NAFTIFINE HYDROCHLORIDE- naftifine hydrochloride cream
Taro Pharmaceuticals U.S.A., Inc.

Naftifine Hydrochloride
Cream USP, 1%

Rx ONLY

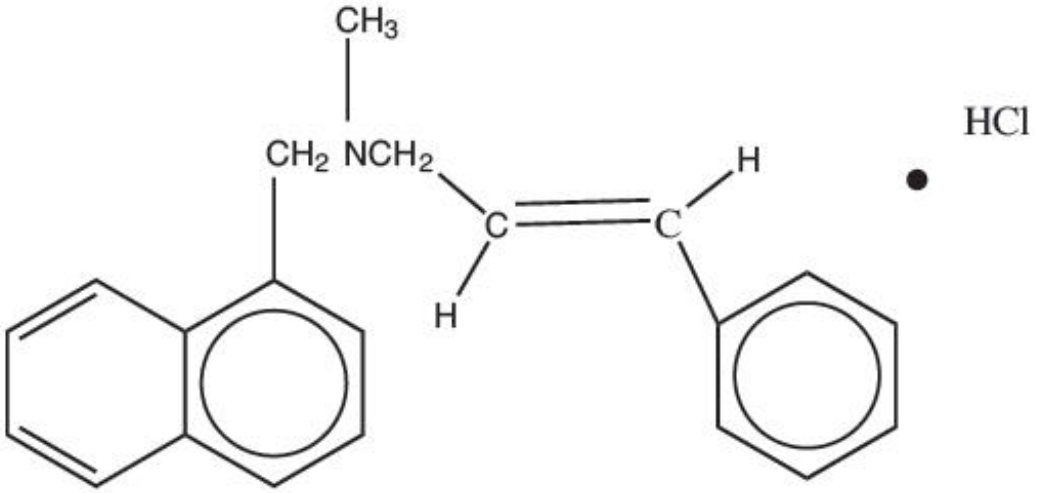
DESCRIPTION

Naftifine Hydrochloride Cream USP, 1% contains the synthetic, broad-spectrum, antifungal agent naftifine hydrochloride. Naftifine Hydrochloride Cream USP, 1% is for topical use only.

CHEMICAL NAME:

(E)-N-Cinnamyl-N-methyl-1-naphthalenemethylamine hydrochloride. Naftifine hydrochloride has an empirical formula of $C_{21}H_{21}N \cdot HCl$ and a molecular weight of 323.86.

Structural Formula



naftifine hydrochloride

Contains

Active Ingredient

Naftifine hydrochloride 1%

Inactive Ingredients

benzyl alcohol, cetyl alcohol, cetyl esters wax, isopropyl myristate, polysorbate 60, purified water, sodium hydroxide, sorbitan monostearate, and stearyl alcohol. Hydrochloric acid may be added to adjust pH.

CLINICAL PHARMACOLOGY

Naftifine hydrochloride is a synthetic allylamine derivative. The following *in vitro* data are available, but their clinical significance is unknown. Naftifine hydrochloride has been shown to exhibit fungicidal activity *in vitro* against a broad spectrum of organisms, including *Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans, Epidermophyton floccosum, Microsporum canis, Microsporum audouini,* and *Microsporum gypseum;* and fungistatic activity against *Candida* species, including *Candida*

albicans. Naftifine Hydrochloride Cream USP, 1% has only been shown to be clinically effective against the disease entities listed in the INDICATIONS AND USAGE section.

Although the exact mechanism of action against fungi is not known, naftifine hydrochloride appears to interfere with sterol biosynthesis by inhibiting the enzyme squalene 2, 3-epoxidase. This inhibition of enzyme activity results in decreased amounts of sterols, especially ergosterol, and a corresponding accumulation of squalene in the cells.

Pharmacokinetics

In vitro and *in vivo* bioavailability studies have demonstrated that naftifine penetrates the stratum corneum in sufficient concentration to inhibit the growth of dermatophytes.

Following a single topical application of 1% naftifine cream to the skin of healthy subjects, systemic absorption of naftifine was approximately 6% of the applied dose. Naftifine and/or its metabolites are excreted via the urine and feces with a half-life of approximately two to three days.

INDICATIONS AND USAGE

Naftifine Hydrochloride Cream USP, 1% is indicated for the topical treatment of tinea pedis, tinea cruris and tinea corporis caused by the organisms *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum*.

CONTRAINDICATIONS

Naftifine Hydrochloride Cream USP, 1% is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS

Naftifine Hydrochloride Cream USP, 1% is for topical use only and not for ophthalmic use.

