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### Abbreviated Class Update: Topical Antifungal Agents

**Month/Year of Review:** March 2014

**PDL Class:** Dermatologic – Topical antifungal

**New drug:** LUZU® (luliconazole) cream

**End date of literature search:** January 2014

**Date of Last Review:** March 2013

**Source Document:** OSU College of Pharmacy

**Manufacturer:** Valeant Pharmaceuticals

#### Current Status of PDL Class:

- Preferred Agents: MICONAZOLE CREAM, NYSTATIN CREAM/OINTMENT
- Non Preferred Agents: BUTENAFINE (MENTAX®), BENZOID ACID/SALICYCLIC ACID OINTMENT (BENSAL HP®)CHLOROXYLENOL, CICLOPIROX CREAM, CLOTRIMAZOLE SOLUTION/CREAM, ECONAZOLE CREAM, KETOCONAZOLE SHAMPOO/CREAM, NAFTIFINE (NAFTIN®), NYSTATIN/TRIAMCINOLONE OINTMENT/CREAM, TERBINAFINE, TOLNAFATE (TINACTIN®), OXICONAZOLE LOTION (OXISTAT®), SERTACONAZOLE (ERTACZO™), SULCONAZOLE CREAM (EXELDERM®), UNDECYLENIC ACID

**PA criteria:** Prior authorization (PA) required for non-preferred agents covering only for a funded diagnosis and trial of generic formulation.

#### Research Questions:

- Is there any new relevant evidence demonstrating differences in efficacy or safety in topical antifungal drugs, suggesting recommended changes to the current PDL?
- Is luliconazole more effective and/or safer than currently available agents?
- Are there subgroups of patients where luliconazole may be more effective or safer than currently available agents?

#### Conclusions:

- There is new low quality evidence from one systematic review and indirect comparisons that there are no statistically significant differences among the antifungals in mycologic cure rate at the end of treatment in the treatment of dermatophytosis.<sup>1</sup>
- There is low quality evidence that butenafine and terbinafine are significantly more efficacious than were clotrimazole, oxiconazole and sertaconazole in sustained cure and terbinafine is statistically superior to ciclopirox for the treatment of dermatophytosis.<sup>1</sup>
- There is low quality evidence based on one published fair quality study that luliconazole is effective and safe for the treatment of tinea cruris and is significantly better than placebo in achieving a complete response (21.2% vs. 4.4%; p<0.001).<sup>2</sup> There are no comparative data between luliconazole and other topical antifungal agents.

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**Recommendations:**

- Maintain luliconazole a non-preferred topical antifungal medication on the PDL due to lack of long term clinical outcomes data and direct comparative data to suggest better tolerability or efficacy than currently available agents.
- Evaluate comparative costs in executive session of other agents.

**Previous Conclusions and Recommendations**

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harm/adverse events

**Reason for Review:**

Since the last review of this class in March 2013, luliconazole (LUZU®) cream was approved by the FDA for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older. This update will examine the new agent's place in therapy and identify any other new relevant comparative effectiveness evidence, high-quality systematic reviews, or evidence-based guidelines for consideration.

**Methods:**

A Medline (Ovid) literature search was conducted for new randomized controlled trials (RCT's) and controlled clinical trials comparing medications head-to-head in the treatment of topical fungal infections with all included drugs and limits for humans, English language with the following search terms: tinea unguium, tinea capitis, tinea corporis, tinea cruris, tinea pedis, lichen planus, pityriasis versicolor, Candidiasis, vulvovaginal candida, blastomycosis, Coccidioidomycosis, Cryptococcosis, mycosis, Histoplasmosis, Onychomycosis, tinea, Chromoblastomycosis, and seborrheic dermatitis. The Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Clinical Evidence, Up To Date, Dynamed, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. The FDA website was searched for new drugs, indications, and safety alerts, and the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines. The primary focus of the evidence is on high quality systematic reviews and evidence based guidelines for this class update. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

