SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Product Name

HYZORAL CREAM (KETOCONAZOLE CREAM 2%W/W)

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SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal Product

HYZORAL CREAM (KETOCONAZOLE CREAM 2%w/w)

2. Qualitative and quantitative composition

Composition:

Ketoconazole USP……2.0 % W/W

Perfume …… Q.S

Cream Base q.s.

Batch Size:1025Kg

Sr. No.	Ingredients	Specification	Label claim	Overages added (In %)	Quantity / 1gm (mg)	Quantity / 30gm Tube (mg)	Quantity of Batch in Kg
1.	Ketoconazole USP	USP	2.00%w/w	-	2.00	60.00	20.50
2.	Macrogol Cetostearyl ether	BP	3.00%w/w	-	3.00	90.00	30.75
3.	Cetostearyl Alcohol	BP	8.00%w/w	-	8.00	240.0	82.00
4.	Methyl Hydroxybenzoate	BP	0.15%w/w	-	0.15	4.500	1.538
5.	Propyl Hydroxybenzoate	BP	0.05%w/w	-	0.05	1.500	0.513
6.	White Soft Paraffin	BP	10.0%w/w	-	10.0	300.0	102.50
7.	Chlorocresol	BP	0.038%w/w	-	0.038	1.140	0.390
8.	Propylene Glycol	BP	5.0%w/w	-	5.0	150.0	51.25
9.	Anhydrous Sodium Sulphite	BP	0.25%w/w	-	0.25	7.500	2.563
10.	Sodium Dihydrogen Phosphate Dihydrate	BP	0.282%w/w	-	0.282	8.460	2.891
11.	Fragrance-Wind Stone NP 21968	IH	0.2%w/w	-	0.2	6.000	2.050
12.	Purified Water	BP	-	-	q.s.	q.s.	q.s. to 1025kg

HYZORAL CREAM
(KETOCONAZOLE CREAM 2%w/w)

3. Pharmaceutical form

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. HYZORAL cream is also indicated for the treatment of cutaneous candidosis (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.

Cutaneous candidosis, tinea corporis, tinea cruris, tinea manus, tinea pedis and tinea (pityriasis) versicolor:

It is recommended that HYZORAL cream be applied once or twice daily to cover the affected and immediate surrounding area.

The usual duration of treatment is: tinea versicolor 2– 3 weeks, yeast infections 2-3 weeks, tinea cruris 2-4 weeks, tinea corporis 3– 4 weeks, tinea pedis 4-6 weeks.

Seborrheic dermatitis:

HYZORAL 2% cream should be applied to the affected areas once or twice daily.

The usual initial duration of treatment in seborrheic dermatitis is 2 to 4 weeks. Maintenance therapy can be applied intermittently (once weekly) in seborrheic dermatitis.

Treatment should be continued until a few days after the disappearance of all symptoms. The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks of treatment. 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 patients

The safety and efficacy of HYZORAL cream in children (17 years of age and younger) has not been established.

4.3 Contraindications

HYZORAL 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

HYZORAL CREAM is not for ophthalmic use.

If coadministered 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 HYZORAL cream in the evening, and to subsequently and gradually withdraw the topical corticosteroid therapy over a period of 2-3 weeks.

HYZORAL Cream contains 6000 mg propylene glycol in each 30 g tube, which is equivalent to 200 mg/g.

HYZORAL CREAM contains cetyl alcohol and stearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

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 HYZORAL CREAM to the skin of non-pregnant humans. (See Pharmacokinetic properties, section 5.2) There are no known risks associated with the use of HYZORAL CREAM in pregnancy or lactation.

4.7 Effects on ability to drive and use machines

HYZORAL CREAM 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 postmarketing 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 paresthesia 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, Imidazole and triazole derivatives

ATC Code: D01AC08

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 HYZORAL CREAM in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of HYZORAL CREAM2% 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

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

6. Pharmaceutical particulars

6.1 Excipients

- Ketoconazole USP
- Macrogol Cetostearyl ether
- Cetostearyl Alcohol
- Methyl Hydroxybenzoate
- Propyl Hydroxybenzoate
- White Soft Paraffin
- Chlorocresol
- Propylene Glycol
- Anhydrous Sodium Sulphite

- Sodium Dihydrogen Phosphate Dihydrate
- Fragrance-Wind Stone NP 21968
- Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at a temperature below 30^0C. in dry place Protect from light.

6.5 Nature and contents of container

30 g Tube Packed in Carton along with Leaflet.

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

Name and address of Manufacturing Site:

GOPALDAS VISRAM & COMPANY LIMITED

Plot No. : A / 590-591, T.T.C. Industrial Area, M.I.D.C.,
Mahape, Navi Mumbai – 400 710, India.

Telephone : 91-22-41111710 / 717

E-Mail: sangeetajagani@gopaldasvisram.com

8. Marketing Authority

SUITELIFE PHARM LTD.

4, Ayo, Davies Close, Off Ekololu Street,

Surulere, Lagos State, Nigeria**.**