DOSSAGE AND ADMINISTRATION

(1)

INDICATIONS AND USAGE

LUZU (luliconazole) Cream, 1% is indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organisms:

• Epidermophyton floccosum.

• Trichophyton rubrum.

• T. mentagrophytes.

• Microsporum audouini.

• Microsporum canis.

• T. schoenleini.

• Cochliobolus heterostrophus.

• Trichosporon beigelii.

• Non-albicans Candida species.

(1)

ADVERSE REACTIONS

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

In three Phase 3 clinical trials, 616 subjects were exposed to LUZU Cream, 1% in adult subjects with interdigital tinea pedis, tinea cruris, or tinea corporis. The most frequently reported adverse reactions, occurring in more than 1% of treated subjects, were application site reactions, which occurred in less than 1% of subjects. (6.1)

6.2 Postmarketing Experience

There are no available data with LUZU Cream, 1% use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

6.3 Postmarketing Data

Postmarketing data for LULICORZINE® (luliconazole) cream, for topical use (0.112% w/w), have been collected from a population of uncertain size, it is not always possible to directly compare drug experiences in the postmarketing setting to the drug experiences observed in controlled clinical trials. (6.3)

7 DRUG INTERACTIONS

7.1 Clinical Pharmacology

7.1.1 Mechanism of Action

Luliconazole inhibits fungal (Candida albicans, Trichophyton rubrum, and Epidermophyton floccosum) glucan synthase, an enzyme responsible for the synthesis of the fungal cell wall. Luliconazole is the R enantiomer (R-354.28) and contains one chiral center. (7.1.1)

7.1.2 Pharmacokinetics

At therapeutic doses, LUZU Cream, 1% is not expected to prolong QTc to any clinically relevant extent. (7.1.2)

8 DOSAGE FORMS AND STRENGTHS

8.1 Pregnancy

Risk Summary

The risk Summary below is based on the available clinical trial data and postmarketing experience. The safety and effectiveness of LUZU Cream, 1% in pregnant women has not been established by evidence from well-controlled trials in adult women. See full prescribing information. (8.1)

8.2 Lactation

There are no available data with luliconazole use in breastfeeding women. (8.2)

9 CONTRAINDICATIONS

9.1 Contraindications

Contraindicated in women who are pregnant or nursing. (9.1)

10 ADVERSE REACTIONS

10.1 Clinical Pharmacology

10.1.1 Mechanism of Action

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11.1.2 Pharmacodynamics

11.2 Pharmacodynamics

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11.3.4 Elimination

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Study 2

The safety and efficacy of LUZU (luliconazole) Cream, 1% was evaluated in a randomized, double-blind, vehicle-controlled, multi-center clinical trial in 256 subjects with a clinical and culture-confirmed diagnosis of tinea corporis. Subjects were randomized to receive LUZU Cream, 1% or vehicle cream.

The mean age of the study population was 40 years (range 14 to 88 years); 72% were male; 36% were White and 64% were Black or African American. Signs and symptoms of tinea corporis included pruritus, positive KOH exam and dermatophyte culture were assessed at baseline, end-of-treatment (Day 7), 2 and 3 weeks post-treatment.

Overall treatment success was defined as complete clearance of signs and symptoms (absence of erythema, scaling and pruritus) and no pruritus

<table>
<thead>
<tr>
<th>Mycological Cure</th>
<th>Vehicle</th>
<th>n ( % )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Clearance</td>
<td>41 (45%)</td>
<td>29 (28%)</td>
</tr>
<tr>
<td>3 Absence of erythema, scaling and pruritus</td>
<td>66 (72%)</td>
<td>51 (48%)</td>
</tr>
<tr>
<td>2 Negative KOH and culture and at most mild erythema and/or scaling</td>
<td>60 (66%)</td>
<td>41 (39%)</td>
</tr>
<tr>
<td>1 Time point failure</td>
<td>5 (5%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Non-Response</td>
<td>4 (4%)</td>
<td>3 (3%)</td>
</tr>
</tbody>
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Mechanism of Resistance

Resistance to antifungal agents is mediated via two primary mechanisms: reduction in drug target abundance or function and development of drug target resistance mutations. Inhibition of fungal lanosterol 14α-demethylase (CYP51A1) is the primary antifungal target of the azole class.

Luliconazole is an antifungal that belongs to the azole class. Although a CYP51A1 inhibitor, the degree of inhibition is at least 25-fold weaker than that of approved azole antifungals. Inhibition of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6, but can inhibit the activity of CYP2B6, 2C8, 2C9 and 2D6.