**Systematic Reviews:**

Rotta I et. al.<sup>1</sup> conducted a mixed-treatment comparison meta-analysis that evaluated and compared the efficacy of topical antifungals used in dermatophytosis treatment. The outcomes evaluated were mycologic cure at the end of treatment and sustained cure. A random-effects Bayesian mixed-treatment comparisons model was applied to combine placebo-controlled RCTs and head to head RCTs. The quality of each study was assessed using the Jadad tool and only studies with a score of 3 or more were included. When looking at direct comparisons, there was a statistically significant difference between clotrimazole and terbinafine, favoring terbinafine (OR 0.24; 95% CI 0.11-0.53). When evaluating sustained cure, there were statistically significant differences between clotrimazole and naftifine (OR 0.35; 95% CI 0.14-0.7), oxiconazole nitrate vs. terbinafine (OR 0.10; 95% CI 0.03-0.32), and naftifine vs. oxiconazole (OR 7,86; 95% CI 2.41-25.60), favoring allylamines in all comparisons.

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The pooled mixed treatment meta-analysis data of the 65 trials identified did not show any statistically significant differences among the antifungals in mycologic cure at the end of treatment. Regarding sustained cure, butenafine and terbinafine were significantly more efficacious than clotrimazole, oxiconazole and sertaconazole. Terbinafine also demonstrated statistical superiority when compared with ciclopirox, and naftifine showed better response compared with oxiconazole. When ranking each agent for efficacy, tioconazole was the therapy that had the greatest probability of being the best treatment considering the mycologic cure at the end of treatment outcome and miconazole was the second most efficient treatment. No inconsistency was detected in the network of evidence for both outcomes, sustaining the validity of the mixed-treatment comparisons results. The authors concluded because of the different costs of the antifungals, pharmacoeconomic analysis is required to identify the most efficient strategy for dermatophytosis management.

**New Guidelines:**

No new or updated guidelines were identified.

**New Safety Alerts, Indications:**

No new safety alerts or indications were found.

**New Drug Evaluation:**

*FDA approved indications:*

luliconazole (LUZU®) was approved by the FDA for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum* and *Epidermophyton floccosum*, in patients 18 years of age and older.<sup>3</sup>

*Potential Off-label Use:*

There were small number of patients under age of 18 were included in the clinical trials, which resulted FDA approval of in adults only. It is potentially used in pediatric population as well.

*Clinical Efficacy Data:*

Approval evidence for the efficacy of luliconazole was based on three randomized, double blind, phase III, placebo controlled, short term (1 or 2 weeks) trials.<sup>4</sup> Two studies evaluated luliconazole in the treatment of tinea pedis and one in tinea cruris. It was not studied in tinea corporis. At the time of this review, only one of these studies was published and was included as primary evidence for review of the efficacy and safety.<sup>2</sup> According to the FDA review, luliconazole resulted in complete clearance (clinical cure and mycological cure) of tinea pedis in 26% in one study and 14% in another study, compared to 2% and 3% in placebo groups, respectively.

Study MP-1000-01<sup>2</sup> is a fair quality study that compared the efficacy and safety of topical luliconazole cream 1% to placebo in patients with tinea cruris. A total of 256 male and female patients aged ≥12 years with clinically evident tinea cruris and eligible for modified intent-to-treat analysis were randomized 2:1 to receive luliconazole cream 1% (n=165) or vehicle (n=91) once daily for 7 days. Efficacy was evaluated at baseline and at days 7, 14, 21, and 28 based on mycology (potassium hydroxide, fungal culture) and clinical signs (erythema, scaling, pruritus). The primary outcome was complete clearance at day 28 (21 days post-treatment). Safety evaluations included adverse events and laboratory assessments. The results showed complete clearance was obtained in 21.2% (35/165) of patients treated with luliconazole cream 1% compared with 4.4% (4/91) treated with vehicle (P<0.001).

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*Clinical Safety:*

During clinical trials with 1% luliconazole cream, the most common adverse reactions were application site reactions which occurred in less than 1% of subjects in both the luliconazole and vehicle arms. Most adverse reactions were mild in severity. The following adverse reactions have been identified during post-marketing use of 1% luliconazole cream: contact dermatitis and cellulitis.

