SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Nizoral 20mg/g Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients;
Propylene glycol, 20% w/w
Stearyl alcohol, 7.5% w/w
Cetyl alcohol, 2.0% w/w
For a 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, Microsporon* 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 cream 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 cruris2-4 weeks;
Tinea corporis 3–4 weeks;

Tinea pedis 4-6 weeks

Seborrheic dermatitis:
Nizoral cream 2% should be applied to the affected areas once or twice daily.

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

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. 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.

Paediatric patients
The safety and efficacy of Nizoral Cream 2% 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 any of the ingredients 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.

This medicine contains 200 mg propylene glycol in each gram of cream.
Propylene glycol may cause skin irritation.
Because this medicine contains propylene glycol, do not use it on open wounds or large areas of broken or damaged skin (such as burns) without checking with your doctor or pharmacist.

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

None stated.

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) 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	**Adverse Drug 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 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 the ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

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 D01AC08

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. The effect on *Malassezia* spp. is very pronounced.

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 Sulphite (E221)
Polysorbate 80
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Tube made of 99.7% aluminum, lined on inner side with heat polymerised epoxyphenol resin with a latex coldseal ring at the end of the tube. The cap is made of 60% polypropylene, 30% calcium carbonate and 10% glyceryl monostearate.

Tubes of 30g.

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

Not special requirements.

7. MARKETING AUTHORISATION HOLDER

STADA Arzneimittel AG, Stadastrasse 2-18, 61118 Bad Vilbel, Germany

8. MARKETING AUTHORISATION NUMBER(S)

Malta: 830/00402

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First Authorisation:02 March 2007
Renewal: 05 October 2012

10. DATE OF REVISION OF THE TEXT

29th November 2023