Antifungals, Topical
Therapeutic Class Review (TCR)

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FDA-APPROVED INDICATIONS

Drug	Tinea pedis	Tinea cruris	Tinea versicolor	Tinea corporis	Cutaneous candidiasis	Other
benzoic acid/ salicylic acid (Bensal HP®)[1]	--	--	--	--	--	Inflammation and irritation associated with common forms of dermatitis including certain eczematoid conditions and complications associated with pyodermas Treatment of insect bites, burns, and fungal infections
butenafine (Mentax®)[2]	X	X	X	X	--	--
ciclopirox (Loprox®)[3,4,5,6]	X	X	X	X	X	Seborrheic scalp dermatitis
ciclopirox (Ciclodan® cream/kit)[7]	X	X	X	X	X	
ciclopirox (Ciclodan™ solution)[8]	--	--	--	--	--	Topical treatment in immunocompetent patients with mild to moderate onychomycosis of fingernails and toenails due to Trichophyton rubrum
ciclopirox (CNL-8™)[9]						
ciclopirox (Penlac®)[10]						
clotrimazole (Alevazol [OTC])[11] (Lotrimin®)[12]	X	X	X	X	X	--
clotrimazole / betamethasone (Lotrisone®)[13]	X	X	--	X	X	--
econazole[14]	X	X	X	X	X	--
econazole (Ecoza™)[15]	X	--	--	--	--	--
efinaconazole (Jublia®)[16]	--	--	--	--	--	Topical treatment of onychomycosis of the toenails due to Trichophyton rubrum and Trichophyton mentagrophytes
ketoconazole cream[17]	X	X	X	X	X	Seborrheic dermatitis
ketoconazole (Extina®)[18]	--	--	--	--	--	Seborrheic dermatitis
ketoconazole (Ketodan™)[19]			--	--	--	Seborrheic dermatitis
ketoconazole (Nizoral Shampoo®)[20]	--	--	X	--	--	--

FDA-Approved Indications (continued)

Drug	Tinea pedis	Tinea cruris	Tinea versicolor	Tinea corporis	Cutaneous candidiasis	Other
ketoconazole (Xolegel®)[21]	--	--	--	--	--	Seborrheic dermatitis
luliconazole (Luzu™)[22]	X	X	--	X	--	Caused by the organism Trichophyton rubrum and Epidermophyton floccosum
miconazole (Azolen™)[23]	X	--	--	X	--	--
miconazole (Fungoid®)[24]	X	--	--	X	--	--
miconazole[25]	X	X	X	X	X	--
miconazole / zinc oxide / white petrolatum (Vusion®)[26]	--	--	--	--	--	Diaper dermatitis (adjunctive treatment)
miconazole (Zeasorb®)[27]	X	X	--	--	--	--
naftifine (Naftin®)[28]	X	X	--	X	--	--
nystatin[29]	--	--	--	--	X	--
nystatin (Pediaderm AF)[30]	--	--	--	--	X	--
nystatin / triamcinolone[31]	--	--	--	--	X	--
oxiconazole (Oxistat®)[32]	X	X	X (cream only)	X	--	--
sertaconazole (Ertaczo®)[33]	X	--	--	--	--	--
sulconazole (Exelderm®)[34]	X	X	X	X	--	--
tavaborole (Kerydin™)[35]	--	--	--	--	--	Topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes
terbinafine (Lamisil®)[36]	X	X	X	X	--	--
tolnaftate (Fungoid-D™)[37]	X	--	--	--	--	--
tolnaftate (Tinactin®)[38]	X	X	X	X	--	--
undecylenic acid (Hongo Cura MS)[39]	X	X	--	X	--	Relief of itching, burning, and cracking
undecylenic acid / zinc undecylenate (Fungi Nail)[40]	X	--	--	X	--	Relief of itching, burning, and cracking
undecylenic acid / zinc undecylenate (Hongo Cura RS)[41]	X	--	--	X	--	Relief of itching, burning, and cracking

Treatment of tinea versicolor requires a legend topical product while the treatment of tinea pedis, tinea cruris, or tinea corporis may be treated with an over-the-counter (OTC) topical agent.

Drug	Manufacturer
benzoic acid/salicylic acid (Bensal HP)	Seven Oaks
butenafine (Mentax)	Mylan Pharmaceuticals
butenafine OTC	Generic
ciclopirox (Ciclodan)	Medimetriks
ciclopirox (CNL-8)	Innocutis Holding
ciclopirox (Loprox)	Generic
ciclopirox (Penlac)	Generic
clotrimazole (Desenex) OTC	Novartis
clotrimazole (Lotrimin)	Generic
clotrimazole OTC (Alevazol)	Generic Capital
clotrimazole/betamethasone (Lotrisone)	Generic
econazole	Generic
econazole (Ecoza)	Quinnova Pharmaceuticals
efinaconazole (Jublia)[42]	Valeant
ketoconazole (Extina)	Stiefel
ketoconazole (Ketodan)	Medimetriks
ketoconazole (Nizoral Shampoo)	Generic
ketoconazole (Xolegel)	Aqua
ketoconazole cream	Generic
luliconazole (Luzu)[43]	Valeant
miconazole (Azolen) OTC	Stratus
miconazole (Fungoid) OTC	Valeant
miconazole OTC	Generic
miconazole (Nuzole)	Vertical Pharmaceuticals
miconazole (Zeasorb) OTC	Stiefel
miconazole / zinc oxide/ white petrolatum (Vusion)	Prestium
naftifine (Naftin)	Merz
nystatin	Generic
nystatin (Pediaderm AF)	Arbor
nystatin/triamcinolone	Generic
oxiconazole (Oxistat)	Sandoz

Drug	Manufacturer
sertaconazole (Ertaczo)	Valeant
sulconazole (Exelderm)	Ranbaxy
tavaborole (Kerydin)[44]	Anacor Pharmaceuticals
terbinafine (Lamisil) OTC	Generic
tolnaftate (Fungoid-D) OTC[45]	Valeant
tolnaftate OTC	Generic
undecylenic acid (Hongo Cura) solution OTC	Kramer
undecylenic acid / zinc undecylenate (Fungi Nail) OTC (Hongo Cura) OTC	Kramer

