เอกสารกำกับยาสำหรับแพทย์ฉบับภาษาอังกฤษ

NIZORAL®

1. Name of the Medicinal Product

1.1 Product Name

NIZORAL® (ketoconazole (INN: Ketoconazole)) 2% Cream

1.2 Strength

Each gram contains 20 mg ketoconazole.

For excipients, see *List of Excipients.*

1.3 Pharmaceutical Dosage Form

Cream for topical application to the skin.

2. Qualitative and Quantitative Composition

Each gram contains 20 mg ketoconazole.

For excipients, see *List of Excipients.*

3. Pharmaceutical Form

Cream for topical application to the skin.

4. Clinical Particulars

4.1 Therapeutic indication

NIZORAL 2% Cream is indicated for topical application in the treatment of dermatophyte infections of the skin: tinea corporis, tinea cruris, tinea manus and tinea pedis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Microsporum canis* and *Epidermophyton floccosum*, as well as in the treatment of cutaneous candidosis and tinea (pityriasis) versicolor.

NIZORAL 2% Cream is also indicated for the treatment of seborrheic dermatitis, a skin condition associated with the presence of *Malassezia furfur*.

4.2 Posology and method of administration

Dosage

Cutaneous candidosis, tinea corporis, tinea cruris, tinea manus, tinea pedis and tinea (pityriasis) versicolor: it is recommended that NIZORAL 2% Cream be applied once daily to cover the affected and immediate surrounding area.

Seborrheic dermatitis: NIZORAL 2% Cream should be applied to the affected area once or twice daily.

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.

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 disappearance of all symptoms. The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks of treatment.

Special populations

Pediatrics

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

Administration

Topical administration to the skin.

4.3 Contraindication

NIZORAL 2% Cream is contraindicated in individuals with a known hypersensitivity to any of its ingredients.

4.4 Special warning and precautions

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.

4.5 Interaction with other medicinal products and other forms of interactions

None known.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Plasma concentrations of ketoconazole are not detectable after topical application 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.

Breast-feeding

There are no adequate and well-controlled studies in lactating women. There are no known risks associated with the use of NIZORAL 2% Cream in lactation.

4.7 Effect on ability to drive and use machine

Not applicable.

4.8 Undesirable effects

Throughout this section, adverse reactions are presented. Adverse reactions are adverse events that were considered to be reasonably associated with the use of ketoconazole based on the comprehensive assessment of the available adverse event information. A causal relationship with ketoconazole cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Clinical trial data

The safety of NIZORAL 2% Cream was evaluated in 1079 subjects in 30 clinical trials where NIZORAL 2% Cream was applied topically to the skin.

Adverse reactions that were reported for ≥1% of NIZORAL 2% Cream-treated subjects are shown in Table 1.

Table 1: Adverse Reactions Reported in ≥1% of 1079 NIZORAL 2% Cream-treated Subjects in 30 Clinical Trials

System Organ Class	%
Preferred Term	
General Disorders and Administration Site Conditions	
Application site erythema	1.0
Application site pruritus	2.0
Skin and Subcutaneous Tissue Disorders	
Skin burning sensation	1.9

Additional adverse reactions that occurred in <1% of NIZORAL 2% Cream-treated subjects in the clinical datasets are listed in Table 2.

Table 2: Adverse Reactions Reported in <1% of 1079 NIZORAL 2% Cream-treated Subjects in 30 Clinical Trials

System Organ Class
Preferred Term
General Disorders and Administration Site Conditions
Application site bleeding
Application site discomfort
Application site dryness
Application site inflammation
Application site irritation
Application site paresthesia
Application site reaction
Immune System Disorders
Hypersensitivity
Skin and Subcutaneous Tissue Disorders
Bullous eruption
Dermatitis contact
Rash
Skin exfoliation
Sticky skin

Postmarketing data

In addition to the adverse reactions reported during clinical studies and listed above, the following adverse reactions have been reported during postmarketing (Tables 3). In table, the frequencies are provided according to the following convention:

Very common	≥ 1/10
Common	≥ 1/100 and < 1/10
Uncommon	≥ 1/1000 and < 1/100
Rare	≥ 1/10000 and < 1/1000
Very rare	< 1/10000, including isolated reports.

In Table 3, adverse reactions are presented by frequency category based on spontaneous reporting rates.

Table 3. Adverse Reactions Identified During Post-marketing Experience with NIZORAL 2% Cream by Frequency Category Estimated from Spontaneous Reporting Rates

Skin and Subcutaneous Tissue Disorders	
Very Rare	Urticaria

4.9 Overdose

Topical Application

Excessive topical application may lead to erythema, edema 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.

Mechanism of action

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

Pharmacodynamic effects

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.

Microbiology

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. Especially the effect on *Malassezia* spp. is very pronounced.

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 seborrheic 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

Preclinical data reveal no special hazard for humans based on conventional studies including primary ocular or dermal irritation, dermal sensitization and repeat-dose dermal toxicity.

Acute dermal and ocular irritation studies with ketoconazole cream formulations in rabbits showed no dermal or ocular irritation. Results from a dermal sensitization study in guinea pigs showed no allergenic or sensitizing potential. In five repeat-dose dermal studies in rabbits, ketoconazole was administered to both abraded and non-abraded skin at a maximum dose of 40 mg/kg. In one study some slight irritation was noted in both the ketoconazole and placebo groups, however, in the remaining studies no dermal or systemic toxic effects were noted. Data from pharmacokinetic studies, of several topical formulations of ketoconazole under exaggerated test conditions in laboratory animals, showed no measurable ketoconazole plasma concentrations.

6. Pharmaceutical Particulars

6.1 List of excipients

The cream formulation consists of cetyl alcohol, isopropyl myristate, polysorbate, propylene glycol, purified water (formulation F12), sodium sulfite, sorbitan stearate, stearyl alcohol.

6.2 Incompatibilities

None known.

6.3 Shelf life

See expiry date on the outer pack.

6.4 Special precautions for storage

Store below 30° C.

Keep out of reach of children

6.5 Nature and contents of container

NIZORAL 2% Cream is supplied in tubes of 15 g

Instructions for Use and Handling

To open the tube, unscrew the cap. Then pierce the seal of the tube with the pin on the top of the cap.

7. Marketing Authorization Holder

See below

Date of revision of the text

11 Apr 2024 (CCDS version 04-Oct-2017 hybrid with UK SmPC 10-Apr-2019 section 4.2)

Manufactured by

Janssen Pharmaceutica NV, Beerse, Belgium

Product Name	Marketing Authorization Numbers	Date of Authorization
NIZORAL®	1C 15165/63	28 December 2020

Imported by

Janssen-Cilag Ltd., Bangkok, Thailand

To report Suspected Adverse Reactions, please contact us at aepqcjacth@its.jnj.com

For any product information, please contact us at medinfosea@its.jnj.com

Warnings according to Ministry of Public Health announcement

Do not use in patient allergic to this drug