NAME OF THE MEDICINAL PRODUCT
NIZORAL® 2% Cream

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each gram contains 20 mg ketoconazole.
For excipients, see List of Excipients.

PHARMACEUTICAL FORM
Cream for topical application to the skin.

CLINICAL PARTICULARS
Therapeutic Indications
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 seborrhoeic dermatitis, a skin condition related with the presence of *Malassezia furfur*.
Posology and Method of 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 daily to cover the affected and immediate surrounding area.
Seborrhoeic dermatitis: NIZORAL® 2% Cream should be applied to the affected area once or twice daily depending on the severity of infection.
Treatment should be continued for a sufficient period, at least 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.
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 duration of treatment in seborrhoeic dermatitis is 2 to 4 weeks. Maintenance therapy is applied once or twice weekly in seborrhoeic dermatitis.
Contraindications
NIZORAL® 2% Cream is contraindicated in individuals with a known hypersensitivity to any of its ingredients.
Special Warnings and Special Precautions for Use
NIZORAL® 2% Cream is not for ophthalmic use.
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 steroid therapy over a period of 2-3 weeks.
Interactions with Other Medicinal Products and Other Forms of Interaction
None known.
Pregnancy and Lactation
There are no adequate and well-controlled studies in pregnant or lactating 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 or lactation.

Effects on Ability to Drive and Use Machines

Not applicable.

Undesirable Effects

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

Table 1: Adverse Drug 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 drug reactions that occurred in <1% of NIZORAL® 2% Cream-treated subjects in the clinical datasets are listed in Table 2.

Table 2: Adverse Drug 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 paraesthesia
Application site reaction
Immune System Disorders
Hypersensitivity
Skin and Subcutaneous Tissue Disorders
Bullous eruption
Dermatitis contact
Rash
Skin exfoliation
Sticky skin

Post-marketing experience

Adverse drug reactions first identified during post-marketing experience with NIZORAL® 2% Cream is included in Table 3. In table 3, 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, ADRs are presented by frequency category based on spontaneous reporting rates.

Table 3: Adverse Drug 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

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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

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. Especially 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.

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

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.

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.

PHARMACEUTICAL PARTICULARS

List of Excipients

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

Incompatibilities

None known.

Shelf Life

Observe expiry date on the outer pack.

Special Precautions for Storage

Store between 15 and 30° C.
Keep out of reach of children

Nature and Contents of Container

NIZORAL® 2% Cream is supplied in tubes of 15 g and 30 g.

Instructions for Use and Handling

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

MANUFACTURED BY

See outer carton.

DATE OF REVISION OF THE TEXT

December 2011