OVERVIEW

Tinea cruris, corporis, and pedis, named for the body sites involved, are superficial fungal infections (dermatophytosis) caused by three genera of dermatophytes: *Trichophyton*, *Microsporum*, and *Epidermophyton.*[46] These dermatophytes are a homogenous group of fungi that live on the keratin of the stratum corneum, nails, and hair. The estimated lifetime risk of acquiring tinea infections is between 10 and 20%.[47]

Dryness of the skin's outer layer discourages colonization by microorganisms, and shedding of epidermal cells keeps many microbes from establishing residence. With inhibition or failure of the skin's protective mechanisms, cutaneous infection may occur with subsequent pruritus, redness, and scaling. Since dermatophytes require keratin for growth, they are restricted to hair, nails, and superficial skin; therefore, most can be treated with topical antifungal medications.[48]

Tinea pedis (athlete's foot) is one of the most common superficial fungal infections of the skin and is most often caused by the dermatophytes *Trichophyton rubrum, Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.[49] Affected skin is usually pruritic with scaling plaques on the soles extending to the lateral aspect of the feet and interdigital spaces. Tinea cruris is a dermatophyte infection of the groin (jock itch) also caused by *T. rubrum, T. mentagrophytes*, and *E. floccosum.* This condition affects the skin of the medial and upper parts of the thighs, usually bilaterally, with severe pruritus. Tinea corporis (ringworm on the skin) refers to tinea anywhere on the body except the scalp, beard, feet, or hands. *Trichophyton* and *Microsporum* are usually the causative organisms. Each lesion may have one or several concentric rings with red papules or plaques in the center. As the lesion progresses, the center may clear, leaving post-inflammatory hypopigmentation or hyperpigmentation.

Tinea versicolor, a common superficial fungal infection, is caused by *Malassezia* species (formerly *Pityrosporon*).[50] This organism is part of the normal flora in most individuals but is capable of becoming pathogenic under certain conditions. The most distinctive clinical feature is the change in pigmentation on the affected sites. Mild scaling and pruritus are usually the only other sequelae.

Cutaneous candidiasis, usually caused by *Candida albicans*, may colonize occluded areas or folds of the skin, producing infection in areas, such as the groin, axillae, and interdigital spaces. Clinical manifestations include erythema, scaling, maceration, vesicles, and pustules.

Onychomycosis is a fungal infection of the nailbed (skin beneath the nail plate) with secondary involvement of the nailplate (visible part of the nail on fingers and toes). The main pathogens responsible for onychomycosis are dermatophytes, yeasts, and molds. Despite significant improvements, approximately 20% of patients with onychomycosis still fail on antifungal therapy. More common in toenails than fingernails, they often cause the end of the nail to separate from the nail bed. Additionally, debris (white, green, yellow, or black) may build up under the nail plate and discolor the nail bed.[51]

Seborrheic dermatitis is one of the more common cutaneous diseases.[52] One proposed etiology is overgrowth of yeast, which normally inhabits sebaceous skin of the scalp, eyebrows, and central face. The disease typically occurs in 3 age groups, which are infancy, middle age, and seniors. Seborrheic dermatitis in adults typically involves the scalp, face, neck, mid upper chest, and intertriginous zones (axillae, groin, and submammary).

PHARMACOLOGY[53]

The mechanism of action of benzoic acid/salicylic acid (Bensal HP) is unknown. It has been demonstrated that benzoic acid/salicylic acid (Bensal HP) reduces methicillin-resistant *Staphylococcus aureus* (MRSA) protected by biofilms in wounds using porcine models and stimulates re-epithelialization of second-degree burns in porcine models.

Undecylenic (Hongo Cura MS) and undecylenic/zinc undecylenate (Fungi Nail, Hongo Cura RS) acid are organic unsaturated fatty acids derived from castor oil that have 11 carbons in the fatty acid chain. The exact mechanism of action of undecylenic/undecylenate acid is unknown. It has been demonstrated that undecylenic/undecylenate acid inhibits morphogenesis of Candida albicans by interference with fatty acid biosynthesis, which can inhibit germ tube (hyphae) formation. Medium-chain fatty acids have also been shown to disrupt the pH of the cell cytoplasm by being proton carriers, which interferes with vial replication mechanism in infected cells. The mechanism of action and effectiveness in fatty acid based antifungal is dependent on the number of carbon atoms in the chain. The more carbon atoms in a chain, the more effective the fatty acid-based antifungal.

The other agents in this category can be divided into 2 principal pharmacologic antifungal groups, the allylamines and the azoles.

Butenafine (Mentax) is structurally and pharmacologically related to the allylamine antifungal agents, which include naftifine (Naftin) and terbinafine (Lamisil). The exact mechanisms of the fungicidal action are unknown for these agents. Presumably, they exert antifungal activity by altering cellular membranes resulting in increased cellular permeability and growth inhibition. They may also interfere with sterol biosynthesis at an earlier stage than do the imidazole derivatives. They are active against many fungi and yeasts. Tolnaftate (Tinactin) works in a similar manner to these agents, although it is a thiocarbamate antifungal. Shorter time to cure is usually seen with fungicidal agents.

Clotrimazole (Alevazol, Lotrimin, Desenex), econazole (Ecoza), ketoconazole (Extina, Ketodan, Nizoral Shampoo, Xolegel), miconazole (Azolen, Fungoid, Zeasorb, Nuzole, Vusion), oxiconazole (Oxistat), sulconazole (Exelderm), and sertaconazole (Ertaczo) are azole antifungals (imidazole derivatives). The imidazole-derivative azole antifungals exert antifungal activity by altering cell membrane permeability by binding with phospholipids in the fungal cell membrane. They are active against many fungi including dermatophytes and yeasts. The azole antifungals, miconazole, clotrimazole, and

ketoconazole, are fungistatic and generally require epidermal turnover to shed living fungus from the skin.[54]

Efinaconazole (Jublia) is also an azole antifungal. The antifungal activity is attributed to disruption of the normal fungal cell membrane permeability by inhibiting lanosterol demethylase, which leads to a decrease in ergosterol concentration and accumulation of lanosterol.

Tavaborole (Kerydin) is an oxaborole antifungal with activity attributed to inhibition of fungal protein synthesis. This is done by inhibition of aminoacyl-transfer ribonucleic acid (tRNA) synthetase (AARS).[55]

Ciclopirox (Ciclodan, Loprox, Penlac, CNL-8) is thought to act by chelating polyvalent cations (Fe^{+3} or Al^{+3}) resulting in the inhibition of the metal dependent enzymes responsible for the degradation of peroxides within the fungal cell. Ciclopirox is active against many genera of fungi, including dermatophytes and yeast.

