CLOTRIMAZOLE- clotrimazole lozenge
Roxane Laboratories, Inc

CLOTRIMAZOLE TROCHE
(clotrimazole lozenges) USP

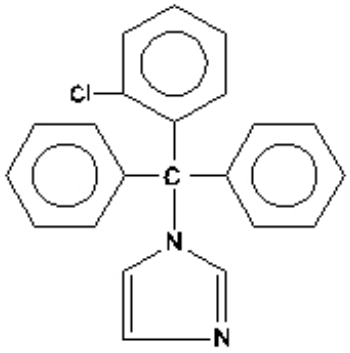
FOR TOPICAL ORAL ADMINISTRATION

Rx only

DESCRIPTION

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

Structural Formula:



$C_{22}H_{17}ClN_2$

The troche dosage form is a large, slowly dissolving tablet (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 troche 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 troche 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 troche.

INDICATIONS AND USAGE

Clotrimazole Troches (clotrimazole lozenges) USP 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 Troches (clotrimazole lozenges) USP 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 Troches (clotrimazole lozenges) USP are contraindicated in patients who are hypersensitive to any of its components.

WARNING

Clotrimazole Troches (clotrimazole lozenges) USP 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 troches; 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 troche 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 troches 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 troches 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 troches; 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 troche.

OVERDOSAGE

No data available.

DRUG ABUSE AND DEPENDENCE

No data available.

DOSAGE AND ADMINISTRATION

Clotrimazole Troches (clotrimazole lozenges) USP are administered only as a lozenge that must be slowly dissolved in the mouth. The recommended dose is one troche five times a day for fourteen consecutive days. Only limited data are available on the safety and effectiveness of the clotrimazole troche 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 troche three times daily for the duration of chemotherapy or until steroids are reduced to maintenance levels.

HOW SUPPLIED

Clotrimazole Troches (clotrimazole lozenges) USP are white, flat face tablets that are plain on one side and embossed with “54 552” on the other side.

Clotrimazole Troche (clotrimazole lozenges) USP, 10 mg

0054-4146-22: Bottles of 70

0054-4146-23: Bottles of 140

0054-8146-22: 7 x 10 Unit-Dose Tablets

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

Roxane Laboratories, Inc.

