CLOTRIMAZOLE- clotrimazole lozenge
Rising Pharma Holdings, Inc.

Clotrimazole Lozenges USP 10 mg

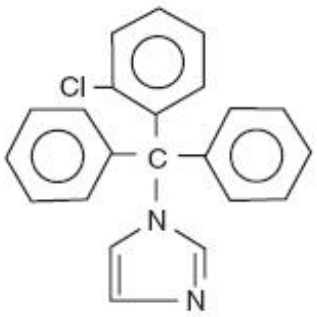
FOR TOPICAL ORAL ADMINISTRATION

Rx only

DESCRIPTION

Each Clotrimazole lozenge USP contains 10 mg clotrimazole USP [1-(o-chloro-α,α-diphenylbenzyl) imidazole], a synthetic antifungal agent, for topical use in the mouth.

Structural Formula:



Chemical Formula: $C_{22}H_{17}ClN_2$

The lozenge dosage form is a large, slowly dissolving lozenge containing 10 mg of clotrimazole USP dispersed in croscarmellose sodium, dextrates, magnesium stearate, microcrystalline cellulose and povidone.

CLINICAL PHARMACOLOGY

Clotrimazole is a broad-spectrum antifungal agent that inhibits the growth of pathogenic yeasts by altering the permeability of cell membranes. The action of clotrimazole is fungistatic at concentrations of drug up to 20 mcg/mL and may be fungicidal *in vitro* against *Candida albicans* and other species of the genus *Candida* at higher concentrations. No single-step or multiple-step resistance to clotrimazole has developed during successive passages of *Candida albicans* in the laboratory; however, individual organism tolerance has been observed during successive passages in the laboratory. Such *in vitro* tolerance has resolved once the organism has been removed from the antifungal environment.

After oral administration of a 10 mg clotrimazole lozenge to healthy volunteers, concentrations sufficient to inhibit most species of *Candida* persist in saliva for up to three hours following the approximately 30 minutes needed for a lozenge to dissolve. The long term persistence of drug in saliva appears to be related to the slow release of clotrimazole from the oral mucosa to which the drug is apparently bound. Repetitive dosing at three hour intervals maintains salivary levels above the minimum inhibitory concentrations of most strains of *Candida*; however, the relationship between *in vitro*

susceptibility of pathogenic fungi to clotrimazole and prophylaxis or cure of infections in humans has not been established.

In another study, the mean serum concentrations were 4.98 ± 3.7 and 3.23 ± 1.4 nanograms/mL of clotrimazole at 30 and 60 minutes, respectively, after administration as a lozenge.

INDICATIONS AND USAGE

Clotrimazole Lozenges are indicated for the local treatment of oropharyngeal candidiasis. The diagnosis should be confirmed by a KOH smear and/or culture prior to treatment.

Clotrimazole Lozenges are also indicated prophylactically to reduce the incidence of oropharyngeal candidiasis in patients immunocompromised by conditions that include chemotherapy, radiotherapy, or steroid therapy utilized in the treatment of leukemia, solid tumors, or renal transplantation. There are no data from adequate and well-controlled trials to establish the safety and efficacy of this product for prophylactic use in patients immunocompromised by etiologies other than those listed in the previous sentence. (See DOSAGE AND ADMINISTRATION.)

CONTRAINDICATIONS

Clotrimazole Lozenges are contraindicated in patients who are hypersensitive to any of its components.

WARNING

Clotrimazole Lozenges are not indicated for the treatment of systemic mycoses including systemic candidiasis.

PRECAUTIONS

Abnormal liver function tests have been reported in patients treated with clotrimazole lozenges; elevated SGOT levels were reported in about 15% of patients in the clinical trials. In most cases the elevations were minimal and it was often impossible to distinguish effects of clotrimazole from those of other therapy and the underlying disease (malignancy in most cases). Periodic assessment of hepatic function is advisable particularly in patients with pre-existing hepatic impairment.

Since patients must be instructed to allow each lozenge to dissolve slowly in the mouth in order to achieve maximum effect of the medication, they must be of such an age and physical and/or mental condition to comprehend such instructions.

Carcinogenesis

An 18 month dosing study with clotrimazole in rats has not revealed any carcinogenic effect.

Use In Pregnancy

Pregnancy Category C:

Clotrimazole has been shown to be embryotoxic in rats and mice when given in doses 100 times the adult human dose (in mg/kg), possibly secondary to maternal toxicity. The drug was not teratogenic in mice, rabbits, and rats when given in doses up to 200, 180, and 100 times the human dose.

Clotrimazole given orally to mice from nine weeks before mating through weaning at a dose 120 times the human dose was associated with impairment of mating, decreased number of viable young, and decreased survival to weaning. No effects were observed at 60 times the human dose. When the drug was given to rats during a similar time period at 50 times the human dose, there was a slight decrease in the number of pups per litter and decreased pup viability.

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

Pediatric Use

Safety and effectiveness of clotrimazole in children below the age of 3 years have not been established; therefore, its use in such patients is not recommended.

The safety and efficacy of the prophylactic use of clotrimazole lozenges in children have not been established.