Nystatin Pediaderm AF) exerts its antifungal activity by binding to sterols in the fungal cell membrane. As a result of this binding, the membrane is no longer able to function as a selective barrier, and potassium and other cellular constituents are lost.

PHARMACOKINETICS[56,57,58,59,60,61,62 63,64,65,66,67,68,69,70,71]

Due to the nature of topical application, all products minimally expose the systemic circulation.

Cream: Creams are oil-in-water emulsions and are generally less greasy than ointments. Creams are usually less effective than ointments.

Gel: Gels consist of a solid, jelly-like material that is mostly liquid, but contains a substantially dilute crosslinked system that gives the gel the property of thixotropy (the gel is solid until the material is agitated and then becomes liquid). They can also be a highly absorbent drug delivery system with natural or synthetic polymers and can act as reservoirs in topical drug delivery.

Lotion: Lotions are diluted creams.

Ointment: Ointments are best at delivering drug to the skin and provide a barrier.

Solutions: Solutions are typically alcoholic liquids and are especially useful for the scalp because they do not coat the hair.

Lacquer: Nail lacquers are topical solutions intended only for use on fingernails and toenails and immediately adjacent skin.

Foam: Foam is a topical product that can be used on the scalp, body, and face. It quickly dissolves leaving minimal residue.

Powder: Powders are beneficial due to their ease of application but generally are less effective than other formulations. Due to their lack of absorption, they can be used over large areas and sometimes are used preventatively in patients prone to tinea pedis and tinea cruris.

CONTRAINDICATIONS/WARNINGS

Hypersensitivity to any component of these agents is considered a contraindication for use.[72] These are topical agents and not intended for ophthalmic, vaginal, or oral use.[73]

Benzoic acid/salicylic acid (Bensal HP) is contraindicated in patients with hypersensitivity type reactions to topical polyethylene glycols.[74]

Ciclopirox (Ciclodan, CNL-8, Loprox, Penlac,) should be avoided in patients with a history of seizure disorders or immunosuppression.[75,76,77]

Combination products containing corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression if applied over large surface areas, associated with prolonged use, used under occlusive dressings, or used in combination with other topical corticosteroids. If HPA suppression is noted, then, if possible, the drug should be discontinued or the application reduced in frequency.[78,79]

Xolegel contains 34% dehydrated alcohol. Extina and Ecoza contain alcohol and propane/butane. So fire, flame, or smoking during and immediately following application of these products should be avoided.[80,81] Do not store containers in sunlight or expose containers to heat or temperatures above 120°F (49°C), even when empty.[82]

Effects, such as hepatitis, lowered testosterone, and ACTH-induced corticosteroid serum levels have been seen with oral ketoconazole; however, these adverse events have not been observed with topical ketoconazole.[83]

Loprox shampoo has had some rare reports of hair discoloration occurring on patients with light colored hair.[84]

Miconazole (Vusion) should not be used to prevent diaper dermatitis, as in an adult institutional setting. Preventative use may lead to the development of resistance.[85]

Undecylenic (Hongo Cura MS) and undecylenic/zinc undecylenate (Fungi Nail, Hongo Cura RS) should not be used to treat or prevent diaper rash.[86]

DRUG INTERACTIONS[87,88,89]

Significant drug interactions with the topical agents have not been noted, with the exception of econazole and luliconazole.

Concomitant administration of warfarin and econazole has resulted in the enhancement of the anticoagulant effect. Monitoring International Normalized Ratio (INR) and/or prothrombin time may be indicated especially for patients who apply econazole to large body surface areas, in the genital area, or under occlusion.

Based on an in vitro assessment, luliconazole has the potential to inhibit cytochrome P-450 (CYP) enzymes 1A2, 2C9, 2C19, 2D6, and 3A4. At therapeutic doses, luliconazole may also inhibit the activity of CYP2C19 and CYP3A4; however, the potential inhibitory activity is theoretical as there have been no *in vivo* drug interaction trials conducted to evaluate the effect of luliconazole on other drugs that are substrates of CYP2C19 and CYP3A4.

ADVERSE EFFECTS

Drug	Burning	Itching	Application Site Reaction	Erythema
benzoic acid/salicylic acid (Bensal HP)[90]	reported	nr	nr	nr
butenafine (Mentax)[91]	<2	<2	<2	<2
Ciclopirox (Ciclodan® cream/kit)[92]	reported	reported	reported	nr
ciclopirox (Ciclodan solution, CNL-8, Penlac,)[93, 94, 95, 96]	1	nr	1	5
ciclopirox (Loprox)[97, 98, 99, 100]	7-34	1-5	1-5	1
clotrimazole (Alevazol)[101] (Desenex)[102] (Lotrimin)[103]	reported	reported	reported	reported
clotrimazole/betamethasone (Lotrisone)[104]	reported	reported	reported	reported
econazole[105]	reported	reported	3	reported
econazole (Ecoza)[106]	nr	nr	< 1	nr
efinaconazole (Jublia)[107]	nr	nr	4.9*	nr
ketoconazole (Extina)[108]	10	≤1	6	≤1
ketoconazole (Ketodan)[109]	10	≤1	6	≤1
ketoconazole (Nizoral Shampoo)[110]	nr	<3	<3	nr
ketoconazole (Xolegel)[111]	4	<1	reported	<1
ketoconazole cream[112]	5	reported	reported	nr
luliconazole (Luzu)[113]	nr	nr	<1	nr
miconazole ()[114]	reported	reported	reported	nr
miconazole (Zeasorb)[115]	nr	nr	nr	nr
miconazole tincture (Azolen, Fungoid)[116, 117]	nr	nr	nr	nr
miconazole/zinc oxide/ white petrolatum (Vusion)[118]	reported	reported	reported	reported
naftifine (Naftin 1% cream)[119]	6	≥2	reported	2%
naftifine (Naftin 1% gel)[120]	5%	1	reported	0.5
naftifine (Naftin 2% cream)[121]	reported	≥ 1	reported	reported
naftifine (Naftin 2% gel)[122]	reported	reported	2%	reported
nystatin[123]	nr	nr	reported	nr
nystatin (Pediaderm AF)[124]	nr	nr	reported	nr
nystatin/ triamcinolone[125]	reported	reported	reported	nr
oxiconazole (Oxistat)[126]	0.7-1.4	0.4-1.6	0.4	0.2
sertaconazole (Ertaczo)[127]	reported	nr	reported	nr

