

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nizoral 20 mg/g Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketoconazole 2% w/w (each gram of cream contains 20 mg).

Excipients with known effect;
propylene glycol, 20%w/w
stearyl alcohol, 7.5%w/w
cetyl alcohol, 2.0%w/w

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream
White odourless cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nizoral cream is indicated 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, Microsporum and Epidermophyton species.

Nizoral cream is also indicated for the treatment of cutaneous candidosis (including external application in vulvitis), *Tinea (pityriasis) versicolor* and in the treatment of seborrhoeic dermatitis, a skin condition related to the presence of *Malassezia furfur* (previously called *Pityrosporum ovale*).

4.2 Posology and method of administration

Nizoral Cream is for use in adults.

For cutaneous administration.

Cutaneous candidosis, tinea corporis, tinea cruris, tinea manus, tinea pedis and tinea (pityriasis) versicolor: It is recommended that Nizoral 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 infection 2-3 weeks, tinea cruris 2-4 weeks, tinea corporis 3-4 weeks, tinea pedis 4-6 weeks.

Seborrheic dermatitis: Nizoral 2% Cream should be applied to the affected areas once or twice daily. The usual initial duration of treatment for seborrheic dermatitis is 2 to 4 weeks. Maintenance therapy can be applied intermittently (once weekly) in seborrheic dermatitis.

The treatment should be continued, until a few days after disappearance of all symptoms. The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks of treatment. General measures with regard to hygiene should be observed to control sources of infection or re-infection.

Paediatric patients

The safety and efficacy of Nizoral 2% Cream in children (17 years of age and younger) has not been established.

4.3 Contraindications

Nizoral cream is contra-indicated in patients with a known hypersensitivity to ketoconazole or any ingredient of the cream formulation.

4.4 Special warnings and precautions for use

Significant absorption is unlikely after topical application to unbroken skin.

Nizoral cream is not for ophthalmic use.

Nizoral cream contains cetyl alcohol, stearyl alcohol and propylene glycol which may cause skin irritations (e.g: contact dermatitis).

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 Nizoral cream in the evening, and to subsequently and gradually withdraw the steroid therapy over a period of 2-3 weeks.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

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 Ketoconazole on pregnancy or on the health of the foetus/newborn child. Animal studies have shown reproductive toxicity following oral administration of ketoconazole. (see Preclinical safety data, section 5.3). Plasma concentrations of ketoconazole are not detectable after topical administration of Nizoral 2% Cream to the skin of non-pregnant humans. There are no known risks associated with the use of Nizoral 2% Cream in pregnancy or lactation

4.7 Effects on ability to drive and use machines

This medicine 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) ADRs were (with % incidence): application site pruritus (2%), skin burning sensation (1.9%), and application site erythema (1%).

Including the above-mentioned adverse drug reactions (ADRs), the following table displays ADRs 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

Frequency Category

Common

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

Immune System Disorders

Skin and subcutaneous Tissue Disorders

General disorders and administration site conditions

Adverse Drug Reactions		
Uncommon ($\geq 1/1,000$ to <1/100)	Not Known	
	Hypersensitivity	

Skin burning sensation	Bullous eruption Dermatitis contact Rash Skin exfoliation Sticky skin	Urticaria
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	

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 via HPRA Pharmacovigilance, website: www.hpra.ie; E-mail.

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: Imidazole and triazole derivatives

ATC code: D01 AC08

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

Ketoconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane.

Nizoral cream acts rapidly on pruritus which is commonly seen in dermatophyte and yeast infections, as well as skin conditions related to the presence of *Malassezia* spp. This symptomatic improvement often occurs before the first signs of healing are observed.

5.2 Pharmacokinetic properties

Plasma concentrations of ketoconazole were not detectable after topical administration of Nizoral Cream in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of Nizoral 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 including primary ocular or dermal irritation, dermal sensitisation and repeat-dose dermal toxicity.

Ketoconazole has been shown to be teratogenic (syndactylia and oligodactylia) in the rat when given orally in the diet at 80 mg/kg/day; a dose that is 10 times above the maximum human oral dose on a mg/kg basis and more than 6000 times the plasma detection limit which was not reached in animal topical studies conducted by the Market Authorisation Holder.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
Stearyl alcohol
Cetyl alcohol
Sorbitan stearate
Polysorbate 60
Isopropyl myristate
Sodium sulfite
Polysorbate 80
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Lined aluminium tube, with a polypropylene screw cap, containing either 15g* or 30g cream.

*Not all pack sizes may be marketed.

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.

6.6 Special precautions for disposal

No special requirements.

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

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
Waterford Road
Clonmel, Co. Tipperary
E91 D768
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/315/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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