Geriatric Use

Clinical studies of clotrimazole did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

Abnormal liver function tests have been reported in patients treated with clotrimazole lozenges; elevated SGOT levels were reported in about 15% of patients in the clinical trials (See PRECAUTIONS).

Nausea, vomiting, unpleasant mouth sensations and pruritus have also been reported with the use of the lozenge.

To report SUSPECTED ADVERSE REACTIONS, contact Rising Pharma Holdings, Inc. at 1-844-874-7464 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

OVERDOSAGE

No data available.

DRUG ABUSE AND DEPENDENCE

No data available.

DOSAGE AND ADMINISTRATION

Clotrimazole Lozenges are administered only as a lozenge that must be slowly dissolved in the mouth. The recommended dose is one lozenge five times a day for fourteen consecutive days. Only limited data are available on the safety and effectiveness of the clotrimazole lozenge after prolonged administration; therefore, therapy should be limited to short term use, if possible.

For prophylaxis to reduce the incidence of oropharyngeal candidiasis in patients immunocompromised by conditions that include chemotherapy, radiotherapy, or steroid therapy utilized in the treatment of leukemia, solid tumors, or renal transplantation, the recommended dose is one lozenge three times daily for the duration of chemotherapy or until steroids are reduced to maintenance levels.

HOW SUPPLIED

Clotrimazole Lozenges USP

10 mg lozenge is supplied as white to off white, round, flat face beveled edge lozenge debossed with “227” on one side and “P” on the other side.

NDC 16571-686-07: Bottle of 70 Lozenges with child-resistant closure.

NDC 16571-686-14: Bottle of 140 Lozenges with child-resistant closure.

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Avoid freezing.

Manufactured by:

Unique Pharmaceutical Laboratories

(A Div. of J.B. Chemicals & Pharmaceuticals Ltd.)

Mumbai 400 030, India

Distributed by:

Rising Pharma Holdings, Inc.

East Brunswick, NJ 08816

138676

Revised: 03/2024

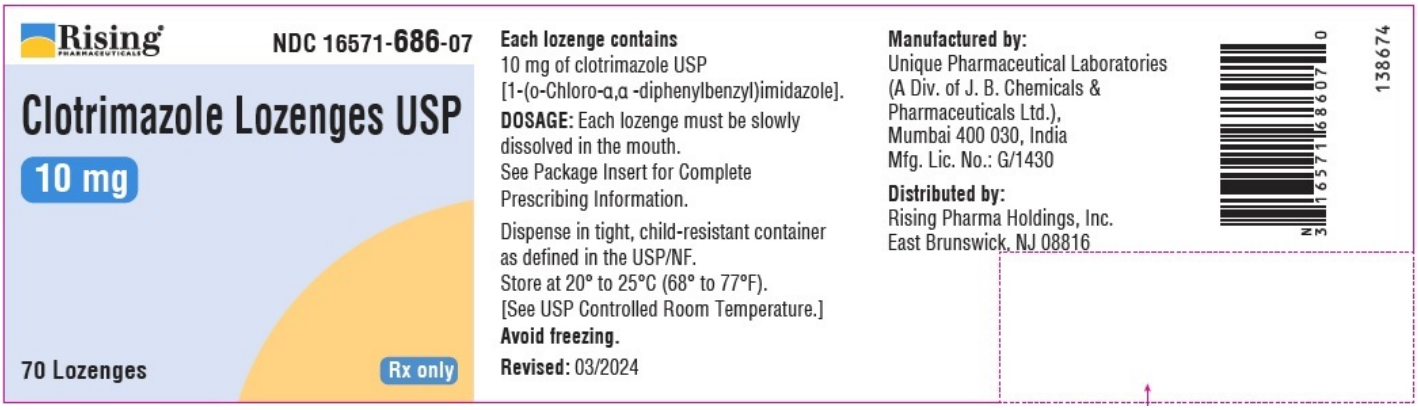
PRINCIPAL DISPLAY PANEL

NDC 16571-**686**-07

Clotrimazole Lozenges USP

10 mg

70 Lozenges



CLOTRIMAZOLE

clotrimazole lozenge

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:16571-686
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CLOTRIMAZOLE (UNII: G07GZ97H65) (CLOTRIMAZOLE - UNII:G07GZ97H65)	CLOTRIMAZOLE	10 mg

Inactive Ingredients	
Ingredient Name	**Strength**
DEXTRATES (UNII: G263MI44RU)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
POVIDONE K30 (UNII: U725QWY32X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics			
Color	WHITE (white to off-white)	**Score**	no score
Shape	ROUND	**Size**	16mm
Flavor		**Imprint Code**	227;P
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:16571-686-07	70 in 1 BOTTLE; Type 0: Not a Combination Product	05/01/2024	
2	NDC:16571-686-14	140 in 1 BOTTLE; Type 0: Not a Combination Product	05/01/2024	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA215641	05/01/2024	

Labeler - Rising Pharma Holdings, Inc. (116880195)

Registrant - Unique Pharmaceutical Laboratories (650434645)

Establishment

Name	Address	ID/FEI	Business Operations
Unique Pharmaceutical Laboratories		650434645	manufacture(16571-686)

Revised: 4/2024 Rising Pharma Holdings, Inc.