**COMPARATIVE CLINICAL EFFICACY**

**Study Endpoints:**

- 1) Clinical and mycologic cure at day 28 (21 days post-treatment)
- 2) Effective treatment at days 7, 14, 21, or 28

**Relevant Study Endpoint:**

- 1) Safety and tolerability in all patients

	Drug Regimens	Patient Population	N	Duration	Outcomes/ Efficacy Results (CI, p-values)	ARR/ NNT	Safety Results (CI, p-values)	ARR/ NNH	Quality Rating; Internal Validity Risk of Bias/ External Validity Concerns
Study MP-1000-01 Jones T et al. <sup>2</sup> Phase III, multi-center, RCT, DB,PC and vehicle controlled	L: luliconazole 1% cream once daily x 7 days P: Vehicle cream once daily x 7 days	Age ≥ 12 y/o Mean age: L/P: 41.1/39.1 Race (%of white): L/P: 59.4%/54.9% Fungal culture results (% of positive): L/P: 100%/100%  Inclusion Criteria: Mycologic diagnosis to tinea cruris confirmed by KOH testing. Good baseline health.  Exclusion Criteria: Use of a topical antifungal or systemic antifungal or abx or patients who are immunocompromised.	N= 256 (MITT Population) L = 165 P = 91	7 days treatment	<u>Primary outcomes:</u> Complete mycologic and clinical clearance : L: 21.2% P: 4.4% (p < 0.001)  <u>Secondary outcomes:</u> Clinical cure: L: 24.2% P: 6.6% ( p < 0.001) Mycologic cure: L: 78.2% P: 45.1% (p < 0.001)	16.8%/6   17.6%/5.7  33.1%/3	<u>Overall TEAEs:</u> L: 11.3% P: 16.9%  <u>The most frequent TEAEs:</u> L: Headache: 1.6% Nasopharyngitis: 1.6% Dysmenorrheal (1.0%) P: Headache: 2.5%	NA	<b>Quality Rating: Fair</b>  <b>Internal Validity: RoB</b> <u>Selection:</u> Low bias; clear randomization and allocation concealment. Populations were similar at baseline. <u>Performance:</u> Low bias; blinding adequate, blinding of patients Detection: Low bias; blinding of monitors. <u>Attrition:</u> Low attrition L/P: 0.6%/2.2% <u>MITT analysis:</u> No adjustment made for covariates.  <b>External Validity:</b> <u>Patient Characteristics:</u> General healthy baseline status. <u>Setting:</u> Multi-centers study at 27 sites. <u>Outcomes</u> <ul style="list-style-type: none"> <li>• Short term study.</li> <li>• Small sample size</li> <li>• Controlled settings</li> <li>• Unknown recurrence rate</li> </ul>
<sup>1</sup> <b>Study design abbreviations:</b> DB = double-blind, RCT = randomized trial, PC = placebo-controlled, PG = parallel -group, XO = crossover. <sup>2</sup> <b>Results abbreviations:</b> RRR = relative risk reduction, RR =relative risk, OR= Odds Ratio, HR = Hazard Ratio, ARR = absolute risk reduction, NNT = number needed to treat, NNH = number needed to harm, CI = confidence interval <sup>3</sup> <b>NNT/NNH</b> are reported only for statistically significant results <sup>4</sup> <b>Quality Rating:</b> (Good- likely valid, Fair- likely valid/possibly valid, Poor- fatal flaw-not valid)									

**New Trials:**

Author: B Liang, Pharm.D

Date: March 2014

A total of 279 citations resulted from initial literature search. After review of titles for inclusion, four potentially relevant comparative randomized trials were identified through abstract review for appropriate medication, indication, study design, and outcomes (Appendix 2). These trials are briefly described in table 1:

