1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed.

Module I Administrative Information
Product Name: SKIZORALCREAM
Generic Name - Ketoconazole Cream BP 2% w/w

Summary Product Characteristics

1. Name of the proprietary product:

Name of the nonproprietary International Product:

Ketoconazole Cream BP 2% w/w

Route of Administration: Topical Cream

2. QUALITY AND QUANTITATIVE COMPOSITION:

No.	Ingredients	Specification	Quantity in mg with O.A/Tube
Active Ingredient			
1.	Ketoconazole	BP	630.0 mg
Excipients			
2	Methyl Paraben	BP	22.50
3	Propyl Paraben	BP	7.50
4	White soft paraffin	BP	2400.0
5	Light liquid paraffin	BP	375.0
6	Ceta macrogol 1000	BP	375.0
7	Cetosteryl Alcohol	BP	1500.0
8	Propylene Glycol	USP	900.0
9	Glycerin	BP	900.0
10	Disodium Edetate	BP	15.00

Where, USP: United State Pharmacopoeia, BP: British Pharmacopoeia, IH: In-House q.s:Quantity Sufficient.

3. PHARMACEUTICAL FORM: Topical Cream

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

For topical application in the treatment of dermatophyte infections of the skin such as tinea corporis, tinea cruris, tinea manus and tinea pedis infections due to Trichophyton spp, Microsporon spp and Epidermophyton spp. Skizoral cream is also indicated for the treatment of cutaneous candidiasis (including vulvitis), tinea (pityriasis) versicolor and seborrhoeic dermatitis caused by Malassezia (previously called Pityrosporum) spp.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION:

Ketoconazole cream is for use in adults.

Tinea pedis:

Skizoralcream should be applied to the affected areas twice daily. The usual duration of treatment for mild infections is 1 week. For more severe or extensive infections (eg involving the sole or sides of the feet) treatment should be continued until a few days after all signs and symptoms have disappeared in order to prevent relapse.

For other infections:

Skizoral cream should be applied to the affected areas once or twice daily, depending on the severity of the infection.

The treatment should be continued until a few days after the disappearance of all signs and symptoms. The usual duration of treatment is: tinea versicolor 2–3 weeks, tinea corporis 3–4 weeks.

The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks. General measures in regard to hygiene should be observed to control sources of infection or reinfection.

Seborrhoeic dermatitis is a chronic condition and relapse is highly likely.

Method of administration: Cutaneous administration.

Paediatrics

There are limited data on the use of ketoconazole 2% cream in paediatric patients.

4.3 CONTRAINDICATIONS:

Skizoral cream is contra-indicated in patients with a known hypersensitivity to any of the ingredients or to ketoconazole itself.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Skizoral cream is not for ophthalmic use.

If administered with a topical corticosteroid, to prevent a rebound effect after stopping a prolonged treatment with topical corticosteroids it is recommended to continue applying a mild topical corticosteroid in the morning and to apply Skizoral cream in the evening, and to subsequently and gradually withdraw the topical corticosteroid therapy over a period of 2-3 weeks.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS:

No interaction studies have been performed.

4.6 PREGNANCY AND LACTATION:

There are no adequate and well-controlled studies in pregnant or lactating women. Data on a limited number of exposed pregnancies indicate no adverse effects of topical ketoconazole on pregnancy or on the health of the foetus/newborn child. Animal studies have shown reproductive toxicity at doses that are not relevant to the topical administration of ketoconazole.

Plasma concentrations of ketoconazole are not detectable after topical application of Skizoral Cream to the skin of non-pregnant humans. There are no known risks associated with the use of Skizoral Cream in pregnancy or lactation.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINE:
Skizoral has no influence on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS:
The safety of ketoconazole cream was evaluated in 1079 subjects who participated in 30 clinical trials. Ketoconazole cream was applied topically to the skin. Based on pooled safety data from these clinical trials, the most commonly reported (≥1% incidence) adverse reactions were (with % incidence): application site pruritus (2%), skin burning sensation (1.9%), and application site erythema (1%).
Including the above-mentioned adverse reactions, the following table displays adverse reactions that have been reported with the use of ketoconazole cream from either clinical trial or post marketing experiences. The displayed frequency categories use the following convention:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not Known (cannot be estimated from the available clinical trial data).

System Organ Class	**Adverse Reactions**		
	Frequency Category		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorders		Hypersensitivity	
Skin and Subcutaneous Tissue Disorders	Skin burning sensation	Bullous eruption Dermatitis contact Rash Skin exfoliation Sticky skin	Urticaria
General Disorders and Administration Site Conditions	Application site erythema Application site pruritus	Application site bleeding Application site discomfort Application site dryness Application site inflammation Application site irritation Application site paraesthesia Application site reaction	

4.9 OVERDOSE:
Topical Application
Excessive topical application may lead to erythema, oedema and a burning sensation, which will disappear upon discontinuation of the treatment.
Ingestion
In the event of accidental ingestion, supportive and symptomatic measures should be carried out.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group:
Antifungals for Topical Use,
ATC code: D01A C08

Mode of action:

Usually, ketoconazole cream acts rapidly on pruritus, which is commonly seen in dermatophyte and yeast infections, as well as skin conditions associated with the presence of Malassezia spp. This symptomatic improvement is observed before the first signs of healing are observed.

Ketoconazole, a synthetic imidazole dioxolane derivative, has a potent antimycotic activity against dermatophytes such as Trichophyton spp., *Epidermophyton floccosum* and Microsporum spp. and against yeasts, including Malassezia spp. and Candida spp. The effect on Malassezia spp. is particularly pronounced.

A study in 250 patients has shown that application twice daily for 7 days of ketoconazole 2% cream vs clotrimazole 1% cream for 4 weeks on both feet demonstrated efficacy in patients with tinea pedis (athlete's foot) presenting lesions between the toes. The primary efficacy endpoint was negative microscopic KOH examination at 4 weeks. Ketoconazole 2% treatment showed equivalent efficacy to 4 weeks clotrimazole 1% treatment. There was no evidence of relapse following treatment with ketoconazole cream at 8 weeks.

5.2 PHARMACOKINETIC PROPERTIES:

Plasma concentrations of ketoconazole were not detectable after topical administration of Skizoral Cream in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of Skizoral cream was applied daily on 40% of the body surface area, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

5.3 PRECLINICAL SAFETY DATA:

Preclinical data reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS:

6.1 LIST OF EXCEPIENTS:

Methyl Paraben	BP
Propyl Paraben	BP
White soft paraffin	BP
Light liquid paraffin	BP
Cetamacrogol 1000	BP
Cetosteryl Alcohol	BP
Propylene Glycol	USP
Glycerin	BP
Disodium Edetate	BP

6.2 INCOMPATIBILITIES:

Not Applicable

6.3 SHELF-LIFE:

36 months from date of manufacturing.

6.4 SPECIAL PRECAUTIONS FOR STORAGE:
Do not Freeze.
Store in cool, dry & dark place.
Keep out of reach of children.

6.5 NATURE AND CONTENT OF CONTAINER:
A Lami tube containing 30 gm of Cream packed in carton along with pack insert.

7. MARKETING AUTHORISATION HOLDER

LESANTO LABORATORIES
Plot no: 9, 10, 11 & 20, Survey no: 53, Near
Railway Bridge, Palghar (E).

8. MARKETING AUTHORISATION NUMBER(S)
Not Applicable

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Not Applicable

10. DATE OF REVISION OF THE TEXT - July-2022