There have been many recent additions to the armamentarium—from new dosing protocols to new drugs—for treating onychomycosis and other fungal infections. Beyond clinical issues that need to be addressed, aesthetically, onychomycosis and fungal infections can bother patients. Ahead, we’ll review the latest research on what’s available.

**Luliconazole Cream 1%**. Luzu Cream 1% (luliconazole, Valeant) is FDA approved for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis, caused by *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older. It is the first topical azole antifungal agent approved to treat tinea cruris and tinea corporis with a one-week, once-daily treatment regimen. Interdigital tinea pedis is approved with a two-week, once-daily treatment.

In a Phase II study of luliconazole for the treatment of interdigital tinea pedis, complete clearance was achieved in 26.8% and 45.7% subjects in the two-week and four-week treatment groups at two weeks post-treatment, respectively. The study found that the antifungal affect persisted several weeks post-treatment, resulting in increased rates of mycologic and clinical cure. Four weeks post-treatment complete clearance rates were 53.7 percent and 62.9 percent for the two-week and four-week treatment groups, respectively.

When comparing *in vitro* and *in vivo* antidermatophyte activities, luliconazole exhibited strong antifungal activity against *Trichophyton spp*—its minimum inhibitory concentration (MIC) was one to four times lower than that of lanoconazole or terbinafine. Seven-day topical therapy with 0.5% solution luliconazole was shown to be more effective than lanoconazole or terbinafine (0.5%). Only luliconazole achieved complete mycologic cure.

Efinaconazole. The FDA approved Jublia (efinaconazole 10% topical solution, Valeant) earlier this year as the first topical triazole for the treatment of onychomycosis of the toenails. Jublia was completely cured compared to 3.3 and 5.5 percent of patients treated with vehicle, respectively.

In a multicenter, randomized, double-blind, vehicle-controlled Phase II study investigating the efficacy and safety of efinaconazole in distal lateral subungual onychomycosis (DLSO), 135 subjects were randomized in a 2:2:2:1 ratio to receive efinaconazole 10% solution (with or without semiocclusion), efinaconazole 5% solution, or vehicle, once daily for 36 weeks with one four-week post-treatment follow-up. Efficacy assessments included complete cure, mycologic cure, clinical efficacy. At follow-up, complete cure was numerically higher in all active groups (16-26 percent) compared with vehicle (nine percent). Mycologic cure rates with efinaconazole 10% semiocclusion, efinaconazole 10%, and efinaconazole 5% were 83 percent, 87 percent, and 87 percent, respectively. Efinaconazole 10% (with or without semiocclusion) demonstrated significantly greater clinical efficacy and treatment effectiveness compared to vehicle.

It has also been shown that efinaconazole has a higher percentage of drug unbound to keratin resulting in greater cumulative nail permeation compared to ciclopirox.4

**Tavaborole.** The FDA approved the New Drug Application for Kerydin (tavaborole, Anacor Pharmaceuticals) topical solution 5%, the first oxaborole antifungal approved for the topical treatment of onychomycosis of the toenails due to *Trichophyton rubrum* or *Trichophyton mentagrophytes*.

Kerydin is a clear, colorless, alcohol-based solution applied with a dropper to the infected toenail once daily for 48 weeks. Debridement of the nail is not required during the treatment period. Due to its topical application, Kerydin has low systemic absorption and has not demonstrated systemic side effects.

Kerydin’s efficacy and safety were evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. Kerydin or vehicle was applied once daily for 48 weeks in subjects with 20-60 percent clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement. A total of 1,194 subjects (795 Kerydin, 399 Vehicle) 18 to 88 years of age, participated in these two trials. The primary efficacy endpoint was complete cure (0 percent...
Econazole 1% Foam. Econza (econazole foam 1%, Quinnova) is FDA approved for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older. Econza Foam combines the proven antifungal efficacy of econazole nitrate with the skin-restoring properties of Proderm Technology. Proven to kill fungi that cause interdigital tinea pedis when applied once-daily for four weeks, its unique, alcohol-free foam delivery helps protect and restore skin, penetrating quickly and drying rapidly without the greasy residue that is common among other creams and gels.