Study	Comparison	Population	Primary Outcome	Results
Goldust M et. al, <sup>5</sup> 2013	Sertaconazole 2% cream (N =30) vs. hydrocortisone 1% cream (N =30) twice a day for 4 weeks.	Patients with seborrheic dermatitis	Not defined - Efficacy of the treatment.	The highest level of satisfaction (90%) was observed 28 days after using sertaconazole and the level of satisfaction was 83.3% in hydrocortisone group. Relapse of the disease one month after stopping treatment was not observed in either group.
Goldust M et. al, <sup>6</sup> 2013	Sertaconazole 2% cream (N =30) vs. tacrolimus 3% cream (N =30) twice a day for 4 weeks.	Patients with seborrheic dermatitis	Not defined - Efficacy of the treatment.	The highest level of satisfaction (90%) was observed 28 days after sertaconazole use. Only 83.3% satisfaction was noted in the tacrolimus group ( $p = 0.006$ ).
Goldust M et. al, <sup>7</sup>	Sertaconazole 2% cream (N =64) vs. clotrimazole 1% cream (N =64) twice a day for 4 weeks.	Patients with seborrheic dermatitis	Not defined - Efficacy of the treatment.	The highest level of satisfaction (87.6%) was observed 28 days after sertaconazole administration and in clotrimazole group it was 50%. Relapse of the disease one month after stopping treatment was not observed in either group.
Tietz, H.-J et al, <sup>8</sup> 2013	Bifonazole (N = 347) vs. placebo ( N = 345) for 4 weeks	Patients mild-to-moderate onychomycosis after non-surgical nail ablation with urea paste.	The primary endpoint of the study was the overall cure rate comprising clinical cure and mycological cure (both microscopy and culture negative) in the target nail assessed 2 weeks.	Overall cure rate was superior in bifonazole-treated group (54.8% vs. 42.2% for placebo; $P = 0.0024$ ). The clinical cure rate was high in both treatment groups (86.6% bifonazole vs. 82.8% placebo), but proportion with mycological cure was higher with bifonazole treatment (64.5%) vs. placebo treatment 49.0%, ( $P = 0.0001$ ).

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## References:

1. Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NLMC, Correr CJ. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol.* 2013;149(3):341–349. doi:10.1001/jamadermatol.2013.1721.
2. Jones TM, Jarratt MT, Mendez-Moguel I, et al. A Randomized, Multicenter, Double-Blind, Vehicle-Controlled Study Evaluating the Efficacy and Safety of Luliconazole Cream 1% Once Daily for 7 Days in Patients Aged [greater than or equal to] 12 Years With Tinea Cruris. *Journal of Drugs in Dermatology.* 2014;13(1):32+.
3. Luzu Prescribing Information. Available at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/204153s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204153s000lbl.pdf). Accessed January 11, 2014.
4. FDA Medical Review. Available at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2013/204153Orig1s000MedR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204153Orig1s000MedR.pdf). Accessed January 11, 2014.
5. Goldust M, Ranjkesh MR, Amirinia M, Golphoroushan F, Rezaee E, Rezazadeh Saatlou MA. Sertaconazole 2% cream versus hydrocortisone 1% cream in the treatment of seborrheic dermatitis. *J Dermatolog Treat.* 2013. doi:10.3109/09546634.2012.755251.
6. Goldust M, Rezaee E, Raghifar R, Hemayat S. Treatment of seborrheic dermatitis: the efficiency of sertaconazole 2% cream vs. tacrolimus 0.03% cream. *Ann Parasitol.* 2013;59(2):73–77.
7. Goldust M, Rezaee E, Rouhani S. Double blind study of sertaconazole 2% cream vs. clotrimazole 1% cream in treatment of seborrheic dermatitis. *Ann Parasitol.* 2013;59(1):25–29.
8. Tietz H-J, Hay R, Querner S, Delcker A, Kurka P, Merk HF. Efficacy of 4 weeks topical bifonazole treatment for onychomycosis after nail ablation with 40% urea: a double-blind, randomized, placebo-controlled multicenter study. *Mycoses.* 2013;56(4):414–421. doi:10.1111/myc.12037.

