

SUMMARY PRODUCT CHARACTERISTIC (SPC)

KETOCONAZOLE

2% Shampoo

BRAND NAME – Ketoconazole

INTERNATIONAL NON-PROPERTY NAME – Ketoconazole

COMPOSITION

Each ml of shampoo contains:

active ingredient: ketoconazole – 20mg;

inactive ingredients: cocamide DEA, cocamidopropyl betaine, sodium laureth sulfate, diazolidinyl urea, hydrochloric acid(conc), triethanolamine 98 %, sodium chloride, flavor apple,color red E-129, water deionized

DOSAGE FORM

Shampoo

A red, transparent, viscous liquid.

PHARMACOLOGICAL GROUP AND ATC CODE

Antifungal; D01AC08.

PHARMACOLOGICAL ACTION

Mechanism of Action

Ketoconazole usually is fungistatic in action, but may be fungicidal at high concentrations after prolonged incubation or against very susceptible organisms.

Like other azole antifungal agents, ketoconazole presumably exerts its antifungal activity by altering and damaging cellular membranes, resulting in increased membrane permeability, secondary metabolic effects, and growth inhibition of fungal cells. Although the exact mechanism of action of ketoconazole has not been fully determined, it has been suggested that the fungistatic activity of the drug may result from interference with ergosterol synthesis, probably via inhibition of C-14 demethylation of sterol intermediates (e.g., lanosterol). The fungicidal activity of ketoconazole at high concentrations may result from a direct physiochemical effect of the drug on the fungal cell membrane.

Ketoconazole 2% shampoo is an imidazole antifungal administered topically for scale washing. It is given in candidiasis and dermatophyte infections of the scalp for prophylaxis and treatment. It indicated for treatment of dandruff and seborrheic dermatitis. It has been given for the prophylaxis of fungal infections in immunocompromised patients, although fluconazole or itraconazole are usually preferred. It has been recommended that, because of its erratic absorption and slow therapeutic response, ketoconazole should not be used for the treatment of life-

threatening fungal infections, including fungal meningitis, or for severe infections in immunocompromised patients.

Antimicrobial action and microbial sensitivity.

Ketoconazole is a broad-spectrum synthetic antifungal agent which inhibits the growth of the following common dermatophytes and yeasts by altering the permeability of the cell membrane: dermatophytes: *Trichophyton rubrum*, *T. mentagrophytes*, *T. tonsurans*, *Microsporum canis*, *M. audouini*, *M. gypseum* and *Epidermophyton floccosum*; yeast: *Candida albicans*, *C. tropicalis*, *Pityrosporum ovale* and *Pityrosporum orbiculare* (*M. furfur*). Development of resistance by these microorganisms to ketoconazole has not been reported.

Ketoconazole has activity against some Gram-positive bacteria and some antiprotozoal activity against *Leishmania* spp. There are rare reports of *Candida albicans* acquiring resistance to ketoconazole. Pharmacological activity of ketoconazole depends on its concentration in different pharmaceutical forms.

Resistance.

The emergence of strains of *Candida* spp. resistant to ketoconazole has become increasingly important, particularly in immunocompromised patients receiving long-term prophylaxis with fluconazole. In addition to resistance in *C. albicans*, infections with *C. dubliniensis*, *C. glabrata*, and *C. krusei*, all of which may be less sensitive to ketoconazole than *C. albicans*, have been noted in these patients, and secondary resistance of *C. glabrata* has been reported during ketoconazole therapy.

PHARMACOKINETICS

Ketoconazole 2% shampoo was not detected in plasma in 39 patients who shampooed 4-10 times per week for 6 months, or in 33 patients who shampooed 2-3 times per week for 3-26 months (mean: 16 months). Systemic absorption following topical application in healthy subjects practically absents and has not any notable clinical effect.

USES

Ketoconazole 2% shampoo is used for the treatment of fungal infections, pityriasis versicolor and conditions like seborrheic dermatitis and dandruff. Shampoo controls flaking, scaling and itching, associated with dandruff.

