For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

LULI-EASE

1. Generic Name

Luliconazole Cream I.P. 1% w/w

2. Qualitative and quantitative Composition:

Luliconazole I.P. …… 1.0% w/w

Preservatives:

Methylparaben I.P. ……. 0.14% w/w

Benzyl Alcohol I.P. ……. 1.0% w/w

In a cream base ……..... q.s.

The list of excipients used are Methyl paraben, Benzyl alcohol, Polysorbate, Cetostearyl Alcohol, Propylene Glycol, Isopropyl Myristate, Butylated Hydroxy Toluene, Medium Chain Triglycerides, Stearic acid and Sodium Hydroxide.

3. Dosage form and strength

Dosage form: Cream

Strength: 1% w/w

4. Clinical particulars

4.1. Therapeutic indication

For the treatment of cutaneous mycosis viz. Tinea pedis, Tinea corporis, Tinea cruris.

4.2. Posology and method of administration

Posology

For the treatment of interdigital tinea pedis (athlete's foot that is between the toes)
Adults: Apply a thin layer of cream topically to affected areas, and approximately 1 inch of the immediate surrounding areas, once daily for 2 weeks.

Children and Adolescents 12 to 17 years: Apply a thin layer of cream topically to affected areas, and approximately 1 inch of the immediate surrounding areas, once daily for 2 weeks.

For the treatment of tinea cruris (jock itch or ringworm) and tinea corporis (Ringworm of body):

Adults: Apply topically to affected areas, and approximately 1 inch of the immediate surrounding areas, once daily for 1 week.

Children and Adolescents 12 to 17 years: Apply topically to affected areas, and approximately 1 inch of the immediate surrounding areas, once daily for 1 week.

Method of administration

For Topical Use

4.3. Contraindications

- Hypersensitivity to the active substance or any of the excipients listed.
- Do not use the cream for ophthalmic, oral or intravaginal use.

4.4. Special warnings and precautions for use

It is for external use only. Do not let the cream get into your eyes, nose, mouth or other mucous membranes and do not swallow it.

Avoid ocular exposure to luliconazole; do not administer by ophthalmic administration. If ocular exposure occurs, treat by immediately flushing the affected eye with cool, clean water. Wash hands before and after application. Use exactly as a stated dose by a physician.

4.5. Drugs interactions

The potential of luliconazole to inhibit cytochrome P-450 (CYP) enzymes 1A2, 2C9, 2C19, 2D6, Page 3 of 7 and 3A4 was evaluated in vitro. Based on in vitro assessment, luliconazole at therapeutic doses, particularly when applied to patients with moderate to severe tinea cruris, may inhibit the activity of CYP2C19 and CYP3A4. However, no in vivo drug interaction trials have been conducted to evaluate the effect of luliconazole on other drugs that are substrates of CYP2C19 and CYP3A4.

Luliconazole is not expected to inhibit CYPs 1A2, 2C9 and 2D6 based on in vitro assessment. The induction potential of luliconazole on CYP enzymes has not been evaluated.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no adequate and well-controlled studies of luliconazole in pregnant women. Luliconazole should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

The animal multiples of human exposure calculations in another study were based on daily dose body surface area (BSA) comparisons (mg/m2) for the reproductive toxicology studies described in this section. The Maximum Recommended Human Dose (MRHD) was set at 8 g 1% cream per day (1.33 mg/kg/day for a 60 kg individual which is equivalent to 49.2 mg/m2 /day).

Systemic embryofoetal development studies were conducted in rats and rabbits. Subcutaneous doses of 1, 5 and 25 mg/kg/day luliconazole were administered during the period of organogenesis (gestational days 7-17) to pregnant female rats. No treatment-related effects on maternal toxicity or malformations were noted at 25 mg/kg/day (3 times the MRHD based on BSA comparisons). Increased incidences of skeletal variation (14th rib) were noted at 25 mg/kg/day. No treatment related effects on skeletal variation were noted at 5 mg/kg/day (0.6 times the MRHD based on BSA comparisons).

Subcutaneous doses of 4, 20 and 100 mg/kg/day luliconazole were administered during the period of organogenesis (gestational days 6-18) to pregnant female rabbits. No treatment-related effects on maternal toxicity, embryo fetal toxicity or malformations were noted at 100 mg/kg/day (24 times the MRHD based on BSA comparisons).

In a pre-and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day luliconazole were administered from the beginning of organogenesis (gestation day 7) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryo fetal toxicity (increased prenatal pup mortality, reduced live litter sizes and increased postnatal pup mortality) was noted at 25 mg/kg/day. No embryo fetal toxicity was noted at 5 mg/kg/day (0.6 times the MRHD based on BSA comparisons). No treatment effects on postnatal development were noted at 25 mg/kg/day (3 times the MRHD based on BSA comparisons).