Adverse Effects (continued)

Drug	Burning	Itching	Application Site Reaction	Erythema
sulconazole (Exelderm)[128]	3	3	reported	1
tavaborole (Kerydin)[129]	nr	nr	4	1.6
terbinafine (Lamisil)[130]	1-2	1-2	1-2	nr
tolnaftate cream (Fungoid-D)	nr	nr	nr	nr
tolnaftate (Tinactin)[131]	nr	nr	reported	nr
undecylenic acid (Hongo Cura) spray	nr	nr	nr	nr
undecylenic acid/ zinc undecylenate (Fungi Nail) (Hongo Cura RS) ointment	nr	nr	nr	nr

Adverse effects are indicated as percentage occurrence. Adverse effects data are compiled from package inserts and cannot be considered comparative or all inclusive. nr = not reported

* Application site reactions for efinaconazole were defined as site dermatitis, site vesicles, and site pain.

**Application site reactions for tavaborole were defined as exfoliation and dermatitis.

The incidence of nail disorders, such as shape change, irritation, ingrown toenail, discoloration, and application site reactions were similar between ciclopirox (Ciclodan, CNL-8, Penlac,) and vehicle.

SPECIAL POPULATIONS

Pediatrics

Fungal infections can occur in children and may frequently present as tinea corporis (includes ringworm), diaper dermatitis, and tinea capitis. Infants and young children may experience diaper dermatitis when infected with *Candida sp.*, which may respond rapidly to topical therapy including ciclopirox, nystatin, and several other agents in this class.[132] Drugs which have safety and effectiveness data for children include clotrimazole, miconazole, tolnaftate, and undecylenic/zinc undecylenate which can be used in patients ages 2 years and older; Vusion may be used in children 4 weeks of age and older.[133] In addition, butenafine (Mentax), econazole (Ecoza), ketoconazole gel (Xolegel), ketoconazole foam (Extina, Ketodan), and sertaconazole (Ertaczo) are approved for use in children ages 12 years and older.[134] Oxiconazole (Oxistat) cream may be used in pediatric patients for tinea corporis, tinea cruris, tinea pedis, and tinea versicolor; however, these approved indications rarely occur in children less than the age of 12 years.[135] Ciclopirox cream and suspension can be used in patients aged 10 years and older, nail lacquer in patients aged 12 years and older, and gel and shampoo in patients aged 16 years and older. Nystatin (Pediaderm AF) can be used at any age, including infancy, while the combination product nystatin/triamcinolone can be used in children 2 months of age and older. Clotrimazole/betamethasone is not recommended for those less than 17 years of age.[136] Safety and effectiveness of econazole, efinaconazole (Jublia), ketoconazole cream, luliconazole (Luzu), naftifine (Naftin), sulconazole (Exelderm), tavaborole (Kerydin), and terbinafine (Lamisil) for pediatric patients have not been established.[137,138,139,140,141,142]

Pregnancy[143]

All agents in this category are Pregnancy Category B with the exception of benzoic acid/salicylic acid (Bensal HP), clotrimazole/betamethasone, econazole (Ecoza), efinaconazole (Jublia), ketoconazole cream, ketoconazole (Extina, Ketodan, Nizoral, Xolegel), luliconazole (Luzu), miconazole (Azolen, Fungoid, Zeasorb, Vusion), nystatin, nystatin/triamcinolone, sertaconazole (Ertaczo), sulconazole (Exelderm), tavaborole (Kerydin), and tolnaftate, which are Pregnancy Category C.

Undecylenic/zinc undecylenate has not been assigned a specific FDA pregnancy risk category rating.

DOSAGES

Drug	Frequency of Application	Rx Availability	OTC Availability
benzoic acid/ salicylic acid (Bensal HP)[144]	Twice daily for 7 days	6%/3% ointment	--
butenafine (Mentax)[145]	Once to twice daily for 1 to 4 weeks	1% cream	Lotrimin Ultra 1% cream
ciclopirox (Loprox)[146, 147, 148, 149]	Gel, topical suspension: twice daily for 4 weeks Shampoo: Apply 5 mL to scalp as directed twice a week for 4 weeks; a minimum of 3 days should occur between applications	0.77% gel 0.77% TS suspension 1% shampoo	--
Ciclopirox (Ciclodan)[150]	Cream, kit : twice daily for 4 weeks	0.77% cream 0.77% cream (co-packaged with skin cleanser combination #23 (Rehyla™) cleanser	--
ciclopirox (Ciclodan)[151]	Once daily (preferably at bedtime or 8 hours before washing) to all affected nails for 48 weeks; daily applications should be made over the previous coat and removed with alcohol every 7 days	8% nail lacquer topical solution	--
ciclopirox (Penlac)[152]			
ciclopirox (CNL-8)[153]			
clotrimazole	2 to 4 times daily for up to 4 weeks	--	AF 1% cream 1% solution
clotrimazole (Lotrimin)[154]	2 to 4 times daily for up to 4 weeks	1% cream 1% solution	AF 1% cream AF 1% solution
clotrimazole (Alevazol)[155]	2 to 4 times daily for up to 4 weeks	--	1% ointment
clotrimazole / betamethasone (Lotrisone)[156]	Twice daily for 2 to 4 weeks	1% / 0.05% cream 1% / 0.05% lotion	--
econazole[157]	Once to twice daily for 2 to 4 weeks	1% cream	--

Dosages (continued)

