Product Name: NAFROZORAL CREAM(KETACANAZOLE CREAM BP 2% W/W)

1 NAME OF THE MEDICINAL PRODUCT

NAFROZORAL CREAM (KETACANAZOLE CREAM BP 2% W/W)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gm contains:
Ketoconazole BP ..... 2% w/w
Cream Base..... q.s.

Sr. No.	Ingredients	Specification	Label claim (In % w/w)	Overages (in %)	Each 30 gm contains (in mg)	Reason for inclusion
1.	Ketoconazole	BP	2 %	8	648.00	Medicament
2.	Cetyl Alcohol	BP	-	-	600.00	Emulsifier
3.	Polysorbate 80 (Tween 80)	BP	-	-	30.00	Emulsifying agent
4.	Propylene Glycol	BP	-	-	6000.00	Solvent
5.	Isopropyl Myristate	BP	-	-	300.00	Solvent
6.	Stearyl Alcohol	BP	-	-	2250.00	Emulsifier
7.	Sorbitan Mon stearate (Span-60)	BP	-	-	600.00	Emulsifying agent
8.	Polysorbate 60 (Tween-60)	BP	-	-	450.00	Emulsifying agent
9.	Sodium Sulphite	BP	-	-	60.00	Antioxidant
10.	Purified Water	BP	-	-	19110	Aq. base

3 PHARMACEUTICAL FORMS

Topical Cream. A white coloured cream

4 CLINICAL PARTICULARS

4.1 Therapeutic Indication.

The topical application of ketoconazole is used 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.

Ketoconazole 2% 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.

Tinea pedis:

Ketoconazole 2% cream 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:

Ketoconazole 2% 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

Ketoconazole 2% cream is contra-indicated in patients with a known hypersensitivity to any of the ingredients or to ketoconazole itself.

4.4 Special warnings and precaution for use.

Ketoconazole 2% 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 Ketoconazole 2% 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 product 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 Ketoconazole 2% Cream to the skin of non-pregnant humans. (See Pharmacokinetic properties, section 5.2) There are no known risks associated with the use of Ketoconazole 2% Cream in pregnancy or lactation.

4.7 Effect on the ability to drive and use machine.

Ketoconazole 2% cream has no influence on the ability to drive and use machines.

4.8 Undesirable effect.

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.

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 Microsporumspp. 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 withtinea 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 Ketoconazole 2% Cream in adults on the skin. In one study in infants with seborrhoeic dermatitis(n = 19), where approximately 40 g of Ketoconazole 2% 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.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetyl Alcohol
Polysorbate 80 (Tween 80)
Propylene Glycol
Isopropyl Myristate
Stearyl Alcohol
Sorbitan Mon stearate (Span-60)
Polysorbate 60 (Tween-60)
Sodium Sulphite
Purified Water

6.2 Incompatibilities

unknown

6.3 Shelf-life
36 months

6.4 Special precautions for storage
Do not store above 30°C. Store in a dry place.

6.5 Nature and composition of immediate packaging

20 gm cream packed in a printed lami tube placed in inner carton. Such 10 inner carton placed in outer carton

6.6 Special precautions for the disposal of unused veterinary medicinal productsor waste materials
None.

7. Marketing authorisation holder
NAFRO PHARMA NIGERIA LTD
Suite B16, Amori shopping Plaza,
113, Idimu Road, Orelope Egbeda Lagos,Nigeria

Manufacturer Name

Astamed Healthcare (I) Pvt. Ltd.

Plot No. 2 & 3, Phase-II, Genesis Ind. Complex,

Kolgaon, Palghar-401404, Maharashtra, India

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text