

# Optimizing Topical Therapy for Onychomycosis: The Importance of Patient Education

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Onychomycosis is a fungal infection of the nail unit due to dermatophytes, yeasts, and nondermatophyte molds (NDMs). It accounts for approximately 50% of all nail disorders seen in clinical practice and is estimated to affect 10% to 12% of the US population.<sup>1,2</sup> Oral medications approved by the US Food and Drug Administration (FDA) include terbinafine and itraconazole, which have demonstrated good efficacy in treating onychomycosis but are associated with potential drug-drug interactions and systemic side effects.<sup>3,4</sup> Although liver failure associated with these drugs is rare,<sup>5</sup> many patients are anxious about systemic adverse events and therefore prefer to use topical therapies for onychomycosis.

Many patients desire topical therapy but not every patient is an appropriate candidate. Patients who will likely respond well to topical therapy include those with superficial onychomycosis, distal lateral subungual onychomycosis that involves less than 50% of the nail plate surface area (without matrix involvement and a nail plate thickness less than 2 mm), and only up to 3 or 4 nails affected.<sup>6</sup> In patients who have contraindications to oral therapy, topical therapy may be the only treatment option. To maximize efficacy of FDA-approved topical agents for onychomycosis therapy, patient education is of utmost importance. Failure to properly counsel the patient on proper medication application may result in decreased antifungal efficacy; poor patient compliance due to lack of improvement; and progression of disease, leading to increased onychodystrophy and pain.

Before initiating therapy, patients should be counseled that treatment with topical drugs is long, requiring daily application of the medication for 6 months for fingernails and 12 months for toenails, based on average nail growth rates (2–3 mm per month for fingernails; 1 mm per month for toenails).<sup>7</sup> Patients also are advised to avoid nail polish application during the course of therapy, as clinical trials were performed without nail polish and the true efficacy

with nail polish is unknown.<sup>8–10</sup> Because patients who have had onychomycosis for shorter durations generally have better cure rates than those who have disease for longer durations, it is prudent to initiate topical therapy as early as possible.<sup>11,12</sup> Treating the feet with an antifungal while treating the nails for onychomycosis further enhances efficacy.<sup>13,14</sup> There are 3 FDA-approved topical therapies for onychomycosis: ciclopirox nail lacquer 8%, efinaconazole solution 10%, and tavaborole solution 5%.<sup>15–17</sup>

Ciclopirox is a hydroxypyridone with broad-spectrum antimicrobial activity against dermatophytes, NDMs, yeasts, and bacteria. Its mechanism of action is to chelate polyvalent cations, such as Fe<sup>3+</sup>, and inhibit fungal metal-dependent enzymes responsible for the degradation of toxic metabolites.<sup>15</sup> Ciclopirox nail lacquer 8% was FDA approved for the treatment of onychomycosis in 1999, making it the first topical approved for this purpose. Its indication is for immunocompetent patients with mild to moderate onychomycosis (*Trichophyton rubrum*) without lunula involvement, with mycologic cure rates of 29% to 36% and complete cure rates of 5.5% to 8.5% (toenails).<sup>15</sup> It is the only FDA-approved topical treatment for both fingernails and toenails. Using a brush applicator, it is applied daily to the nail plate and its undersurface, hyponychium, and 5 mm of the surrounding skin. It is important to counsel the patient to remove the lacquer from the nail plate weekly because failure to do so will result in accumulation of numerous layers of medication, such that the active drug cannot reach the site of infection (Figures 1 and 2). The nail plate also should be trimmed and filed weekly by the patient, with monthly clipping/debridement by a physician recommended.<sup>6,15</sup>

Efinaconazole is a triazole with antifungal activity against dermatophytes, NDMs, and *Candida* species. Its mechanism of action is inhibition of lanosterol 14 $\alpha$ -demethylase, an enzyme involved in the biosynthesis of ergosterol, which is a component of the fungal cell membrane. Efinaconazole solution 10% was FDA approved in June 2014 for the

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**FIGURE 1.** Appearance of the great toenail after application of ciclopirox nail lacquer 8% daily for 6 months without weekly removal of the lacquer. The great toenail shows accumulation of multiple layers of medication, preventing penetration of the active drug to the site of infection. Prior to presenting to our office, the patient was not counseled on proper application.



**FIGURE 2.** After vigorous rubbing of the great toenail with alcohol and clipping the lacquer accumulation, the numerous layers of medication were removed from the nail plate. The patient was then counseled on proper medication application.

treatment of toenail onychomycosis due to *T rubrum* and *Trichophyton mentagrophytes*, with package insert mycologic cure rates of 53.4% to 55.2% and complete cure rates of 15.2% to 17.8%.<sup>9,16</sup> It is applied with a brush applicator to the nail plate, as well as its undersurface, nail folds, and hyponychium. Two drops are recommended for the great toenail and one drop for all other toenails, and no removal of the solution or debridement is required.<sup>6,16</sup>

Tavaborole is a benzoxaborole with antifungal activity against dermatophytes, NDMs, and yeasts. Its mechanism of action is inhibition of fungal aminoacyl transfer RNA synthetase, thus impeding protein synthesis.<sup>18</sup> Tavaborole solution 5% was FDA approved in July 2014 for the treatment of toenail onychomycosis due to *T rubrum* and *T mentagrophytes*, with mycologic cure rates of 31.1% and 35.9% and complete cure rates of 6.5% and 9.1%, respectively.<sup>11,17</sup> It is applied with a glass pointed-tip dropper to the nail plate, such that the entire nail is covered as well as under the nail tip. No removal of the solution or debridement is required.<sup>17</sup>

Topical therapies for onychomycosis require long treatment durations, thus excellent compliance and adherence to the treatment protocol are vital to maximize efficacy. Dermatologists who prescribe ciclopirox nail lacquer 8% should counsel patients to remove the lacquer with alcohol weekly, such that the antifungal penetrates the nail plate to reach the site of infection. Monthly debridement also must be clarified before initiating therapy. With all topical therapy for onychomycosis, it is important to treat early, treat concurrently for tinea pedis, and avoid use of nail polish so that patients have the best possible cure rates.

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