Drug	Frequency of Application	Rx Availability	OTC Availability
econazole (Ecoza) [158]	Once daily for 4 weeks	1% foam	--
efinaconazole (Jublia) [159]	Apply once daily for 48 weeks to the toenail, toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate using the integrated flow-through brush applicator	10% solution	--
ketoconazole (Extina)[160]	Twice daily for 4 weeks	2% foam	--
ketoconazole cream[161]	Cream: once daily for 2 to 6 weeks depending on indication; apply twice daily for 4 weeks or until clinical clearing for seborrheic dermatitis	2% cream	--
ketoconazole (Ketodan)[162]	Twice daily for 4 weeks	2% foam 2% foam combo package (co-packaged with skin cleanser combination #23 (Rehyla™) cleanser)	--
ketoconazole (Xolegel)[163]	Daily for 2 weeks	2% gel	--
ketoconazole (Nizoral Shampoo)[164]	Shampoo 2%: use as directed twice a week for 4 weeks Shampoo 1%: use every 3 to 4 days for up to 8 weeks	2% shampoo	A-D 1% shampoo
luliconazole (Luzu)[165]	Apply a thin layer to the affected area and approximately 1 inch on the immediate surrounding area(s) once daily for 1 week (tinea cruris and corporis) or 2 weeks (tinea pedis)	1% cream	--
miconazole (Azolen, Fungoid tincture)[166]	Apply thin layer twice a day (morning and night) on skin, under nails, and surrounding cuticle areas.	--	2% tincture
miconazole ([167,168]	Twice daily for 2 to 4 weeks	2% cream	2% powder (Lotrimin AF) 2% liquid (Lotrimin AF) 2% cream 2% spray 2% gel 2% ointment 2% cream (Nuzole)

Dosages (continued)

Drug	Frequency of Application	Rx Availability	OTC Availability
miconazole (Zeasorb)[169]	Twice daily for 2 to 4 weeks	--	2% alcohol-gel 2% powder
miconazole / zinc oxide / white petrolatum (Vusion)[170]	Apply at each diaper change for 7 days	0.25% / 15% / 81.35% ointment	--
naftifine (Naftin)[171]	Cream: daily for 4 weeks Gel: twice daily for 4 weeks	1% cream 1% gel	--
naftifine (Naftin)[172]	Cream: once daily for 2 weeks Gel: once daily for 2 weeks	2% cream 2% gel	--
nystatin[173,174]	Cream, ointment: twice daily until healing is complete Powder: 2 to 3 times daily until healing is complete	100,000 units / gm cream 100,000 units / gm powder 100,000 units / gm ointment Nyata™ Kit: 100,000 units / gm powder (three 15 gm bottles) copackaged with Curatin™ exfoliating serum (114 gm)	--
nystatin (Pediaderm AF)[175]	Twice daily until healing is complete	Pediaderm AF Complete Kit 100,000 units / gm cream	--
nystatin / triamcinolone[176]	Twice daily	100,000 units / gm / 0.1% cream 100,000 units / gm / 0.1% ointment	--
oxiconazole (Oxistat)[177]	Once to twice daily for 2 to 4 weeks	1% cream 1% lotion	--
sertaconazole (Ertaczo)[178]	Twice daily for 4 weeks	2% cream	--
sulconazole (Exelderm)[179]	Once to twice daily for 2 to 4 weeks	1% cream 1% solution	--
tavaborole (Kerydin) [180]	Apply once daily for 48 weeks to entire toenail surface	5% solution	--
terbinafine (Lamisil)[181]	Cream: twice daily for 1 to 2 weeks Spray: once or twice daily for 1 week Gel: once daily for 1 week	--	1% cream 1% spray 1% gel
tolnaftate	Twice daily for 2 to 4 weeks	--	1% cream 1% powder 1% powder spray 1% solution 1% liquid spray

Dosages (continued)

Drug	Frequency of Application	Rx Availability	OTC Availability
tolnaftate (Fungoid-D)[182]	Apply thin layer once to twice daily (morning and/or night)	--	1% cream
tolnaftate (Tinactin)[183]	Twice daily for 2 to 4 weeks	--	1% cream 1% powder 1% powder spray 1% liquid spray
undecylenic acid (Hongo Cura)	Tinea cruris: twice daily (morning and night) for 2 weeks Tinea pedis and corporis: twice daily (morning and night) for 4 weeks	--	25% spray
undecylenic acid / zinc undecylenate (Fungi Nail) (Hongo Cura)	Twice daily (morning and night) for 4 weeks	--	5%-20% ointment

In general, tinea corporis and tinea cruris require treatment for 2 weeks, whereas tinea pedis may require treatment for up to 4 weeks.[184] Treatment should continue for at least 1 week after symptoms have resolved.[185] Therapy with ciclopirox (Penlac, CNL-8) is recommended for 48 weeks.

CLINICAL TRIALS

Search Strategies

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved topical use of all drugs in this class. Studies included for analysis in the review were published in English, performed with human participants, and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80% of participants entering the investigation. Despite some inherent bias found in all studies, including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship and/or funding must be considered, the studies in this review have also been evaluated for validity and importance.

Tinea Corporis

tolnaftate cream (Tinactin) verses undecylenic/zinc undecylenate cream verses placebo

Ninety seven subjects with dermatophytosis of the glabrous skin and groin, were randomly assigned to receive 1% tolnaftate, 3% undecylenic acid and its zinc salt (zinc undecylenate), or placebo cream in a double-blind manner.[186] Thirty three subjects received 1% tolnaftate cream and 21 of those subjects were cured clinically and mycologically. Thirty two subjects received 3% undecylenic acid and 20% zinc undecylenate cream of which 21 subjects were cured clinically and mycologically. In contrast, only 3 of the 32 subjects that received the placebo cream were cured clinically and mycological. Treatments with tolnaftate and undecylenic/zinc undecylenate appeared safe and effective in dermatophytoses of the glabrous skin.

Tinea Cruris and Tinea Corporis

butenafine (Mentax) versus clotrimazole (Lotrimin)

Eighty patients, diagnosed with tinea cruris or tinea corporis, were randomly assigned to butenafine once daily for 2 weeks or clotrimazole twice daily for 4 weeks in a double-blind manner.[187] Follow-up was done at 1, 2, 4, and 8 weeks. At the end of 1 week, butenafine recipients exhibited higher clinical cure rate compared to clotrimazole recipients (26.5 versus 2.9%, respectively), as well as higher mycological cure (61.7 versus 17.6%, respectively); however, this difference was not statistically significant at 4 and 8 weeks of treatment.