ADMINISTRATION

Shampoo should be applied on scalp for 3-5 minutes once daily and then washed away with warm water. For treatment of dandruff and seborrheic dermatitis it is used twice in a week during 3-4 weeks, then as needed to control dandruff or seborrheic dermatitis. If the condition is worsens or fails to improve it shampoo

may be applied for two to four weeks additionally. or patient should see a physician. If the scalp is broken or inflamed, the patient should not use product. For treatment of pityriasis versicolor shampoo should be applied once daily for 5 following days.

For prophylaxis of dandruff and seborrheic dermatitis shampoo is applied once daily for a week or two weeks. Shampoo should not be used for prolonged periods without consulting a physician. Maximal duration of treating lasts up to 9 weeks. Medical consultation is needed when symptoms are persist, or others are appeared.

For prophylaxis apply once daily for up to 3 days before sun exposure, leave preparation on for 3–5 minutes before rinsing.

ADVERSE EFFECTS

As in case of use of other shampoos local irritation, pruritus or contact dermatitis may observed after application of ketoconazole shampoo (as result of irritation or allergic reactions). Hair may become fatty or dry. However, when using a Ketoconazole as 20 mg/g shampoo these effects are rare.

In rare cases, primarily in patients with chemically damaged or gray hair, change in hair color observed.

Adverse reactions identified in clinical studies: Adverse reactions, observed in $\geq 1\%$ of patients after application Ketoconazole shampoo 2% on the hairy parts heads or skin, is not revealed. Adverse reactions, observed in $\leq 1\%$ of patients, after application of Ketoconazole 2% shampoo on the hairy parts heads or skin, are follows:

Eye disorders : eye irritation, increased lacrimation.

General disorders and administration site conditions: application site erythema, application site irritation, application site pruritus, application site reaction , hypersensitivity, pruritus, pustules, skin reactions.

Immune system disorders: hypersensitivity.

Infections and Infestations: folliculitis.

Nervous System Disorders: dysgeusia

Skin and subcutaneous tissue disorders acne, alopecia, dermatitis contact, dry skin, hair texture abnormal, skin burning sensation, skin rash, skin exfoliation.

Adverse effects have been identified during post-marketing studies, listed below according to the following classification:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $\leq 1/10$)

Uncommon ($\geq 1/1,000$ to $\leq 1/100$)

Rare ($\geq 1/10,000$ to $\leq 1/1,000$)

Very rare ($< 1/10,000$) including isolated reports

Skin and Subcutaneous Tissue Disturbances

Violations of the skin and subcutaneous tissue:

Very rare: angioedema, urticarial, hair colour changes

PRECAUTIONS AND CONTRAINDICATIONS

Scalp damage on surface for application. High hypersensitivity to drug components. Shampoo intended for external use. Avoid its occasional connection with the eyes, nose, mouth, opened wounds. When indicated in patients, treating with topical GCS for a long time, usage of them should be interrupted for 2-3 weeks to avoid withdrawal [abstinence] syndrome. In case of inflammation or irritation doctor advice is needed. Supportive measures should be done when shampoo occasional is used internally.

Pregnancy and breast-feeding

Ketoconazole for topical use lists to Category B. Via to (for its) negligible systemic absorption it is not contraindicated in pregnancy and during breast feeding.

No adverse effects were seen in a breast-feed infant whose mother was applying ketoconazole topically. The American Academy of Pediatrics considers that the use of ketoconazole is therefore usually compatible with breast feeding.

Pediatric Precautions

Ketoconazole shampoo has not been systematically studied in children of any age. There is essentially no information to date on use of the drug in children younger than 12 years of age. Although ketoconazole has been used in a limited number of children, it is contraindicated for children under age of 12 years.

OVERDOSAGE

There no observed of overdose in using Ketoconazole 2 % shampoo , as the product intended for topical use. In case of accidental ingestion, supportive or symptomatic measures should be carried out. In order to avoid aspiration, neither emesis nor gastric lavage should be instigated.

DRUG INTERACTIONS

There is not any case of systemic absorption of Ketoconazole during its usage. Any drug interactions are excluded.

PRESENTATION

90 ml of shampoo in a plastic bottle (inside package)

The 1 bottle with leaflet packed in cardboard box(outer package)

STORAGE CONDITIONS

Store at a temperature not higher than 25 ° C, in a dry place, out of the reach of children. Protect from light.

Expiry date

3 years.

DISPENSION

Without prescription

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MARKETING AUTHORIZATION HOLDER**“ARPIMED” LLC**

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