

CLOTRIMAZOLE- clotrimazole lozenge
Hikma Pharmaceuticals USA USA Inc.

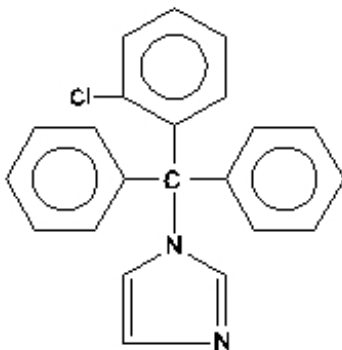
Clotrimazole Troche(lozenges) USP
FOR TOPICAL ORAL ADMINISTRATION

Rx only

DESCRIPTION

Each Clotrimazole Troche (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:



$C_{22}H_{17}ClN_2$

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

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

WARNING

Clotrimazole is 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 is 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 Troche (lozenges) USP

10 mg troche is supplied as white, round, flat face beveled edge troche with product identification “54 552” on one side and plain on the other side.

NDC 0054-4146-22: Bottle of 70 Troches

NDC 0054-4146-23: Bottle of 140 Troches

NDC 0054-8146-22: 7x10 Unit-Dose Troches

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

Avoid freezing.

Distributed by: **Hikma**

Pharmaceuticals USA Inc.

Berkeley Heights, NJ 07922

C50000435/01

Revised July 2021

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Each troche contains
10 mg clotrimazole, USP.

[1-(o-chloro- α , α -diphe-
nylbenzyl) imidazole].

DOSAGE: Each troche
must be slowly dissolved
in the mouth.

See Package Insert for
Complete Prescribing
Information.

Dispense in tight, child-
resistant container as
defined in the USP/NF.

Store at 20° to 25°C
(68° to 77°F).

[See USP Controlled
Room Temperature.]

Avoid freezing.

NDC 0054-4146-22 70 Troches

Clotrimazole Troche (lozenges), USP

10 mg

Distributed by: **Hikma
Pharmaceuticals USA Inc.**
Berkeley Heights, NJ 07922

R_x only

hikma.



C50000434/01

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 0054-8146-22

7 x 10 Unit-Dose
Troches

Each troche contains
10 mg clotrimazole,
USP.

[1-(o-chloro- α ,
 α -diphenylbenzyl)
imidazole].

Clotrimazole

Troche (lozenges), USP

10 mg

Glue

R_x only

DOSAGE: Each troche must be slowly dissolved in the mouth.

See Package Insert for Complete Prescribing Information.

This unit-dose package is not child-resistant. If dispensed for outpatient use, a child-resistant container should be utilized.

For Institutional Use Only.

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

Avoid freezing.

C50000436/01

Distributed by: **Hikma
Pharmaceuticals USA Inc.**
Berkeley Heights, NJ 07922



hikma.

CLOTRIMAZOLE

clotrimazole lozenge

Product Information

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

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CLOTRIMAZOLE (UNII: G07GZ97H65) (CLOTRIMAZOLE - UNII:G07GZ97H65)	CLOTRIMAZOLE	10 mg

Inactive Ingredients

Ingredient Name	Strength
CROSCARMELOSE SODIUM (UNII: M28OL1HH48)	
DEXTRATES (UNII: G263MI44RU)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	

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; Type 0: Not a Combination Product	07/29/2004	
2	NDC:0054-4146-23	140 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	07/29/2004	

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	Item Code (Source)	NDC:0054-8146
Route of Administration	ORAL, TOPICAL		

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Ingredient Name	Basis of Strength	Strength
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Ingredient Name	Strength
CROSCARMELOSE SODIUM (UNII: M28OL1HH48)	
DEXTRATES (UNII: G263MI44RU)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	

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	07/29/2004	07/31/2025
1		1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076387	07/29/2004	07/31/2025

Labeler - Hikma Pharmaceuticals USA USA Inc. (080189610)**Establishment**

Name	Address	ID/FEI	Business Operations
West-Ward Columbus Inc.		058839929	MANUFACTURE(0054-4146, 0054-8146)

Revised: 7/2021

Hikma Pharmaceuticals USA USA Inc.