METAPHARMACEUTICAL

TECHNICAL DATA SHEET

1165-TDS-ENG-2026

KETOCONAZOL (EUR. PH.)		
DESCRIPTION DCI: KETOCONAZOLE	DESCRIPTION DOE: KETOCONAZOL	
CAS Nº: 65277-42-1	EC Nº: 265-667-4	AEMPS CODE: 3882A
MOL. WEIGHT: 531.44	MOL. FORMULA: C26H28Cl2N4O4	ARTICLE CODE: 1165

ATTRIBUTES	SHOULD BE
Appearance	White or almost white powder
Solubility	Practically insoluble in water, freely soluble in methylene chloride, soluble in methanol, sparingly soluble in ethanol (96 %)
Identification A	Complies
Appearance of solution	Clear and not more intensely coloured than ref. solution BY4
Optical rotation	-0.10º / +0.10º
Related substances	
Impurity D	=< 0.2 %
Unspecified impurities	=< 0.10 %
Total impurities	=< 0.3 %
Loss on drying	=< 0.5 %
Sulfated ash	=< 0.1 %
Assay	99.0 - 101.0 %

COMPLIES WITH

European Pharmacopoeia 12.1

STORAGE

Store in a cool and dry place. Protect from light.

REMARKS

Ketoconazole is subjected to the requirements of the ICH Q3D "Elemental Impurities" guideline and the requirements of guides EMA/CHMP/ICH/82260/2006.

Absence of N-nitrosamines impurities has been ensured after a risk evaluation according to ICH Q9, ICH M7 and in accordance with guidelines EMA/428592/2019 Rev 2 and EMA/189634/2019.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE, among others, are available upon request.

All methods of analysis are validated by official pharmacopoeias or are validated by internal methods of the manufacturer, which can be obtained at specific request.

Properties and uses
KETOCONAZOLEE is a synthetic imidazole antifungal with fungistatic action, broad spectrum (dermatophytes, yeasts, and Trichomonas), which alters the permeability of the cell membrane of sensitive fungi by inhibiting the synthesis of ergosterol. When administered orally, maximum blood levels are observed after about 2 hours of administration. The absorption is greater when the pH decreases. It is widely distributed in the tissues, although it does not seem to penetrate into detectable doses in the CSF, and it passes into breast milk. It binds in large proportion to plasma proteins. It is metabolized extensively in the liver to inactive metabolites, the main route of excretion being biliary, and to a lesser extent the urinary one. It has been observed that the elimination is biphasic, with an initial half-life of 2 h and a final half-life of 8 h. Systemic absorption by topical or vaginal route is minimal.

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It has been shown to be effective orally in the treatment of superficial and systemic infections caused by several pathogenic fungi. It is used orally for the treatment of candidiasis, systemic blastomycosis, coccidioidomycosis, paracoccidioidomycosis, cryptococcosis, histoplasmosis, chromomycosis, sporotrichosis disseminated, gastrointestinal fungal infections, fungal pneumonia, paronychia, athlete's foot, tinea (body, crural, and versicolor), Onychomycosis, and fungal septicemia.
However, its use is not recommended in the treatment of fungal meningitis due to its erratic absorption through the CSF. It is also not appropriate for serious infections in patients at risk.
It is also used in the prophylaxis of fungal infections in immunosuppressed patients, although its use is not advisable when the infection is already established.
Topically, it is used in candidiasis, candidiasic intégrigo, tinea, and pityriasis versicolor in the form of cream, gel, pastes, or powders, and for seborrheic dermatitis and dandruff in the form of shampoos.
Due to the risk of hepatotoxicity, its use in non-systemic infections is reserved for serious infections not susceptible to topical therapy or resistant to other treatments.

Precautions
Do not administer to patients who have been receiving griseofulvin for up to one month, since there is a risk of hepatotoxicity.
In patients with achlorhydria it is advisable to administer this medication orally associated with citrus juices or cola. It is advisable to control liver function in individuals with alcoholism or liver failure.
During the first days of therapy, the driving of vehicles and the handling of dangerous machinery is discouraged.
In the vaginal application, the application at bedtime is recommended, to favor local action and vaginal absorption.
Typically contact with the eyes and the use of occlusive bandages or that allow perspiration should be avoided, since it can favor the development of yeasts, with the consequent skin irritation.
It is advisable to wash and dry the area to be treated.

Interactions
It may potentiate the effect or toxicity of oral anticoagulants, antihistamines H1 (such as astemizole and terfenadine), chlordiazepoxide, methylprdnisolone, quinidine, and cyclosporine.
Its action is reduced by antacids, anti-ulcers (cimetidine, omeprazole, lansoprazole, sucralfate ...), and antiepileptic drugs (such as phenytoin).

Other observations
It is photosensitive.
It is easily oxidizable (with time it can give a pink coloration in the formulations that can be avoided by adding BHT 0.03 - 0.1%, sodium metabisulfite 0.05%, or ascorbic acid 0.5%).
It is not advisable to give more than one month of expiration to the master formulas with KETOCONAZOLE.

Compounding examples

Shampoo for seborrheic dermatitis
KETOCONAZOLE - **2%**
Salicylic acid - **2%**
Antioxidant c.s.
Sulfonated anionic detergent, c.s.p. - **200 mL**

Modus operandi: Predispose KETOCONAZOLE in 5% methylidene glycerol, and salicylic acid in a little Tagat-L. Add them to the detergent at a speed of agitation such that it does not form too much foam. Adjust the final pH to 3 - 4 with lactic acid.

Emulsion of KETOCONAZOLE and hydrocortisone
KETOCONAZOLE - **2%**
Hydrocortisone - **1%**
Antioxidant c.s.
Emulsion O / W, c.s.p. - **100 g**

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KETOCONAZOLE paste
KETOCONAZOLE - **2%**
Talc - **25 g**
Zinc oxide - **25 g**
Glycerin - **25 g**
Antioxidant c.s.
Distilled water c.s.p. - **100 g**

Modus operandi: Moisten the KETOCONAZOLE with a little glycerin in mortar. Make the pasta to the water and incorporate it little by little, homogenizing well with the pistil.

KETOCONAZOLE Gel
KETOCONAZOLE - **2%**
Antioxidant c.s.
Carbopol gel c.s.p. - **100 g**

Aqueous solution of KETOCONAZOLE
KETOCONAZOLE - **2%**
Antioxidant c.s.
Purified water c.s.p. - **100 mL**

Modus operandi: KETOCONAZOLE is solubilized simply by lowering the pH to 4 with lactic acid.

KETOCONAZOLE capsules
KETOCONAZOLE - **200 mg**
for a capsule, No. 50

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