## Appendix 1: Specific Drug Information<sup>3</sup>

### CLINICAL PHARMACOLOGY

Luliconazole is an antifungal that belongs to the azole class. Although the exact mechanism of action against dermatophytes is unknown, luliconazole appears to inhibit ergosterol synthesis by inhibiting the enzyme lanosterol demethylase. Inhibition of this enzyme's activity by azoles results in decreased amounts of ergosterol, a constituent of fungal cell membranes, and a corresponding accumulation of lanosterol.

### PHARMACOKINETICS

Luliconazole is the R enantiomer of a chiral molecule. The potential for inter-conversion between R and S enantiomers in humans has not been assessed. Information on the pharmacokinetics of luliconazole presented below refers to both R enantiomer and S enantiomer, if any, combined. Luliconazole is >99% protein bound in plasma. In a pharmacokinetic trial, 12 subjects with moderate to severe tinea pedis and 8 subjects with moderate to severe tinea cruris applied a mean daily amount of approximately 3.5 grams of LUZU Cream, 1% to the affected and surrounding areas once daily for 15 days. Plasma concentrations of luliconazole on Day 15 were measurable in all subjects and fluctuated little during the 24 hour interval. In subjects with tinea pedis, the mean  $\pm$  SD of the maximum concentration (C<sub>max</sub>) was 0.40  $\pm$  0.76 ng/mL after the first dose and 0.93  $\pm$  1.23 ng/mL after the final dose. The mean time to reach C<sub>max</sub> (T<sub>max</sub>) was 16.9  $\pm$  9.39 hours after the first dose and 5.8  $\pm$  7.61 hours after the final dose. Exposure to luliconazole, as expressed by area under the concentration time curve (AUC<sub>0-24</sub>) was 6.88  $\pm$  14.50 ng\*hr/mL after the first dose and 18.74  $\pm$  27.05 ng\*hr/mL after the final dose. In subjects with tinea cruris, the mean  $\pm$  SD C<sub>max</sub> was 4.91  $\pm$  2.51 ng/mL after the first dose and 7.36  $\pm$  2.66 ng/mL after the final dose. The mean T<sub>max</sub> was 21.0  $\pm$  5.55 hours after the first dose and 6.5  $\pm$  8.25 hours after the final dose. Exposure to luliconazole, as expressed by AUC<sub>0-24</sub> was 85.1  $\pm$  43.69 ng\*hr/mL after the first dose and 121.74  $\pm$  53.36 ng\*hr/mL after the final dose.

### DOSE & AVAILABILITY

STRENGTH	FORM	ROUTE	FREQUENCY	RENAL ADJ	HEPATIC ADJ	Pediatric Dose	Elderly Dose	OTHER DOSING CONSIDERATIONS
1%	cream	topical	Daily	NA	NA	The safety and effectiveness in pediatric patients have not been established.	No dose adjustment is necessary for the elderly.	Geriatric patients might experience greater sensitivity.

### DRUG SAFETY

*Serious (REMS, Black Box Warnings, Contraindications):* There are no Serious Drug Safety concerns or contradictions for luliconazole at this time.

*Warnings and Precautions:* None.

*Pregnancy Category:* C.

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*Look-alike / Sound-alike (LA/SA) Error Risk Potential:*

No look-alike/sound-alike drugs have been found to have error risk potential.

*Adverse Reactions*

During clinical trials with 1% luliconazole cream, the most common adverse reactions were application site reactions which occurred in less than 1% of subjects in both the luliconazole and vehicle arms. Most adverse reactions were mild in severity. The following adverse reactions have been identified during post-marketing use of 1% luliconazole cream: contact dermatitis and cellulitis.

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## Appendix 2:

### Systematic Review

1. Rotta I, Ziegelmann PK, Otuki MF, Riveros BS, Bernardo NLMC, Correr CJ. Efficacy of topical antifungals in the treatment of dermatophytosis: a mixed-treatment comparison meta-analysis involving 14 treatments. *JAMA Dermatol.* 2013;149(3):341–349.

