KETOCONAZOLE- ketoconazole cream
E. Fougera & Co. a division of Fougera Pharmaceuticals, LLC

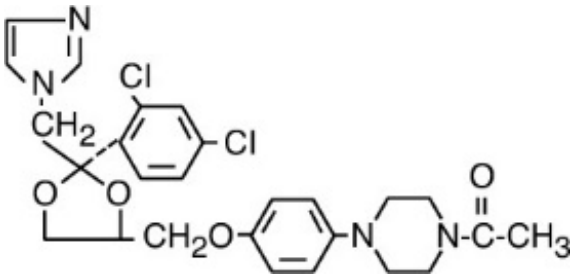
KETOCONAZOLE CREAM 2%

Rx only

DESCRIPTION

Ketoconazole Cream 2%, for topical administration only, contains the broad-spectrum synthetic antifungal agent, ketoconazole 2%, formulated in an aqueous cream vehicle consisting of propylene glycol, stearyl and cetyl alcohols, sorbitan monostearate, polysorbate 60, isopropyl myristate, sodium sulfite anhydrous, polysorbate 80 and purified water.

Ketoconazole is *cis*-1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine and has the following structural formula:



CLINICAL PHARMACOLOGY

When Ketoconazole Cream 2% was applied dermally to intact or abraded skin of Beagle dogs for 28 consecutive days at a dose of 80 mg, there were no detectable plasma levels using an assay method having a lower detection limit of 2 ng/ml.

After a single topical application to the chest, back and arms of normal volunteers, systemic absorption of ketoconazole was not detected at the 5 ng/ml level in blood over a 72-hour period.

Two dermal irritancy studies, a human sensitization test, a phototoxicity study and a photoallergy study conducted in 38 male and 62 female volunteers showed no contact sensitization of the delayed hypersensitivity type, no irritation, no phototoxicity and no photoallergenic potential due to Ketoconazole Cream 2%.

Microbiology: Ketoconazole is a broad spectrum synthetic antifungal agent which inhibits the *in vitro* 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;* yeasts: *Candida albicans, Malassezia ovale (Pityrosporum ovale)* and *C. tropicalis;* and the organism responsible for tinea versicolor, *Malassezia furfur (Pityrosporum orbiculare)*. Only those organisms listed in the INDICATIONS AND USAGE Section have been proven to be clinically affected. Development of resistance to

ketoconazole has not been reported.

Mode of Action:*In vitro* studies suggest that ketoconazole impairs the synthesis of ergosterol, which is a vital component of fungal cell membranes. It is postulated that the therapeutic effect of ketoconazole in seborrheic dermatitis is due to the reduction of M. ovale, but this has not yet been proven.

INDICATIONS AND USAGE

Ketoconazole Cream 2% is indicated for the topical treatment of tinea corporis, tinea cruris and tinea pedis caused by *Trichophyton rubrum, T. mentagrophytes* and *Epidermophyton floccosum;* in the treatment of tinea (pityriasis) versicolor caused by *Malassezia furfur (Pityrosporum orbiculare)*; in the treatment of cutaneous candidiasis caused by *Candida spp.* and in the treatment of seborrheic dermatitis.

CONTRAINDICATIONS

Ketoconazole Cream 2% is contraindicated in persons who have shown hypersensitivity to the active or excipient ingredients of this formulation.

WARNINGS

Ketoconazole Cream 2% is not for ophthalmic use.

Ketoconazole Cream 2% contains sodium sulfite anhydrous, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

General: If a reaction suggesting sensitivity or chemical irritation should occur, use of the medication should be discontinued. Hepatitis (1:10,000 reported incidence) and, at high doses, lowered testosterone and ACTH induced corticosteroid serum levels have been seen with orally administered ketoconazole; these effects have not been seen with topical ketoconazole.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A long-term feeding study in Swiss Albino mice and in Wistar rats showed no evidence of oncogenic activity. The dominant lethal mutation test in male and female mice revealed that single oral doses of ketoconazole as high as 80 mg/kg produced no mutation in any stage of germ cell development. The Ames'*Salmonella* microsomal activator assay was also negative.