PRECAUTIONS

General

Naftifine Hydrochloride Cream USP, 1% is for external use only. If irritation or sensitivity develops with the use of Naftifine Hydrochloride Cream USP, 1%, treatment should be discontinued and appropriate therapy instituted.

Diagnosis of the disease should be confirmed either by direct microscopic examination of a mounting of infected tissue in a solution of potassium hydroxide or by culture on an appropriate medium.

Information for patients

The patient should be told to:

1. Avoid the use of occlusive dressings or wrappings unless otherwise directed by the physician.
2. Keep Naftifine Hydrochloride Cream USP, 1% away from the eyes, nose, mouth and other mucous membranes.

Carcinogenesis, mutagenesis, impairment of fertility

In a 2-year dermal carcinogenicity study, naftifine hydrochloride cream was administered to Sprague-Dawley rats at topical doses of 1%, 2% and 3% (10 mg/kg/day, 20 mg/kg/day, and 30 mg/kg/day naftifine hydrochloride). No drug-related tumors were noted in this study up to the highest dose evaluated in this study of 30 mg/kg/day [3.6 times the maximum recommended human dose (MRHD) based on mg/m^2 comparison].

Naftifine hydrochloride revealed no evidence of mutagenic or clastogenic potential based on the results of two *in vitro* genotoxicity tests (Ames assay and Chinese hamster ovary cell chromosome aberration assay) and one *in vivo* genotoxicity test (mouse bone marrow micronucleus assay).

Oral administration of naftifine hydrochloride to rats, throughout mating, gestation, parturition and lactation, demonstrated no effects on growth, fertility or reproduction, at doses up to 100 mg/kg/day (12 times MRHD based on mg/m^2 comparison).

Pregnancy

Teratogenic Effects

Reproduction studies have been performed in rats and rabbits (via oral administration) at doses 150 times or more than the topical human dose and have revealed no evidence of impaired fertility or harm to the fetus due to naftifine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Naftifine Hydrochloride Cream USP, 1% is administered to a nursing woman.

Pediatric use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

During clinical trials with Naftifine Hydrochloride Cream USP, 1%, the incidence of adverse reactions was as follows: burning/stinging (6%), dryness (3%), erythema (2%), itching (2%), local irritation (2%).

DOSAGE AND ADMINISTRATION

A sufficient quantity of Naftifine Hydrochloride Cream USP, 1% should be gently massaged into the affected and surrounding skin areas once a day. The hands should be washed after application. If no clinical improvement is seen after four weeks of treatment with Naftifine Hydrochloride Cream USP, 1%, the patient should be re-evaluated.

HOW SUPPLIED

Naftifine Hydrochloride Cream USP, 1% is supplied in the following sizes:
15 g - NDC 51672-1362-1 (tube)
30 g - NDC 51672-1362-2 (tube)
60 g - NDC 51672-1362-3 (tube)
90 g - NDC 51672-1362-8 (tube)

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

Manufactured by:
Taro Pharmaceuticals Inc., Brampton, Ontario, Canada L6T 1C1

Distributed by:
Taro Pharmaceuticals U.S.A., Inc., Hawthorne, NY 10532

TARO is a registered trademark of Taro Pharmaceuticals U.S.A., Inc.

