

## **NIZORAL SHAMPOO**

### **Product Information**

#### **1. Trade Name of the Medicinal Product**

Nizoral Shampoo

#### **2. Qualitative and Quantitative Composition**

Each gram contains 20 mg ketoconazole

For Excipients, see *List of Excipients*.

#### **3. Pharmaceutical Form**

Shampoo for topical application to the scalp or skin

#### **4. Clinical Particulars**

##### **4.1 Therapeutic Indications**

Topical treatment of Seborrhoeic Dermatitis including dandruff resulting from proven fungal infection including Pityriasis versicolor.

##### **4.2 Posology and Method of Administration**

###### **Dosage**

Usually, a palmful of shampoo suffices for one wash.

###### **Treatment**

Adults, Elderly and Adolescence :

Pityriasis versicolor: once daily for a maximum of 5 days.

- Seborrheic dermatitis and dandruff: twice weekly for 2 to 4 weeks.

###### **Special populations**

###### **Pediatrics**

The safe and effective use of Nizoral Shampoo 2% in infants and children under the age of 12 years has not been established.

###### **Administration**

Topical application to the scalp or skin.

The infected areas of the skin or the scalp should be thoroughly washed with NIZORAL Shampoo 2%, which should be left on the skin/scalp for 3 to 5 minutes before rinsing.

### **4.3 Contraindications**

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

### **4.4 Special Warning and Precautions for Use**

In patients who have been on prolonged treatment with topical corticosteroids, it is recommended that the steroid therapy be gradually withdrawn over the period of 2 to 3 weeks, while using NIZORAL Shampoo 2%, to prevent any potential rebound effect.

Avoid contact with the eyes.

If the shampoo should get into the eyes, they should be irrigated with water.

### **4.5 Interactions with other Medicaments and other forms of Interaction**

None known.

### **4.6 Pregnancy and lactation**

There are no adequate and well-controlled studies in pregnant women.

Plasma concentrations of ketoconazole were not detectable after topical administration of NIZORAL Shampoo 2% to the scalp of non-pregnant humans. Plasma levels were detected after topical administration of NIZORAL Shampoo 2% on the whole body.

There are no known risks associated with the use of NIZORAL Shampoo 2% 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 Shampoo 2% in lactation.

### **4.7 Effects on Ability to Drive and Use Machines**

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 Shampoo 2% was evaluated in 2890 subjects in 22 clinical trials where NIZORAL Shampoo was administered topically to the scalp and/or skin.

No adverse reactions were reported in  $\geq 1\%$  of NIZORAL Shampoo 2% - treated subjects.

Adverse reactions that occurred in  $<1\%$  of NIZORAL Shampoo 2% - treated subjects in the clinical datasets are listed in table 1.

<b>Table 1. Adverse Reactions Reported in <math>&lt;1\%</math> of 2890 NIZORAL Shampoo 2%-treated Subjects in 22 Clinical Trials</b>
<b>System Organ Class</b>
Preferred Term
<b>Eye Disorders</b>
Eye irritation
Increased lacrimation
<b>General Disorders and Administration Site Conditions</b>
Application site erythema
Application site irritation
Application site hypersensitivity
Application site pruritus
Application site pustules
Application site reaction
<b>Immune System Disorders</b>
Hypersensitivity
<b>Infections and Infestations</b>
Folliculitis
<b>Nervous System Disorders</b>
Dysgeusia
<b>Skin and Subcutaneous Tissue Disorders</b>
Acne
Alopecia
Dermatitis contact
Dry skin
Hair texture abnormal
Rash
Skin burning sensation
Skin disorder
Skin exfoliation

#### 4.9.1 Post-marketing experience

In addition to the adverse reactions reported during clinical studies and listed above, the following adverse reactions have been reported during postmarketing experience (Tables 2). In each table, the frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000, including isolated reports

In Table 2, adverse reactions are presented by frequency category based on spontaneous reporting rates.

<b>Table 2. Adverse Reactions Identified During Post-marketing Experience with NIZORAL Shampoo 2% by Frequency Category Estimated from Spontaneous Reporting Rates</b>	
<b>Skin and Subcutaneous Tissue Disorders</b>	
<i>Very rare</i>	Angioedema, Urticaria, Hair colour changes

#### 4.9 Overdose

In the event of accidental ingestion, supportive and symptomatic measures should be carried out. To avoid aspiration, emesis or gastric lavage should be performed.

### 5. Pharmacological Properties

#### 5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Antifungals for Topical Use, Imidazole and triazole derivatives; ATC code: D01AC08.

##### Mechanism of action

Ketoconazole, is a synthetic imidazole dioxolane derivative with potent antifungal activity.

##### Pharmacodynamic effects

NIZORAL Shampoo 2% rapidly relieves scaling and pruritus, which are usually associated with seborrheic dermatitis, pityriasis capitis (dandruff) and pityriasis versicolor.

##### Microbiology

Ketoconazole has a potent antifungal activity against dermatophytes, such as *Trichophyton* spp., *Epidermophyton* spp., *Microsporum* spp., and yeasts, such as *Candida* spp. and *Malassezia* spp. (*Pityrosporum* spp.).

## 5.2 Pharmacokinetic Properties

Plasma concentrations of ketoconazole were not detectable after topical administration of NIZORAL Shampoo 2% on the scalp. Plasma levels were detected after topical administration of NIZORAL Shampoo 2% on the whole body.

## 5.3 Preclinical Safety Data

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

Acute single dose oral toxicity studies of the shampoo formulation in rodents showed a safety margin of about 83 to 125 times (on a mg/kg basis) when compared to a single use clinical dose of a 2% shampoo formulation. Acute dermal and ocular irritation studies in rabbits with ketoconazole shampoo formulations showed minimal irritation with good reversibility. In a chronic (6-months) dermal toxicity study in rabbits, dosed up to 50 mg/kg/day, results showed that the shampoo formulation did not result in dermal or systemic toxic effects and showed no potential for sensitization.

## 6. Pharmaceutical Particulars

### 6.1 List of Excipients

Sodium lauryl ether sulphate  
Disodium monolauryl ether sulphosuccinate  
Coconut fatty acid diethanolamide  
Laurdimonium hydrolysed animal collagen  
Macrogol 120 methyl glucose dioleate  
Sodium chloride  
Concentrated hydrochloric acid  
Imidurea  
Sodium hydroxide  
Perfume bouquet  
Erythrosine sodium (E172)  
Purified water

### 6.2 Incompatibilities

None known.

### 6.3 Special Precautions for storage

Store at 25°C or below  
Keep out of reach of children

**6.4 Nature and contents of container**

100 ml white high density polyethylene (HDPE) bottle with polypropylene (PP) cap.

**6.5 Instructions for use/handling**

Not applicable

**Manufacturer :**

Janssen Pharmaceutica, Beerse Belgium

**License Holder:**

J-C Health Care Ltd.

Kibbutz Shefayim 6099000, Israel.