Pregnancy: Teratogenic effects: Pregnancy Category C:

Ketoconazole has been shown to be teratogenic (syndactylia and oligodactylia) in the rat when given orally in the diet at 80 mg/kg/day, (10 times the maximum recommended human oral dose). However, these effects may be related to maternal toxicity, which was seen at this and higher dose levels.

There are no adequate and well-controlled studies in pregnant women. Ketoconazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether Ketoconazole Cream 2% administered topically could result in sufficient systemic absorption to produce detectable quantities in breast milk. Nevertheless, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

During clinical trials 45 (5.0%) of 905 patients treated with Ketoconazole Cream 2% and 5 (2.4%) of 208 patients treated with placebo reported side effects consisting mainly of severe irritation, pruritus and stinging. One of the patients treated with Ketoconazole Cream developed a painful allergic reaction.

In worldwide postmarketing experience, rare reports of contact dermatitis have been associated with Ketoconazole Cream or one of its excipients, namely sodium sulfite or propylene glycol.

DOSAGE AND ADMINISTRATION

Cutaneous candidiasis, tinea corporis, tinea cruris, tinea pedis and tinea (pityriasis) versicolor: It is recommended that Ketoconazole Cream 2% be applied once daily to cover the affected and immediate surrounding area. Clinical improvement may be seen fairly soon after treatment is begun; however, candidal infections and tinea cruris and corporis should be treated for two weeks in order to reduce the possibility of recurrence. Patients with tinea versicolor usually require two weeks of treatment. Patients with tinea pedis require six weeks of treatment. *Seborrheic dermatitis:* Ketoconazole Cream 2% should be applied to the affected area twice daily for four weeks or until clinical clearing.

If a patient shows no clinical improvement after the treatment period, the diagnosis should be redetermined.

HOW SUPPLIED

Ketoconazole Cream 2% is supplied as follows:

15 gram NDC 0168-0099-15
30 gram NDC 0168-0099-30
60 gram NDC 0168-0099-60
Store below 77°F (25°C).

E. FOUGERA & CO.
A division of
Fougera
PHARMACEUTICALS INC.
Melville, New York 11747

I299C
R11/11
#39

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CONTAINER

NDC 0168-0099-15

FOUGERA®

KETOCONAZOLE

CREAM 2%

For dermatologic use only.

Rx only

Contains ketoconazole 20 mg/g,
propylene glycol, stearyl and cetyl
alcohols, sorbitan monostearate,
polysorbate 60, isopropyl myristate,
sodium sulfite anhydrous,
polysorbate 80 and purified water.

