

1. NAME OF THE MEDICINAL PRODUCT

(Ketoconazole Cream BP 2.0 % w/w)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Ketoconazole BP.....2.0 % w/w

Cream base.....q.s.

3. PHARMACEUTICAL FORM

Topical Cream

White homogenous cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ketoconazole Cream is indicated 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 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

Posology

Ketoconazole Cream is for use in adults.

Paediatric population

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

Method of administration:

Cutaneous administration.

Tinea pedis:

Ketoconazole 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 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. Seborrheic dermatitis is a chronic condition and relapse is highly likely.

4.3 Contraindications

Ketoconazole 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 cream is not for ophthalmic use.

If co-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 ketoconazole 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 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 cream to the skin of non-pregnant humans. There are no known risks associated with the use of ketoconazole cream in pregnancy or lactation.

4.7 Effects on ability to drive and use machines

Ketoconazole 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 ($\geq 1\%$ 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 ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ 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 ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1,000$ 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	

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.

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: D01A C08

Mechanism 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 ketoconazole cream in adults on the skin. In one study in infants with seborrheic dermatitis (n = 19), where approximately 40 g of ketoconazole 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 excipients

Methyl Paraben, Propyl Paraben, White soft Paraffin, Light Liquid Paraffin, Cetomacrogol 1000, Cetostearyl Alcohol, Propylene Glycol, Glycerin, Disodium Edetate & Purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C in a dry place. Do not freeze. Protect from light.

6.5 Nature and contents of container

ketoconazole cream is a white homogenous cream filled in a 30 gm printed lami tube packed in a printed carton along with leaflet.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

M/s. GENEITH PHARM LTD.

12 Adewale Crescent, Off Ewenla Street,
Off Oshodi, Apapa,
Lagos, Nigeria

8. MARKETING AUTHORISATION NUMBER(S)

BD/26

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/01/2023

10. DATE OF REVISION OF THE TEXT

29/12/2027