1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE DRUG PROUDUCT:

NEOVIRAL CREAM (Ketoconazole Cream 2.0% w/w)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Declaration-

Each gm contains-

Ketoconazole USP 2.0% w/w

Excipients Q.S.

Quantitative Declaration-

BATCH SIZE: 100000 CREAMS

Ingredients	Function	Quantity (%)	Quantity/Batch (in kg)
Ketoconazole USP	Antifungal agent	**0.02 GM**	**0.000020**
Cetamacrogal- 1000 BP	Emulsifying agent, Solubilizing agent	3.000	30.000
Cetostearyl Alcohol BP	Emollient, Emulsifying agent	8.000	80.000
Light Liquid Paraffin BP	Emollient, Lubricant	4.000	40.000
White soft Paraffin BP	Emollient, Ointment Base	17.000	170.000
Propylene Glycol BP	Humectant, Stabilizing agent	7.500	75.0000
Chlorocresol BP	Antimicrobial	0.100	1.000
Sodium Dihydrogen Ortho Phosphate BP	Buffering agent, sequestering agent	0.100	1.000
Disodium Hydrogen Ortho Phosphate BP	Buffering agent, emulsifying agent	0.020	0.200
EDTA Sodium BP	Chelating agent.	0.010	0.100
Purified Water BP	Solvent	q.s.	q.s.
Orthophosphoric acid BP	Alkalizing agent; buffering agent	q.s.	q.s.
Color Erythrosine Supra IH	Colorant	0.285	2.85 g
Fragrance Swiss Rose IH	Aroma Compound	0.1425	1.425

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. 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 Dosage/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 Ketoconazole 2% 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: Ketoconazole 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.

Paediatric patients: The safety and efficacy of Ketoconazole 2% cream in children (17 years of age and younger) has not been established.

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 precautions 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.

Ketoconazole 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 Fertility, 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 Effects on ability to drive and use machines

Ketoconazole 2% 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**		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorders			
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	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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: Yellow Card Scheme Website: https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 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 excess of the maximum human exposure indicating little relevance to clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetamacrogal-1000
Cetostearyl Alcohol
Light Liquid Paraffin
White soft Paraffin
Propylene Glycol
Chlorocresol
Sodium Dihydrogen Ortho Phosphate
Disodium Hydrogen Ortho Phosphate
EDTA Sodium
Purified Water
Orthophosphoric acid
Color Erythrosine Supra
Fragrance Swiss Rose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Storage: Do not freeze. Store below 30°C.

To be used only under medical supervision.

Replace cap securely after use.

Keep all medicines out of reach of children.

For External Use Only.

6.5 Nature and contents of container

30 gm

6.6 Special Precautions for Disposal of a used medicinal product or waste materials derived from such medicinal product and Other Handling of the Product

No special requirements

7. APPLICANT/HOLDER OF CERTIFICATE OG PRODUCT REGISTRATION

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Block 116, Flat 1, Ojokoro Housing Estate, Meiran, Lagos

8. DRUG PRODUCT MANUFACTURER

Cotec Healthcare Pvt. Ltd.

NH No. 74, Roorkee Dehradun Highway, Kishanpur, Roorkee (UK) 247667

9. NAFDAC REGISTRATION NUMBER(S)