In two double-blind, parallel-group, vehicle-controlled, multicenter clinical trials, 495 subjects aged ≥12 years with a clinical diagnosis of interdigital tinea pedis and fungal culture positive for a dermatophyte at baseline received Econza Foam (n=246) or foam vehicle (n=249). Subjects applied Econza Foam or foam vehicle once-daily for four weeks. The primary endpoint was proportion of subjects who achieved a complete cure (negative KOH, negative fungal culture, no evidence of clinical disease as indicated by complete resolution of all signs and symptoms) at two weeks post-treatment (Day 43). Secondary endpoints included mycologic cure (negative KOH and negative culture) and effective treatment (mycologic cure + no or mild erythema and/or scaling and all other signs and symptoms absent).

Econza Foam exhibited superiority over foam vehicle for the primary and secondary endpoints and demonstrated potent antifungal activity against all of the pathogens evaluated with a high mycologic cure rate. The complete cure rate at Day 43 (two weeks post-treatment) was higher in the Econza Foam group (24.3 percent) than in the foam vehicle group (3.6 percent). In addition, higher rates of mycologic cure (67.6 percent vs 16.9 percent) and effective treatment (48.6 percent vs 10.8 percent) were observed with econazole nitrate foam 1% vs the foam vehicle. Econza Foam was safe and well tolerated with a safety profile comparable with the foam vehicle. During clinical trials, the most common adverse reactions were application site reactions, which occurred in less than one percent of subjects in both the Econza Foam and vehicle arms.

Ketoconazole. Xolegel Gel 2% (ketoconazole, Aqua Pharmaceuticals) is currently FDA approved for the topical treatment of seborrheic dermatitis in immunocompetent adults and children 12 years of age and older. Ketoconazole gel 2% has the same side effect precautions as oral ketoconazole on label, but it is doubtful that the side effects are the same. The FDA limited use of ketoconazole oral tablets last year, warning that the oral tablets can cause severe liver injuries and adrenal gland problems and advising that it can lead to harmful drug interactions. The FDA approved label changes and added a new Medication Guide to address these safety issues.

Itraconazole. Itraconazole (Onmel, Merz) once-daily 200mg tablets are FDA approved for once-daily oral treatment of onychomycosis caused by *T. rubrum* or *T. mentagrophytes* in non-immunocompromised patients. Onmel uses Metrex technology to offer a convenient dose with enhanced bioavailability. The 200mg dose has the same active drug and the same warnings as the 100mg tablets. There is no A/B-rated generic substitute for Onmel. Studies of itraconazole 200mg found statistically significant efficacy across all endpoints compared to vehicle at Week 52 (40 weeks after the end of 12-week treatment). It is also noninferior to itraconazole capsules for complete cure of onychomycosis. Safety of itraconazole 200mg is comparable to two 100mg itraconazole capsules.5

This article is based on part of a presentation on new drugs presented at the 2014 Maui Derm, which took place in January 2014 in Hawaii.

5. ONMEL® (itraconazole) 200-mg Tablets. Prescribing Information. Merz Pharmaceuticals, LLC. 2012; Rev 1/12.

Neal Bhatia, MD, FAAD is in private practice in San Diego, CA. Dr. Bhatia has affiliations with Bayer, Dusa, Ferndale, Galderma, Genentech, Leo, Onset, Pharmaderm, Promius, Quinnova, and Valeant Pharmaceuticals.

Ted Rosen, MD is a Professor of Dermatology, Chief of Dermatology Service at Michael E. DeBakey Veterans Affairs Medical Center at Baylor College of Medicine in Houston, TX. Dr. Rosen has affiliations with Anacor, Galderma, Genentech, Merz, Pharmaderm, and Valeant Pharmaceuticals.