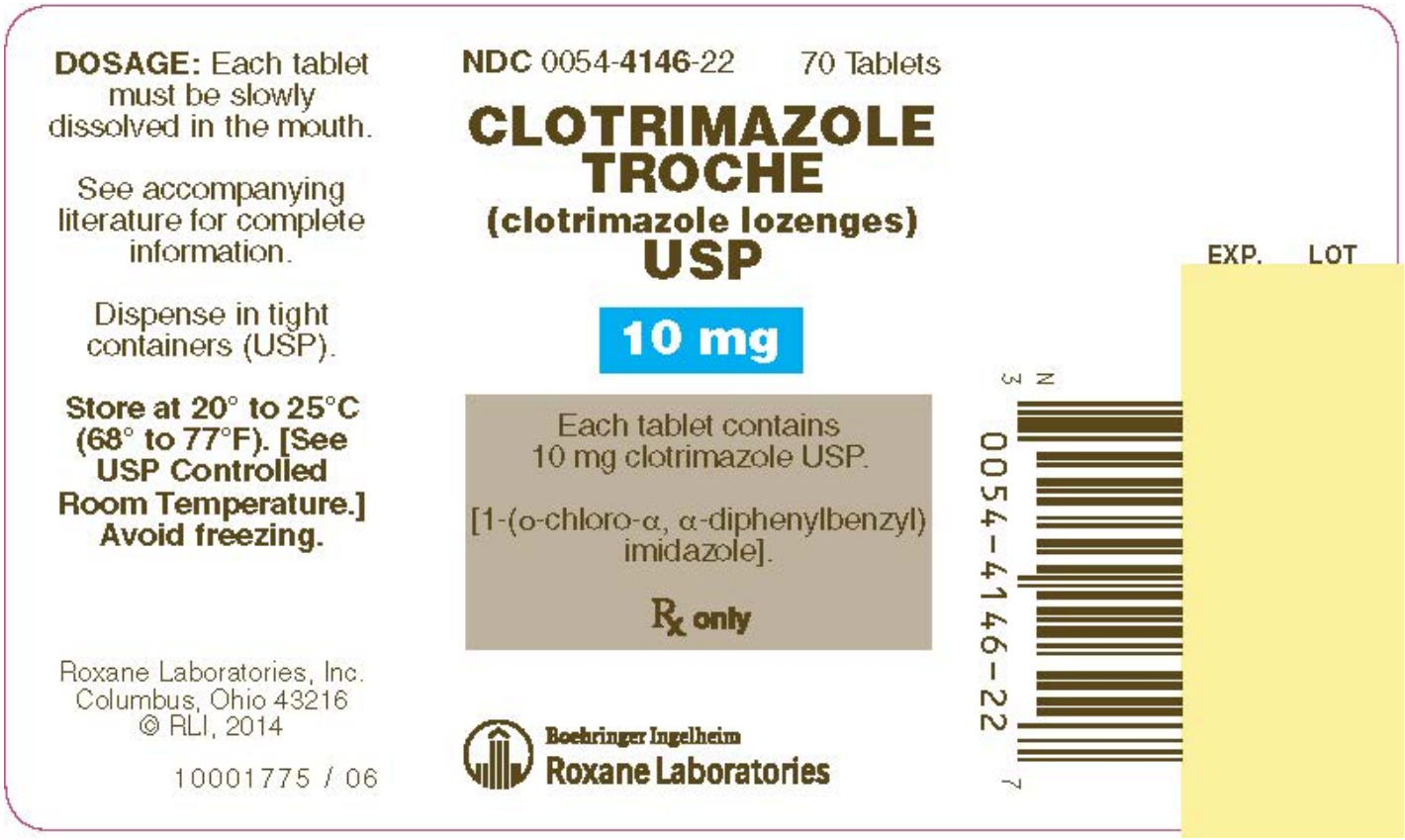
Columbus, Ohio 43216

10001777/08 Revised August 2014

PRINCIPAL DISPLAY PANEL

Roxane Laboratories, Inc.

NDC 0054-4146-22



Package/Label Display Panel

Roxane Laboratories, Inc.

NDC 0054-8146-22

CLOTRIMAZOLE

clotrimazole lozenge

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0054-4146
Route of Administration	ORAL, TOPICAL	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CLOTRIMAZOLE (CLOTRIMAZOLE)	CLOTRIMAZOLE	10 mg

Inactive Ingredients	
Ingredient Name	**Strength**
CROSCARMELLOSE SODIUM	
DEXTRATES	
MAGNESIUM STEARATE	
CELLULOSE, MICROCRYSTALLINE	
POVIDONES	

Product Characteristics			
Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	16mm
Flavor		**Imprint Code**	54;552
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0054-4146-22	70 in 1 BOTTLE, PLASTIC; Combination Product Type = C112160		
2	NDC:0054-4146-23	140 in 1 BOTTLE, PLASTIC; Combination Product Type = C112160		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076387	07/29/2004	

CLOTRIMAZOLE

clotrimazole lozenge

Product Information

Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0054-8146
Route of Administration	ORAL, TOPICAL	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CLOTRIMAZOLE (CLOTRIMAZOLE)	CLOTRIMAZOLE	10 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELLOSE SODIUM	
DEXTRATES	
MAGNESIUM STEARATE	
CELLULOSE, MICROCRYSTALLINE	
POVIDONES	

Product Characteristics

Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	16mm
Flavor		**Imprint Code**	54;552
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0054-8146-22	70 in 1 CARTON		
1		1 in 1 BLISTER PACK; Combination Product Type = C112160		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076387	07/29/2004	

Labeler - Roxane Laboratories, Inc (833490464)

Registrant - Roxane Laboratories, Inc (833490464)

Establishment

Name	Address	ID/FEI	Business Operations
Boehringer Ingelheim Roxane Inc		058839929	MANUFACTURE(0054-4146, 0054-8146)