#### **Abstract**

**Importance:** Considering that most randomized controlled trials compare antifungals with placebo instead of other antifungals, conventional meta-analysis is insufficient to define superiority between the evaluated strategies. To our knowledge, this is the first mixed-treatment comparison meta-analysis on antifungal treatments in the literature and shows all the evidence available at the time of the study.

**Objective:** To evaluate and compare the efficacy of topical antifungals used in dermatophytosis treatment, using mixed-treatment comparisons.

**Evidence Acquisition:** We performed a comprehensive search (up to July 31, 2012) for all entries in MEDLINE, Cochrane Central Register of Controlled Trials, EMBASE, Literatura Latino Americana e do Caribe em Ciências da Saúde, and International Pharmaceutical Abstracts. Randomized controlled trials that compared topical antifungals with one another or with placebo in dermatophytosis treatment were selected for analysis. Methodologic quality of the trials was assessed using the Jadad scale. We excluded studies that scored less than 3 points. The outcomes evaluated were mycologic cure at the end of treatment and sustained cure. A random-effects Bayesian mixed-treatment comparisons model was applied to combine placebo-controlled and direct topical antifungals comparison trials. **RESULTS** Pooled data of the 65 trials identified did not show any statistically significant differences among the antifungals concerning the outcome of mycologic cure at the end of treatment. Regarding the sustained cure outcome, butenafine hydrochloride and terbinafine hydrochloride were significantly more efficacious than were clotrimazole, oxiconazole nitrate, and sertaconazole nitrate. Terbinafine also demonstrated statistical superiority when compared with ciclopirox (ciclopiroxolamine), and naftifine hydrochloride showed better response compared with oxiconazole. No inconsistency was detected in the network of evidence for both outcomes, sustaining the validity of the mixed-treatment comparisons results.

**Conclusions and relevance:** With the outcome mycologic cure at the end of treatment, there was no significant difference among the antifungals. Butenafine, naftifine, and terbinafine might be the best strategies for maintaining cured status. Because of the different costs of the antifungals, pharmacoeconomic analysis is required to identify the most efficient strategy for dermatophytosis management.

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## Randomized Clinical Trials

1. **Goldust M, Ranjkesh MR, Amirinia M, Golforoushan F, Rezaee E, Rezazadeh Saatlou MA. Sertaconazole 2% cream versus hydrocortisone 1% cream in the treatment of seborrheic dermatitis. *J Dermatolog Treat.* 2013 Feb 24. [Epub ahead of print].**

### Abstract

**Objective:** Seborrheic dermatitis (SD) is commonly treated with anti-inflammatory products, including topical corticosteroids. This study was undertaken to compare the efficiency of sertaconazole 2% cream with hydrocortisone 1% cream in the treatment of SD.

**Methods:** In this clinical trial study, 60 SD patients were studied. Thirty patients received local sertaconazole 2% cream and were recommended to use the cream twice a day for 4 weeks. In the control group, 30 patients received hydrocortisone 1% cream and were recommended to use the cream twice a day for 4 weeks. At the start of the study and also 2 and 4 weeks after first visit, the patients were examined by a dermatologist for signs of improvement and control of clinical symptoms.

**Results:** The mean age of the patients was  $32.23 \pm 12.09$ . The highest level of satisfaction (90%) was observed 28 days after using sertaconazole and the level of satisfaction was 83.3% in hydrocortisone group. Relapse of the disease one month after stopping treatment was not observed in both groups treated with sertaconazole 2% cream and hydrocortisone 1% cream.

**Conclusion:** Topical sertaconazole therapy is a considerable advancement in the treatment of SD with corticosteroids. The cure rate was somewhat higher in the sertaconazole group and it can be considered as the nonsteroidal alternative to topical steroid therapy for SD.