luliconazole (Luzu) versus placebo

In a randomized, double-blind, vehicle-controlled, multicenter clinical trial, 256 subjects with a clinical and culture confirmed diagnosis of tinea cruris were evaluated based on the safety and efficacy of luliconazole 1% cream[188,189]. The patients either applied luliconazole 1% cream or vehicle cream to the affected area and approximately 2.5cm (1 inch) of the surrounding area once daily for 7 days. The signs and symptoms of tinea cruris (erythema, scaling, and pruritus), KOH (potassium hydroxide) examination, and dermatophyte culture were assessed at baseline, end-of-treatment (Day 7), and 2 and 3 weeks post-treatment. The treatment success was defined as complete clearance (clinical cure and mycological cure) at 3 weeks post-treatment. Complete clearance in patients with tinea cruris was demonstrated with luliconazole 1% cream. The 3-week post-treatment outcomes for luliconazole 1% cream (n=165) yielded 21% complete clearance, 43% effective treatment, 24% clinical cure, and 78% mycological cure, as compared to the vehicle cream group (n=91) that yielded 4% complete clearance, 19% effective treatment, 7% clinical cure, and 45% mycological cure.

naftifine (Naftin) versus econazole

Patients with tinea cruris or tinea corporis (n=104) were evaluated in a double-blind, randomized study.[190] Naftifine 1% cream or econazole 1% cream were applied to affected areas twice daily for 4 weeks. After 1 week of treatment, naftifine had an overall cure rate of 19% compared with 4% for econazole (p=0.03). Two weeks after the end of treatment, both medications had overall cure rates of approximately 80%. A difference in favor of naftifine, although not statistically significant after the first week, persisted throughout treatment. Three percent of the naftifine patients had adverse effects compared with 13% of the econazole subjects.

Tinea Pedis

econazole foam (Ecoza) versus placebo

In 2 randomized, double-blind, vehicle-controlled, multicenter, clinical trials, 505 patients with interdigital tinea pedis were randomized 1:1 to Ecoza 1% topical foam or vehicle.[191] The patients ranged in age from 12 to 71 years with 5 subjects less than 18 years of age at baseline. Patients applied the assigned medication once daily for 4 weeks. The severity of erythema, scaling, fissuring, maceration, vesiculation, and pruritus were graded using a 4-point scale (none, mild, moderate, severe). Patients had KOH (potassium hydroxide) examination and fungal cultures taken to confirm eligibility. A total of 339 subjects with positive fungal cultures were evaluated for efficacy. Efficacy was evaluated on Day 43, 2-weeks post-treatment with treatment success being defined as complete cure

(negative KOH and fungal culture and no evidence of clinical disease). Complete cure rates at 2-weeks post treatment (Day 43) were 23.2% for Ecoza 1% topical foam and 2.4% for the foam vehicle in trial 1, and 25.3% for Ecoza 1% topical foam and 4.8% for the foam vehicle in trial 2. The effective treatment (mycological cure and no or mild erythema and/or scaling with all other signs and symptoms absent) and mycological cure (negative KOH and Fungal culture) rates were also measured 2-weeks post-treatment (Day 43). The effective treatment rates for trial 1 were 48.8% for Ecoza 1% foam and 10.8% for the foam vehicle, and trial 2 reflected 48.4% for Ecoza and 10.8% for the vehicle. The mycological cure rates in trial 1 were 68.3% for Ecoza and 15.7% for the vehicle; in trial 2, the rates were 67% for Ecoza and 18.1% for the vehicle.

ketoconazole (Nizoral) versus clotrimazole (Lotrimin)

The effects of clotrimazole 1% cream and ketoconazole 2% cream were compared in a double-blind, randomized manner for therapy of interdigital tinea pedis in 106 treated patients.[192] Ketoconazole cream was used twice daily, and clotrimazole cream was administered once daily; both were used for 4 weeks. The number of patients with cure or improvement after 4 weeks was comparable (62% clotrimazole group versus 64% ketoconazole group). The mycological response revealed a negative culture and microscopy in 53.1 versus 52.1% of the patients after 14 days, in 76 versus 79.2% after 28 days, and in 83.7 versus 76.9% after 56 days of observation in clotrimazole versus ketoconazole, respectively. The overall score of the development of tinea-related signs and symptoms did not show relevant differences between the 2 drugs. Better results were obtained under clotrimazole than under ketoconazole for pruritus (97.8 versus 89.6%) and burning/stinging (97.5 versus 89.4%). Treatments appeared comparably safe and tolerable.

luliconazole (Luzu) versus placebo

In 2 randomized, double-blind, vehicle-controlled, multicenter trials, the safety and efficacy of luliconazole 1% cream were evaluated in 423 patients with clinical and culture-confirmed diagnosis of interdigital tinea pedis.[193,194] The randomized patients either applied luliconazole 1% cream or vehicle cream to the entire area of the forefeet, including all interdigital web spaces and approximately 2.5 cm (1 inch) of the surrounding area of the foot, once daily for 14 days. The signs and symptoms of tinea pedis (erythema, scaling, and pruritus), KOH (potassium hydroxide) examination, and dermatophyte culture were assessed at baseline, end-of-treatment (Day 14), and 2- and 4-weeks post-treatment. Success was defined as complete clearance (clinical cure and mycological cure) at 4-weeks post-treatment. Complete clearance in patients with interdigital tinea pedis was demonstrated with luliconazole 1% cream. The 4-week post-treatment outcomes for study one regarding luliconazole cream (n=106) yielded 26% complete clearance, 48% effective treatment, 29% clinical cure, and 62% mycological cure, as compared to the vehicle cream group (n=103) that yielded 2% complete clearance, 10% effective treatment, 8% clinical cure, and 18% mycological cure. The 4-week post-treatment outcomes for Study two regarding the luliconazole cream 1% group (n=107) yielded 14% complete clearance, 33% effective treatment, 15% clinical cure, and 56% mycological cure, as compared to the vehicle cream group (n=107) that yielded 3% complete clearance, 15% effective treatment, 4% clinical cure, and 27% mycological cure.

terbinafine (Lamisil) versus clotrimazole (Lotrimin)

A multicenter, randomized, double-blind, parallel-group study in 256 patients with tinea pedis compared the safety and efficacy of the twice daily application of terbinafine 1% cream for 1 week (placebo given for the remaining 3 weeks) with the twice daily application of clotrimazole 1% cream for 4 weeks.[195] Mycological cure and effective treatment were assessed 4 and 6 weeks after commencing therapy. Mycological cure rates at 4 weeks were 93.5% for terbinafine and 73.1% for clotrimazole (p=0.0001). Effective treatment rates at 4 weeks were 89.7% for terbinafine and 58.7% for clotrimazole (p=0.0001), and at 6 weeks were 89.7% for terbinafine and 73.1% for clotrimazole (p=0.002).