NET WT 15 grams

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CARTON

NDC 0168-0099-15

Rx only

FOUGERA®

KETOCONAZOLE

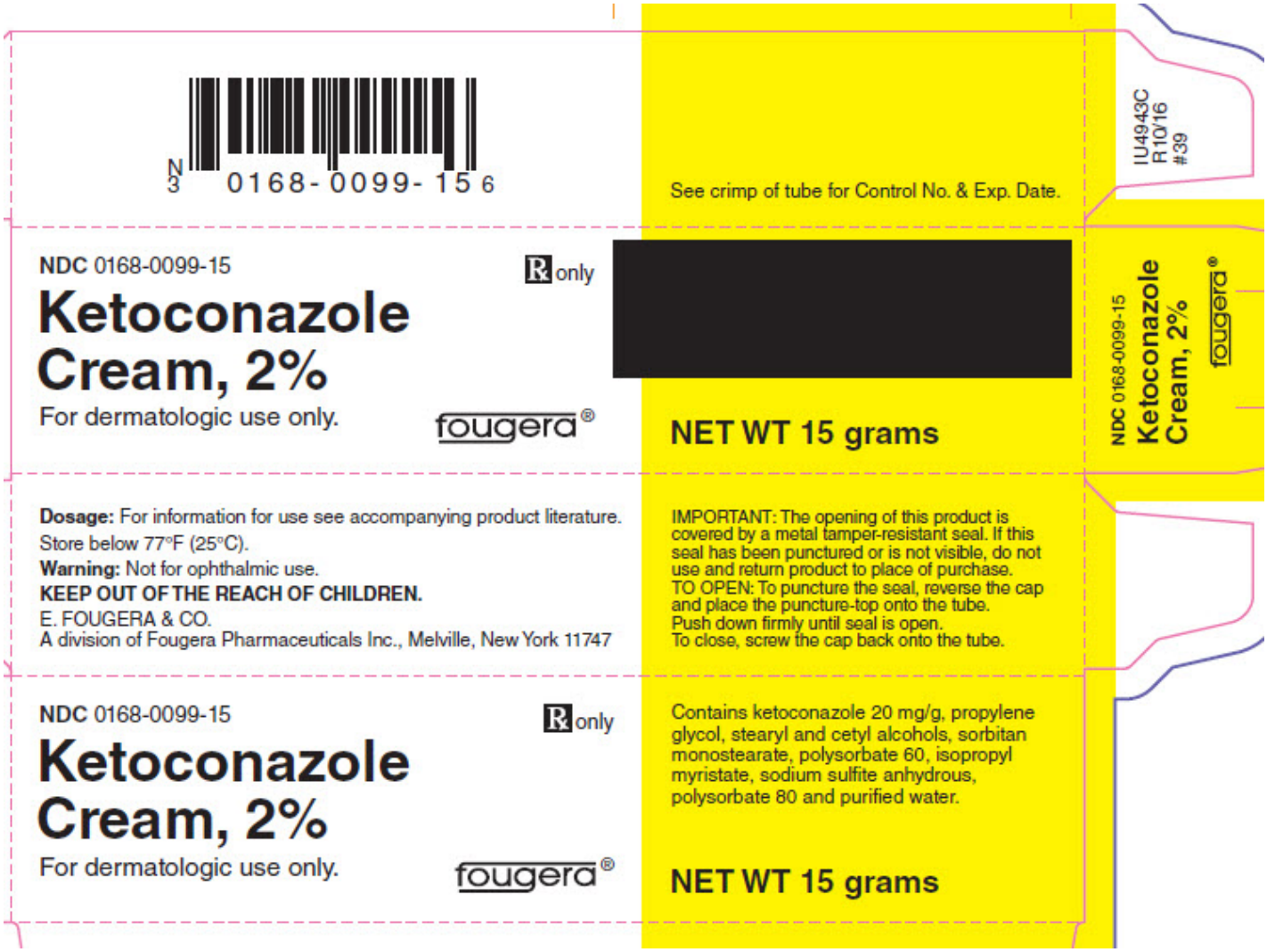
CREAM 2%

For dermatologic use only.

Warning: Not for ophthalmic use.

Keep out of reach of children.

NET WT 15 grams



KETOCONAZOLE ketoconazole cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0168-0099
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ketoconazole (UNII: R9400W927I) (ketoconazole - UNII:R9400W927I)	ketoconazole	20 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
propylene glycol (UNII: 6DC9Q167V3)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
cetyl alcohol (UNII: 936JST6JCN)	
sorbitan monostearate (UNII: NVZ4I0H58X)	
polysorbate 60 (UNII: CAL22UVI4M)	
isopropyl myristate (UNII: 0RE8K4LNJS)	
sodium sulfite (UNII: VTK01UQK3G)	
polysorbate 80 (UNII: 6OZP39ZG8H)	
water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0168-0099-15	1 in 1 CARTON	04/28/2004	
1		15 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:0168-0099-30	1 in 1 CARTON	04/28/2004	
2		30 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:0168-0099-60	1 in 1 CARTON	04/28/2004	
3		60 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076294	04/28/2004	

Labeler - E. Fougera & Co. a division of Fougera Pharmaceuticals, LLC (043838424)