with onychomycosis (mean ± SD age, 55.7 ± 11.7 years) revealed that terbinafine had comparable efficacy and caused no hypoglycemic reactions in this group, who were being treated with insulin or oral hypoglycemics.⁷ The terbinafine prescribing information suggests not using the drug for patients with chronic or active liver disease and recommends checking a pretreatment AST and ALT.⁸

Recommendations from others

Guidelines from the British Association of Dermatologists point out that terbinafine is superior to itraconazole, and consider it a first-line treatment because it has a better cure rate and lower relapse rate.⁹ UpToDate suggests oral terbinafine as initial treatment for onychomycosis at a dose of 250 mg daily for 12 weeks.¹⁰ ■

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FAST TRACK

Do not prescribe terbinafine for patients with chronic or active liver disease