In a double-blind, clinical trial, 429 patients with tinea pedis were randomized to receive terbinafine 1% topical solution twice daily for 1 week followed by a vehicle application for 3 weeks, or clotrimazole 1% solution for 4 weeks.[196] Patients were evaluated at baseline and at weeks 1, 2, 4 (end of treatment), and 8 (end of follow-up). Effective treatment results were similar and were recorded in 83% of terbinafine patients and 82% of clotrimazole patients. Mycological cure and disappearance of signs and symptoms were similar at each assessment visit in the 2 groups. The mycological cure rate was 95% with terbinafine solution and 91% with clotrimazole solution (p=0.05). Mild to moderate adverse events occurred in 4 to 5% of patients in each group.

A multicenter, prospective, randomized, double-blind, parallel-group study compared the efficacy and tolerability of terbinafine 1% cream with clotrimazole 1% cream in the treatment of interdigital tinea pedis.[197] Patients received either terbinafine twice daily for 1 week followed by a placebo cream for 5 weeks or clotrimazole twice daily for 4 weeks. Outcome measures were observed at 1, 4, 8, and 12 weeks after the commencement of the study. Of the 217 patients randomized, 104 had a culture-confirmed dermatophyte infection at baseline. In these patients, 84.6% in the terbinafine group were culture-negative after 1 week compared with only 55.8% in the clotrimazole group. Both agents were well tolerated.

sertaconazole (Ertaczo) versus placebo

A total of 383 patients with tinea pedis were evaluated after receiving either sertaconazole 2% cream twice daily for 4 weeks or vehicle control in 2 randomized, double-blind, parallel group, multicenter studies.[198] Results demonstrated a 70.3% mycologic cure reported in the study group versus 36.7% with the vehicle group (p<0.0001). At week 6, 46.7% of the sertaconazole group had successful treatment outcomes versus 14.9% of the vehicle group (p<0.0001). Both treatment arms were well-tolerated.

Tinea Versicolor

ciclopirox cream (Loprox) versus clotrimazole cream

Two randomized, double-blind, parallel-group, multicenter studies assessed the efficacy and safety of ciclopirox 1% cream in patients with tinea versicolor.[199] The first study compared ciclopirox with the placebo cream vehicle, and the second study compared ciclopirox 1% cream to clotrimazole 1% cream. In both studies, treatments were applied topically twice a day for 14 days. Clinical and mycological cure responses were compared at treatment weeks 1 and 2, and then post-treatment weeks 1 and 2. Results from the first study demonstrated 49% of the ciclopirox treatment group (n=73) were clinically and mycologically cured after 2 weeks versus 24% of the placebo treatment group (n=72; p<0.001). Results from the second study demonstrated that 77% of the patients treated with ciclopirox cream

were clinically and mycologically cured after 2 weeks of treatment versus 45% of patients treated with clotrimazole cream (p<0.001). Two weeks post-treatment, the proportion of patients with combined response was slightly greater in the ciclopirox treatment group versus the clotrimazole treatment group (86% versus 73%, respectively). No adverse effects were observed in either group.

sulconazole (Exelderm) versus miconazole (Monistat)

Sulconazole 1% cream and miconazole 2% cream were compared in the treatment of tinea versicolor in a double-blind, multicenter, randomized clinical trial enrolling 192 patients.[200] The medications were applied twice daily for 3 weeks. Of 181 patients analyzed for efficacy at the end of the treatment trial, 93% of the sulconazole patients and 87% of miconazole patients became KOH-negative. The complete clearing of tinea versicolor lesions occurred in 89% of sulconazole-treated patients and 82% of miconazole-treated patients. Cutaneous adverse effects, predominantly transient itching, were reported in 8 patients receiving sulconazole and in 4 patients receiving miconazole. No systemic adverse events were reported.

Onychomycosis

ciclopirox (Penlac) versus placebo

Two double-blind, vehicle-controlled multicenter studies were performed in the United States to evaluate the use of ciclopirox 8% nail lacquer to treat mild to moderate toenail onychomycosis caused by dermatophytes.[201] A total of 460 patients were randomized to ciclopirox (n=231) or vehicle (n=229). Treatment was applied daily for 48 weeks. At the end of the 48-week treatment period, the mycologic cure rate in study I was 29% for ciclopirox and 11% for the vehicle group. In study II, mycologic cure rates were 36 and 9%, respectively. The most common adverse reactions were transient and localized to the site of action (e.g., erythema and application site reaction).

efinaconazole (Jublia) versus placebo

In 2 phase 3, multicenter, randomized, double blind clinical studies, the safety and efficacy of efinaconazole 10% solution in the treatment of toenail onychomycosis were evaluated.[202,203] A total of 1,655 subjects were involved in the studies (Study 1: n=870, Study 2: n=785) with 20 to 50% clinical involvement. The subjects were randomized 3:1 to efinaconazole or vehicle and received once daily applications for 48 weeks, with 4-week post treatment follow-up. Complete cure rate (0% clinical involvement of target toenail, and both negative KOH examination and fungal culture) was the primary endpoint at 52 weeks and debridement was not performed. With efinaconazole, the mycologic cure rates were significantly greater (Study 1: 55.2%, Study 2: 53.4%) compared with the vehicle (p<0.001). The primary endpoint and complete cure was also significantly greater for efinaconazole (Stud 1: 17.8% versus 3.3%, Study 2: 15.2% versus 5.5%, p<0.001). In study 1 treatment success for efinaconazole ranged from 21.3% to 44.8% and from 17.9% to 40.2% in Study 2, compared with 5.6% to 16.8% and 7% to 15.4%, respectively, with vehicle. Local site reactions (2%) were the adverse events associated with efinaconazole and it was clinically similar to the vehicle.

tavaborole (Kerydin) versus placebo

In 2 multicenter, double-blind, randomized, vehicle-controlled trials, the efficacy and safety of tavaborole 5% solution in the treatment of toenail onychomycosis were evaluated. [204]. A total of 1,194 patients were involved in the trial (Trial 1: n=593, Trial 2: n=601) with 20 to 60% clinical involvement of

the target toenail, without dermatophytomas or lunula (matrix) involvement. At 52 weeks, following a 48-week treatment period, efficacy assessments were made. The complete cure efficacy endpoint included negative mycology (negative KOH wet mount and negative fungal culture) and completely clear nail (no clinical evidence of onychomycosis as evidenced by a normal toenail plate, no onycholysis, and no subungual hyperkeratosis). The complete cure rate for trial 1 regarding tavaborole 5% solution (n=399) yielded 6.5% complete cure, 15.3% complete or almost complete cure, and 31.1% mycological cure. As compared to the vehicle group (n=194) that yielded 0.5% complete cure, 1.5% complete or almost complete cure, and 7.2% mycological cure. The outcomes for trial 2 regarding the tavaborole 5% solution group (n=396) yielded 9.1% complete cure, 17.9% complete or almost complete cure, and 35.9% mycological cure, as compared to the vehicle group (n=205) that yielded 1.5% complete cure, 3.9% complete or almost complete cure, and 12.2% mycological cure.

