1. Name of the medicinal product

Micozol® Cream

2. Qualitative and quantitative composition

Each gram of cream contains Miconazole Nitrate 20 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Cream

4. Clinical particulars

4.1 Therapeutic indications

Micozol® Cream is effective in the treatment of fungal infections of the skin and nails including yeast infections e.g *candida species*, and in other fungi such as *Tinea capitis, T. corporis, T. manuum, T. barbae, T. cruris, T. pedis* (athlete's foot) and in napkin dermatitis.

4.2 Posology and method of administration

.Micozol® Cream is applied to the affected part and rubbed in two or three times daily. Duration of treatment could be up to 2-3 days depending on the extent and the site of the disease.

Method of Administration:

To be applied topically to affected body parts.

4.3 Contraindications

Local irritation and sensitivity reactions may occur, contact dermatitis has been reported. Miconazole cream is contraindicated in individuals who have shown hypersensitivity to Miconazole Nitrate or any of the components.

4.4 Special warnings and precautions for use

When Micozol® cream is used by patients taking oral anticoagulants, the anticoagulant effect should be carefully monitored.

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment Miconazole topical formulations. If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued. Micozol® cream must not come into contact with the mucosa of the eyes.

4.5 Interaction with other medicinal products and other forms of interaction

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application, clinically relevant interactions are rare. However, in patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored.

4.6 Fertility, pregnancy and lactation

Pregnancy

In animals miconazole nitrate has shown no teratogenic effects but is foetotoxic at high oral doses. Only small amounts of miconazole nitrate are absorbed following topical administration. However, as with other imidazoles, miconazole nitrate should be used with caution during pregnancy.

Breast-feeding

Topically applied miconazole is minimally absorbed into the systemic circulation, and it is not known whether miconazole is excreted in human breast milk. Caution should be exercised when using topically applied miconazole products during lactation.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Adverse drug reactions reported among 834 patients who received miconazole nitrate 2% cream (n=426) and/or placebo cream base (n=408) in 21 double- blind clinical trials are presented in Table 1 below. The adverse drug reactions are ranked by frequency, using 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

Adverse reactions obtained from clinical studies and post-marketing surveillance are presented by frequency category based on incidence in clinical trials or epidemiology studies, when known.

Table 1: Adverse reactions reported in clinical trials and post-marketing experience

	Adverse Reactions	
	Frequency Category	
System Organ Class	**Uncommon** (≥1/1,000 to <1/100)	**Not known**
Immune System Disorders		Anaphylactic reaction Hypersensitivity
Skin and Subcutaneous Tissue Disorders	Skin burning sensation Skin inflammation Skin hypopigmentation	Angioedema Urticaria Contact dermatitis Rash Erythema Pruritus
General Disorders and Administration Site Conditions	Application site irritation Application site burning Application site pruritus Application site reaction NOS Application site warmth	

4.9 Overdose

Symptoms

Cutaneous use: Excessive use can result in skin irritation, which usually disappears after discontinuation of therapy.

Treatment

Micozol® cream is intended for cutaneous use, not for oral use. If accidental ingestion of large quantities of the product occurs, use appropriate supportive care

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of action

Miconazole is an azole antifungal used to treat a variety of conditions, including those caused by *Candida* overgrowth. Unique among the azoles, Miconazole is thought to act through three main mechanisms. The primary mechanism of action is through inhibition of the CYP450 14α-lanosterol demethylase enzyme, which results in altered ergosterol production and impaired cell membrane composition and permeability, which in turn leads to cation, phosphate, and low molecular weight protein leakage.

In addition, Miconazole inhibits fungal peroxidase and catalase while not affecting NADH oxidase activity, leading to increased production of reactive oxygen species (ROS).Increased intracellular ROS leads to downstream pleiotropic effects and eventual apoptosis.

Lastly, likely as a result of lanosterol demethylation inhibition, Miconazole causes a rise in intracellular levels of farnesol. This molecule participates in quorum sensing in *Candida*, preventing the transition from yeast to mycelial forms and thereby the formation of biofilms, which are more resistant to antibiotics. In addition, farnesol is an inhibitor of drug efflux ABC transporters, namely *Candida* CaCdr1p and CaCdr2p, which may additionally contribute to increased effectiveness of azole drugs.

Pharmacotherapeutic classification: (Antifungals for dermatological/topical use; imidazole derivative)

ATC code*:* D01A C02.

5.2 Pharmacokinetic properties

Absorption: There is little absorption through skin or mucous membranes when miconazole nitrate is applied topically.

Distribution: Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Metabolism and Excretion: The small amount of miconazole that is absorbed is eliminated predominantly in faeces as both unchanged drug and metabolites.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6. Pharmaceutical particulars

6.1 List of excipients

Liquid paraffin (Heavy)

Stearic acid

Ceto-stearl alcohol

Cetomacrogol 1000

Propylene glycol

Benzyl alcohol

Purified water

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

20g Collapsible Alumnium tubes.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7.0 APPLICANT/MANUFACTURER

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