1.5 Product Information

1.5.1 Summary of Product Characteristics (SPC)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MICOZAL® 2 % cream, tube of 15 g.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains ketoconazole 20 mg
100 g of cream contain ketoconazole 2 g
Excipients with known effect: 100 g of cream contain proplene glycol 10.6 g, stearyl alcohol 8 g and cetyl alcohol 7 g.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream for cutaneous application.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MICOZAL cream is for use in adults.

Micozal cream is indicated in the treatment of dermatophytes or yeast infections of the skin which can be adequately treated using a topical agent because of their location and limited surface extent such as *tinea corporis*, *tinea cruris*, *tinea manus*, *tinea pedis*, cutaneous candidosis and *pityriasis versicolor*.
Others skin infections leading to desquamation such as dermatitis seborrhoeica, in which *Malassezia* (formerly known as *Pityrosporum*) plays a significant role, can also be treated by MICOZAL cream.
Mycosis, for which, a local treatment cannot be applied should be treated by oral route.

4.2 Posology and method of administration

Micozal cream is for use in adults.

- ***Tinea pedis:***

For mild infections, the cream should be applied to the affected areas twice daily during 1 week. For more severe or extensive infections (e.g. involving the sole or sides of the feet or fingernail) treatment should be continued during 2 to 6 weeks or an oral treatment should be considered.

- ***Others dermatophytes infections (tinea corporis, tinea cruris, timea manus, cutaneous candidosis and pityriasis versicolor):***

The cream should be applied to the affected areas once daily, rubbing delicately the skin. The treatment should be continued up to 1 week after the complete disappearance of the lesion. Depending on the type and extent of the infection, the treatment may last 2 to 6 weeks.

- ***Dermatitis seborrhoeica***:

Apply onto the infected area 1 to 2 times daily, depending on the type and extent of the infection.

- ***Paediatric population***

No data concerning the use of 2 % ketoconazol cream are available in paediatric population.

Method of administration
Local skin application

4.3 Contraindications
MICOZAL 2 % cream is contraindicated in patients with a known hypersensitivity to any of the ingredients listed in section 6.1. or to ketoconazole itself.

4.4 Special warnings and precautions for use
Cross-allergy between imidazole derivatives antimycotics can occur.
In case of allergic reaction or if an irritation occurs, the treatment should be discontinued.
MICOZAL 2 % cream is not for ophthalmic use.
In case of simultaneous application with a topical corticosteroid, it is recommended, to prevent a rebound effect after stopping a prolonged treatment with topical corticosteroids, it is recommended to continue applying the corticosteroid in the morning and to apply MICOZAL 2 % cream in the evening, and to subsequently and gradually withdraw the steroid therapy over a period of 2 to 3 weeks.
It is unadvised to use acidic pH soap because it favours the multiplication of *Candida*.
This medicine contains:

- Propylene glycol : this may cause skin irritation
- Stearyl alcohol and cetyl alcohol: these may cause local skin irritations (e.g. contact dermatitis)

Incompatibilities
Not known.
Fertility, pregnancy and lactation
Pregnancy
No effect during pregnancy is expected given the fact that systemic exposure to ketoconazole is negligible.
MICOZAL cream can be used during pregnancy.
Although the active ingredient is not resorbed by percutaneous route, there are no adequate and well-controlled studies in pregnant women. Plasma concentrations of ketoconazole are not detectable after topical application of ketoconazole 2 % w/w cream to the skin of non-pregnant humans.

Breastfeeding
No relevant and well-controlled study has been performed in breastfeeding mothers. No effect on the new born/infant is expected given the fact that, for the breastfeeding mother, the systemic exposure to ketoconazole in topical use is negligible. MICOZAL can thus be used during breastfeeding.

Fertility

The ketoconazole plasmatic concentrations are undetectable following local application of MICOZAL cream. No effect is thus expected on fertility.

Effects on ability to drive and use machines
Not applicable.

4.5 Undesitable 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 frequently 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-mentionned 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 catagories 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) and not known (cannot be estimated from available clinical trial data)

Immune system disorders
Uncommon : hyersensitivity

Skin and Subcutaneous Tissue disorders
Common : skin burning sensation
Uncommon : bullous eruption, contact dermatitis, rash, skin desquamation, clammy skin
Not known : urticaria

General disorders and administration site conditions
Common : application site erythema, application site pruritus.
Uncommon : application site bleeding, application site discomfort, application site dryness, application site inflammation, application site irritation, application site paresthesia, application site reaction.

Reporting of suspected undesirable reactions
Reporting suspected adverse reactions after autorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.6 Overdose

Topical application
Excessive topical application may lead to erythema, oedema and 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: Imidazole and triazole derivatives, ATC code: D01AC08.

Mechanism of action

The mechanism of action lays on the inhibition of fungal cytochrome P-450. The conversion of certain sterols on the cell wall of the yeasts and fungi, as well as the action of certain enzymes bound to the cell wall are blocked. The permeability of the cell wall is affected. Peroxides and ergosterol precursors thus accumulate in the cell, which brings finally the cell to death. The selectivity for the yeasts and the fungi is assured by the specific tendency of the ketoconazole to inhibit the biosynthesis of ergosterol. Yeasts are widely relying on this biosynthesis, ergosterol being in charge of a normal permeability of the cell membranes.
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Pharmacodynamic properties

Ketoconazole cream act normally rapidly against itching, being frequently associated with cutaneous infections by dermatophytes and yeasts, and against skin disorders caused by *Malassezia* spp. This symptomatic improvement appear before the first signs of healing can be observed.

Spectrum

Ketoconazole is a dioxolane-imidazole derivative having fungicidal properties. Dermatophytes (*Trichophyton, Epidermophyton and Microsporum* spp.), yeasts (*Candida* spp., *Malassezia* (formerly known as *Pityrosporum*), *Torulopsis* and *Cryptococcus*), dimorphous fungi and Eumycetes are sensitive to ketoconazole 2 % cream. The effect on *Malassezia* spp. Is particularly pronounced.

5.2 Pharmacokinetic properties

MICOZAL cream concentrates in the *stratum corneum* and in the exterior cell layer of the *spinosum stratum*. The percutaneous absorption is so negligible that no measurable plasmatic rate can be detected. So, systematic results should not be expected.
Plasma concentrations of ketoconazole were not detectable after topical administration of ketoconazole 2 % w/w cream on the skin in adults.
In one study in infants with seborrheic dermatitis (n = 19), where approximately 40 g of cream was applied daily on 40 % of the body surface, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

5.3 Preclinacal safety data

Preclinical data based on conventional trials including eye and primary skin irritation, the skin sensitivity and toxicity at repeated doses revealed no particular risk to human.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients: *sodium sulphite, propylene glycol, stearyl alcohol, cetyl alcohol, polysorbate 60, polysorbate 80, isopropyl myristate, sorbitan stearate, purified water.*

6.2 Incompatibilities

MICAZOL cream should not be mixed with other active substances or excipients.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Keep the tube tightly close.

6.5 Nature and contents of container
Aluminium tube 15 g.

6.6 Special precautions for disposal and other handling
How to open the tube of cream: unscrew the cap and use the other side of the cap to pierce the seal.

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

7. CATEGORY OF DISTRIBUTION

☐ OTC (Over-the counter medicine) ☒ POM (Prescription only medicines)

8. MARKETING AUTHORISATION HOLDER
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10. DATE OF REVISION
September 2017