Seborrheic Dermatitis

ketoconazole foam (Extina) versus ketoconazole cream

A total of 1,162 subjects, aged 12 years or older, with mild to severe seborrheic dermatitis were randomized to receive ketoconazole foam (n=427), vehicle foam (n=420), ketoconazole cream (n=210), or vehicle cream (n=105) twice daily for 4 weeks.[205] The primary endpoint was the proportion of subjects achieving an Investigator's Static Global Assessment score of 0 or 1 at week 4 (treatment success). A significantly greater percentage of subjects achieved treatment success using ketoconazole foam than vehicle foam (56% and 42%, respectively; $p<0.0001$). Ketoconazole foam was well-tolerated with a low incidence of treatment-related adverse events (14%). Ketoconazole foam was shown to be equivalent to ketoconazole cream.

ketoconazole gel (Xolegel) versus vehicle

A randomized phase 3, vehicle-controlled trial was performed on 459 people to evaluate the efficacy of ketoconazole 2% gel in comparison to the vehicle after 2 weeks of treatment in moderate to severe seborrheic dermatitis.[206] The primary endpoint was to evaluate the proportion of patients who had either cleared or almost cleared dermatitis after 28 days. Results indicated that 25.3% of patients treated with ketoconazole 2% gel experienced successful treatment in comparison to 13.9% of patients receiving the vehicle alone ($p=0.0014$). In addition, ketoconazole 2% gel helped to improve erythema, scaling, and pruritus when compared to the vehicle ($p=0.0022$). Few adverse events were reported, but the adverse events that were experienced were mild and moderate and similar between both groups.

Two studies compared the effectiveness of a combination gel containing ketoconazole 2% and desonide 0.05%, each active gel individually, and a vehicle control in 316 patients with moderate to severe seborrheic dermatitis.[207] The primary endpoint was efficacy measured by the proportion of patients who experienced an improvement in scaling and erythema, as well as the investigator global assessment scores. A score of 0 or 1, if the baseline was ≥ 3, defined effective treatment in these patients after 28 days. The comparison of the combination gel to its individual components revealed that the efficacy of ketoconazole alone was comparable to the combination gel, as well as desonide gel alone, for up to 2 weeks after the end of treatment.

META-ANALYSIS

A systematic review was conducted to evaluate topical treatments for fungal infections of the skin and nails of the foot.[208] Authors searched the Cochrane Skin Group Specialized Register (January 2005), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 1, 2005), MEDLINE and EMBASE (from inception to January 2005). The study objectives were to assess the effects of topical treatments in successfully treating fungal infections of the skin of the feet and toenails and in preventing recurrence. In conclusion, allylamines and azoles for athlete's foot consistently produce a much higher percentage of cures than placebo. Allylamines cure slightly more infections than azoles and are now available over-the-counter.

The efficacy and safety of luliconazole cream 1% in the treatment of dermatophytoses in a meta-analysis yielded that the short-term treatment with the product can result in the complete clearance of dermatophytoses.[209] The luliconazole cream 1% was more effective than controlled drugs or vehicle (week 4: odds ratio=1.46, 95% confidence interval =1.12-1.91) and no more adverse events occurred in the luliconazole cream 1% group (week 4: odds ratio=1.01, 95% confidence interval 0.71-1.44). The analysis strengthens the evidence for luliconazole cream 1% being more effective than vehicle, 1% terbinafine, 1% bifonazole, and 0.1% or 0.5% luliconazole.

SUMMARY

Many topical antifungal preparations are available as prescription medications and over-the-counter (OTC) products. Limited data are available regarding comparative efficacy in the treatment of the various fungal infections — tinea cruris, tinea corporis, tinea pedis, and tinea versicolor. In general, tinea corporis and tinea cruris require treatment for 2 weeks, and tinea pedis may require treatment for 4 weeks. Treatment should continue for at least 1 week after symptoms have resolved. Combination therapy (antifungal plus corticosteroid) can be considered when inflammation is present. The safety of the topical agents is inherently limited to local exposure.

Limited data are also lacking in comparative efficacy for the treatment of seborrheic dermatitis. Both ciclopirox (Loprox) and ketoconazole (Extina, Xolegel) have been approved for use in this condition, but superiority has not been established for either agent due to the lack of well designed comparative clinical studies.

Due to the lack of comparative studies with ciclopirox (Ciclodan, CNL-8, Penlac), efinaconazole (Jublia), and tavaborole (Kerydin) for the treatment of onychomycosis, it is difficult to measure its effectiveness versus other indicated products. An oral antifungal, if tolerated, may lead to higher success rates in the treatment of onychomycosis.[210]

The combination product miconazole, zinc oxide, and white petrolatum (Vusion) is indicated as adjunctive treatment for diaper dermatitis in patients 4 weeks and older. The other agents with safety and effectiveness data for children ages 2 years and older are clotrimazole, miconazole, undecylenic, undecylenic/zinc undecylenate, and tolnaftate.

Luliconazole is a new azole agent that has similar antifungal properties as other available azole products. Luliconazole offers once daily dosing and is dosed for a shorter period of time than other azoles. The duration of therapy is 2 weeks for interdigital tinea pedis and 1 week for tinea corporis and cruris.

Based on the limited amount of efficacy data available for these various agents in the treatment of dermatologic fungal infections, choice of therapy is mainly based on clinical judgment with regard to prior treatments and complicating conditions, such as bacterial growth or intense inflammation.

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