Lactation

There is no data on the excretion of luliconazole into human milk. Many drugs are excreted in human milk, caution should be exercised when luliconazole is administered to women who are breastfeeding.

Fertility

In a fertility study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day luliconazole were administered prior to and during mating and through early pregnancy. Treatment-related effects on reproductive function were noted in females (decreased live embryos and decreased corpus luteum) at 5 and 25 mg/kg/day and in males (decreased sperm counts) at 25 mg/kg/day. No treatment related effects on fertility or reproductive function were noted at 1 mg/kg/day (0.1X MRHD based on BSA comparisons).

Pediatric Use

Appropriate studies have not been performed on the relationship of age to the effects of luliconazole topical cream in children younger than 12 years of age to treat tinea pedis and tinea cruris and in children younger than 2 years of age to treat tinea corporis. Safety and efficacy have not been established.

Geriatric Use

Appropriate studies performed to date have not demonstrated geriatric specific problems that would limit the usefulness of luliconazole topical cream in the elderly. However, elderly patients are more sensitive to the effects of this medicine than younger adults.

Children

Age 2 to 12 years: Specific dosage information is not available. Younger than 2 years: Safety and efficacy have not been established.

Hepatic Impairment

No dosage adjustment is required.

Renal Impairment

No dosage adjustment is required.

4.7. Effects on ability to drive and use machines

Luliconazole cream has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The most common adverse reactions reported were application site reactions, contact dermatitis and cellulitis. Most adverse reactions were mild in severity.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com or at email: pv@torrentpharma.com or call on 1800-120-3001.

4.9. Overdose

Overdose treatment should be supportive or symptomatic.

5. Pharmacological properties

5.1. Mechanism of Action

Luliconazole is an azole antifungal. 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.

5.2. Pharmacodynamic properties

Pharmacological classification: 14.1.3 Dermatological and topical preparations: Antifungals. At therapeutic doses, luliconazole is not expected to prolong QTc to any clinically relevant extent.

5.3. Pharmacokinetic properties

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 luliconazole 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 a little during the 24-hour interval. In subjects with tinea pedis, the mean ± SD of the maximum concentration (Cmax) was 0.40 ± 0.76 ng/mL after the first dose and 0.93 ± 1.23 ng/mL after the final dose. The mean time to reach Cmax (Tmax) was 16.9 ± 9.39 hours after the first dose and 5.8 ± 7.61 hours after the final dose. Exposure to luliconazole, as expressed by the area under the concentration-time curve (AUC0-24) was 6.88 ± 14.50 ng*hr/mL after the first dose and 18.74 ± 27.05 ng*hr/mL after the final dose. In subjects with tinea cruris, the mean ± SD Cmax was 4.91 ± 2.51 ng/mL after the first dose and 7.36 ± 2.66 ng/mL after the final dose. The mean Tmax was 21.0 ± 5.55 hours after the first dose and 6.5 ± 8.25 hours after the final dose. Exposure to luliconazole, as expressed by AUC0-24 was 85.1 ± 43.69 ng*hr/mL after the first dose and 121.74 ± 53.36 ng*hr/mL after the final dose.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

The safety and efficacy of luliconazole for interdigital tinea pedis treatment were evaluated in two randomized, double-blind, vehicle-controlled, multi-centre clinical trials in 423 subjects with a clinical and culture-confirmed diagnosis of interdigital tinea pedis. Subjects were randomized to receive luliconazole or vehicle. Subjects applied either luliconazole 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 mean age of the study population was 41 years; 82% were male; 53% were White and 40% were Black or African American. Signs and symptoms of tinea pedis (erythema, scaling, and pruritus), KOH exam and dermatophyte culture were assessed at baseline, end-of-treatment (Day 14), 2- and 4-weeks post-treatment.

Overall treatment success was defined as complete clearance (clinical cure and mycological cure) at 4 weeks post-treatment. Luliconazole demonstrated complete clearance in subjects with interdigital tinea pedis. Treatment outcomes at 4 weeks post-treatment are summarized in Table.

