SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nizoral Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For a full list of excipients, see 6.1.

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, Microsporom spp and Epidermophyton spp.

Nizoral 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.

Cutaneous candidosis, tinea corporis, tinea cruris, tinea manus, tinea pedis and tinea (pityriasis) versicolor: it is recommended that Nizoral 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.

Seborrhoeic dermatitis: Nizoral Cream should be applied to the affected area once or twice daily.

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

Paediatrics patients

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

4.3 Contraindications

Nizoral 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

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

Nizoral cream contains 6000 mg propylene glycol in each 30 g tube, which is equivalent to 200 mg/g.

Nizoral 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 Nizoral 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 Nizoral 2% Cream in pregnancy or lactation.

4.7 Effects on ability to drive and use machines

Nizoral 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		
	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	

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://sideeffects.health.gov.il

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

Stearyl Alcohol

Cetyl Alcohol

Sorbitan Stearate

Polysorbate 60

Isopropyl Myristate

Sodium Sulphite Anhydrous (E221)

Polysorbate 80

Water purified (Ph. Eur)

Propylene Glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

store between 15-30°C.

6.5 Nature and contents of container

Tube of 15g.

6.6 Special precautions for disposal

No special requirements

7 License Holder

J-C Health Care-Cilag Ltd., Kibbutz Shefayim, 6099000, Israel

8 MARKETING AUTHORISATION NUMBER

042-19-25862-00

9 MANUFACTURER

Janssen Pharmaceutica,N.V Beerse, Turnhoutseweg 30, B-2340, Belgium

Approved in Jan-2023

Based on UK SmPC Mar-2021