Revised: May 2018
PK-7357-2 10

PRINCIPAL DISPLAY PANEL - 90 g Tube Carton

NDC 51672-1362-8

90 g

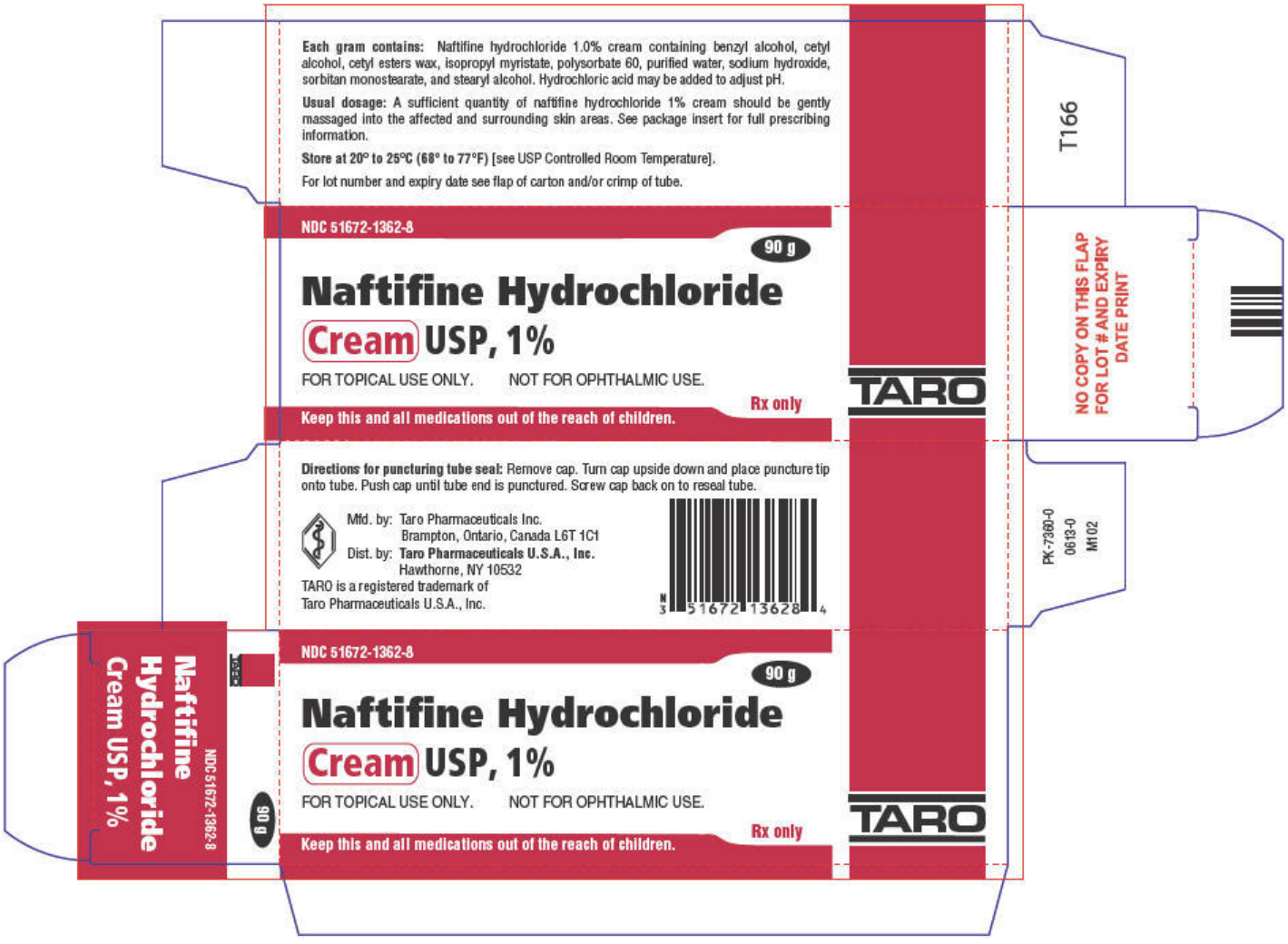
Naftifine Hydrochloride
Cream USP, 1%

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.

Rx only

TARO

Keep this and all medications out of the reach of children.



NAFTIFINE HYDROCHLORIDE

naftifine hydrochloride cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51672-1362
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Naftifine Hydrochloride (UNII: 25UR9N9041) (Naftifine - UNII:4FB1TON47A)	Naftifine Hydrochloride	10 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
benzyl alcohol (UNII: LKG8494WBH)	
cetyl alcohol (UNII: 936JST6JCN)	
cetyl esters wax (UNII: D072FFP9GU)	
isopropyl myristate (UNII: 0RE8K4LNJS)	
polysorbate 60 (UNII: CAL22UVI4M)	
sodium hydroxide (UNII: 55X04QC32I)	
water (UNII: 059QF0KO0R)	
sorbitan monostearate (UNII: NVZ4I0H58X)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
hydrochloric acid (UNII: QTT17582CB)	

Product Characteristics

Color	WHITE	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51672-1362-1	1 in 1 CARTON	09/08/2016	
1		15 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:51672-1362-2	1 in 1 CARTON	09/08/2016	
2		30 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:51672-1362-3	1 in 1 CARTON	09/08/2016	
3		60 g in 1 TUBE; Type 0: Not a Combination Product		
4	NDC:51672-1362-8	1 in 1 CARTON	09/08/2016	
4		90 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	ANDA205975	09/08/2016	

Labeler - Taro Pharmaceuticals U.S.A., Inc. (145186370)

Establishment

Name	Address	ID/FEI	Business Operations
Taro Pharmaceuticals Inc.		206263295	MANUFACTURE(51672-1362)

Revised: 5/2018 Taro Pharmaceuticals U.S.A., Inc.