Table: Efficacy Results at 4 Weeks Post-treatment – Interdigital Tinea Pedis

	Study 1		Study 2	
	Luliconazole N= 106 n %)	**Vehicle Cream N= 103 n (%)**	**Luliconazole N= 107 n (%)**	**Vehicle Cream N= 107 n (%)**
Complete Clearance[1]	28 (26%)	2 (2%)	15 (14 %)	3 (3%)
Effective Treatment[2]	51 (48%)	10 (10%)	35 (33%)	16 (15%)
Clinical Cure[3]	31 (29%)	8 (8%)	16 (15%)	4 (4%)
Mycological Cure[4]	66 (62%)	18 (18%)	60 (56%)	29 (27%)

[1] Proportion of subjects who achieved both clinical cure and mycological cure
[2] Negative KOH and culture and at most mild erythema and/or scaling and no pruritus
[3] Absence of erythema, scaling and pruritus
[4] Negative KOH and negative fungal culture

The safety and efficacy of luliconazole for tinea cruris treatment were evaluated in a randomized, double-blind, vehicle-controlled, multi-centre clinical trial in 256 subjects with a clinical and culture-confirmed diagnosis of tinea cruris. Subjects were randomized to receive luliconazole or vehicle. Subjects applied either luliconazole or vehicle cream to the affected area and approximately 2.5 cm (1 in) of the surrounding area once daily for 7 days.

The mean age of the study population was 40 years; 83% were male; 58% were White and 34% were Black or African American. Signs and symptoms of tinea cruris (erythema, scaling, and pruritus), positive KOH exam and dermatophyte culture were assessed at baseline, end-oftreatment (Day 7), 2 and 3 weeks post-treatment.

Overall treatment success was defined as complete clearance (clinical cure and mycological cure) at 3 weeks post-treatment. Luliconazole demonstrated complete clearance in subjects with tinea cruris. Treatment outcomes at 3 weeks post-treatment are summarized in Table.

Table. Efficacy Results at 3 Weeks Post-treatment - Tinea Cruris

	Luliconazole Cream, 1% N= 165 n (%)	**Vehicle Cream N= 91 n (%)**
Complete Clearance[1]	35 (21%)	4 (4%)
Effective Treatment[2]	71 (43%)	17 (19%)
Clinical Cure[3]	40 (24%)	6 (7%)
Mycological Cure[4]	129 (78%)	41 (45%)

[1] Proportion of subjects who achieved both clinical cure and mycological cure

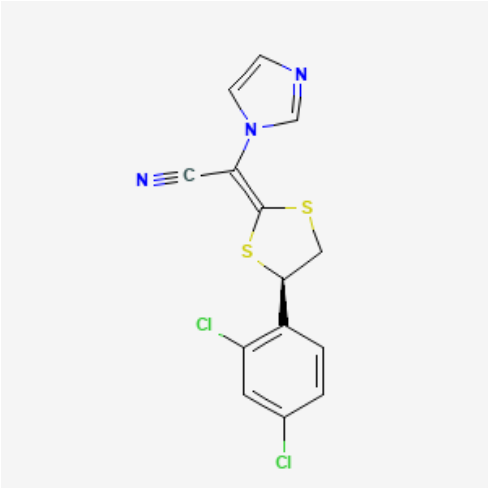
[2] Negative KOH and culture and at most mild erythema and/or scaling and no pruritus

[3] Absence of erythema, scaling and pruritus

[4] Negative KOH and negative fungal culture

7. Description

Luliconazole is (2E)-2-[(4R)-4-(2,4-dichlorophenyl)-1,3-dithiolan-2-ylidene]-2-imidazol-1-ylacetonitrile. The empirical formula is C14H9Cl2N3S2 and its molecular weight is 354.3 g/mol. The chemical structure of Luliconazole is:



Luli- Ease
Luliconazole Cream is white to off white cream filled in Laminated tube.

The list of excipients used are Methyl paraben, Benzyl alcohol, Polysorbate, Cetostearyl Alcohol, Propylene Glycol, Isopropyl Myristate, Butylated Hydroxy Toluene, Medium Chain Triglycerides, Stearic acid and Sodium Hydroxide.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the date of expiry.

8.3. Packaging information

Luliconazole is available in tube of 10 gm & 30 gm.

8.4. Storage and handing instructions

Store at a temperature not exceeding 30^{o}C. Do not Freeze.

Keep the tube tightly closed after use.

For external use only.

Keep out of reach of children.

Avoid contact with eyes, mouth & other mucous membranes.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Manufactured by:

Pure & Cure Healthcare Pvt. Ltd.

(A subsidiary of Akums Drugs & Pharmaceuticals Ltd.)

Plot No. 26A, 27-30, Sector 8A, I.I.E, SIDCUL,

Ranipur, Haridwar-249 403, Uttarakhand.

11. Details of permission or licence number with date

Mfg. Lic. No. is 31/UA/2013, issued on 27.07.2024.

12. Date of revision

NA

MARKETED BY

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IN/ LULI-EASE CREAM /APR-2026/01/PI