# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. Name of the medicinal product
Luliconazole 1 % w/w topical cream
Lucozol

## 2. Qualitative and quantitative composition
Each gram of cream contains 10 mg of luliconazole.

Excipient with known effect
Each gram of cream also contains 10 mg of benzyl alcohol, 0.1 mg of butylated hydroxytoluene and 250 mg of propylene glycol (see section 4.4).

For the full list of excipients, see section 6.1.

## 3. Pharmaceutical form
Topical cream.

Off-white to pale yellow-coloured smooth cream.

## 4. Clinical particulars

### 4.1 Therapeutic indications
Luliconazole is indicated for the topical treatment of fungal infections in people with interdigital tinea pedis (athlete's foot that is between the toes), tinea cruris (jock itch or ringworm) and tinea corporal (ringworm of the body) caused by the organisms.

### 4.2 Posology and method of administration

**Posology**

***For the treatment of interdigital tinea pedis (athlete's foot - 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 - 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**
Topical use.

## 4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
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.

**Specific Populations**

*Pediatric population*
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 population*
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.

*Excipients*
This medicine contains **benzyl alcohol**. Benzyl alcohol may cause mild local irritation.

This medicine **also** contains **butylated hydroxytoluene**. Butylated hydroxytoluene may cause local skin reactions (e.g., contact dermatitis).

This medicine **also** contains **propylene glycol**. Propylene glycol may cause skin irritation, do not use it on open wounds or large areas of broken or damaged skin (such as burns) without checking with your doctor or pharmacist.

## 4.5 Interaction with other medicinal products and other forms of interaction

The potential of luliconazole to inhibit cytochrome P-450 (CYP) enzymes 1A2, 2C9, 2C19, 2D6,

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 Fertility, pregnancy and breastfeeding

**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 ($mg/m^2$) 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 $mg/m^2$/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 ($14^{th}$ 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, embryofetal 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, embryofetal toxicity (increased prenatal pup mortality, reduced live litter sizes and increased postnatal pup mortality) was noted at 25 mg/kg/day. No embryofetal 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 luconazole 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).

### 4.7 Effects on the ability to drive and use machines
The medication has no known influence on the ability to drive or use machinery.

### 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 suspected 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. Healthcare professionals are asked to report any suspected adverse reactions via the e-PV desktop applications (https://drive.google.com/file/d/16hwTz0587ZWtSWadbBAMwQPOD_KSExZP/view) or search for e-PV Mobile applications on the Google Play or Apple App Store.

### 4.9 Overdose
Overdose treatment should be supportive or symptomatic.

## 5. Pharmacological properties

### 5.1 Pharmacodynamic properties
Pharmacological classification: 14.1.3 Dermatological and topical preparations: Antifungals.

*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.

*Pharmacodynamic effects*
At therapeutic doses, luliconazole is not expected to prolong QTc to any clinically relevant extent.

### 5.2 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 ($C_{max}$) 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 $C_{max}$ ($T_{max}$) 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 ($AUC_{0-24}$) 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 $C_{max}$ was 4.91 ± 2.51 ng/mL after the first dose and 7.36 ± 2.66 ng/mL after the final dose. The mean $T_{max}$ 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 $AUC_{0-24}$ was 85.1 ± 43.69 ng*hr/mL after the first dose and 121.74 ± 53.36 ng*hr/mL after the final dose.

### 5.3 Preclinical safety data

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 1.

**Table 1: 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-of-treatment (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 2.

**Table 2. Efficacy Results at 3 Weeks Post-treatment - Tinea Cruris**

| | **LUZU 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

## 6. Pharmaceutical particulars

### 6.1 List of excipients
Medium chain triglycerides
Propylene glycol
Isopropyl myristate
Benzyl alcohol
Polysorbate/ Acrylamide/ Sodium acryloyldimethyl taurate copolymer/ sohexadecane
Butylated hydroxytoluene
Purified water

### 6.2 Incompatibilities
Not applicable.

### 6.3 Shelf life
24 months.

### 6.4 Special precautions for storage
Store below 30°C.

### 6.5 Nature and contents of the container
The cream is packed in a laminated aluminium tube with a cap.

Fill weight: 30 g.

### 6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. APPLICANT

Lincoln Pharmaceuticals Limited
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Ahmedabad - 380060
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## 8. MANUFACTURER

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## 9. REGISTRATION DETAILS

Zimbabwe registration number: 2023/14.1.3/6497
Zimbabwe category for distribution: Pharmacist Initiated Medicines (P.I.M.)

## 10. DATE OF REVISION OF TEXT

January 2024