2. **Goldust M, Rezaee E, Raghifar R, Hemayat S. Treatment of seborrheic dermatitis: the efficiency of sertaconazole 2% cream vs. tacrolimus 0.03% cream. *Ann Parasitol.* 2013;59(2):73–77.**

### Abstract

The treatment of seborrheic dermatitis (SD) includes topical antifungal agents to eradicate *Malassezia* spp. corticosteroids to treat the inflammatory component of the disease, and keratolytics to remove scale and crust. The aim of this study was to compare the efficiency of sertaconazole 2% cream and tacrolimus 0.03% cream in the treatment of seborrheic dermatitis. In this clinical trial study, sixty patients suffering from SD were studied. Thirty patients received local sertaconazole 2% cream with a recommendation to use the cream twice a day for 4 weeks. In the control group, thirty patients received tacrolimus 0.03% cream twice a day for four weeks. At the time of referral, and 2 and 4 weeks after first visit, the patients were examined by a dermatologist to check the improvement of clinical symptoms. The mean ages of the sertaconazole and tacrolimus groups were  $30.98 \pm 12.24$  and  $34.67 \pm 10.82$ , respectively. The highest level of satisfaction (90%) was observed 28 days after sertaconazole use. Only 83.3% satisfaction was noted in the tacrolimus group. The relationship between patient satisfaction and sertaconazole 2% cream receive in 28th day was significant ( $P = 0.006$ ). Sertaconazole 2% cream may be an excellent alternative therapeutic modality for treating seborrheic dermatitis.

3. **Goldust M, Rezaee E, Rouhani S. Double blind study of sertaconazole 2% cream vs. clotrimazole 1% cream in treatment of seborrheic dermatitis. *Ann Parasitol.* 2013;59(1):25–29.**

#### **Abstract**

Treatment of seborrheic dermatitis (SD) is an important issue in dermatology. This study was undertaken to compare efficiency of sertaconazole 2% cream vs. clotrimazole 1% cream for the treatment of seborrheic dermatitis. One hundred twenty eight patients suffering from SD were studied. Patients were randomly divided into two groups. Sixty four patients received local sertaconazole 2% cream and in control group 64 patients received clotrimazole 1% cream. They were recommended to use the cream twice a day for 4 weeks. At the beginning of referring and 2 and 4 weeks after first visit, the patients were examined by a dermatologist to assess improvement of clinical symptoms. The mean age of sertaconazole and clotrimazole group patients was 34.78+/-13.54 and 38.68+/-11.88, respectively. The highest level of satisfaction (87.6%) was observed 28 days after sertaconazole administration and in clotrimazole group it was 50%. Relapse of the disease one month after stopping treatment was not observed in groups treated with sertaconazole 2% cream and clotrimazole 1% cream. This study suggests that sertaconazole 2% cream is an effective and well-tolerated treatment for moderate to severe facial seborrheic dermatitis.

4. **Tietz H-J, Hay R, Querner S, Delcker A, Kurka P, Merk HF. Efficacy of 4 weeks topical bifonazole treatment for onychomycosis after nail ablation with 40% urea: a double-blind, randomized, placebo-controlled multicenter study. *Mycoses.* 2013;56(4):414–421.**

#### **Summary**

Onychomycosis is a common fungal infection most often affecting the toenails. If untreated, it can cause discomfort sufficient to reduce quality of life. To evaluate efficacy and safety of bifonazole cream vs. placebo in onychomycosis treatment after non-surgical nail ablation with urea paste. Fifty-one study centres randomized 692 subjects with mild-to-moderate onychomycosis to receive bifonazole 1% cream or placebo for 4 weeks following non-surgical nail ablation with urea 40% paste over 2–4 weeks. Efficacy of the two phase treatment was evaluated by overall cure of the target nail comprising clinical and mycological cure 2 weeks, 3 and 6 months after end of treatment. At 2 weeks (primary endpoint), overall cure rate was superior in bifonazole-treated group (54.8% vs. 42.2% for placebo;  $P = 0.0024$ ). The clinical cure rate was high in both treatment groups (86.6% bifonazole vs. 82.8% placebo), but proportion with mycological cure was higher with bifonazole treatment (64.5%) vs. placebo treatment 49.0%, ( $P = 0.0001$ ). We observed higher early overall cure rate with 4 weeks topical bifonazole compared with placebo after removal of infected nail parts with urea. This two stage treatment was well tolerated and offers an additional option in topical onychomycosis therapy.