NAFTIFINE HYDROCHLORIDE- naftifine hydrochloride gel
Amneal Pharmaceuticals of New York LLC

Naftifine Hydrochloride Gel, USP 1%
Rx ONLY

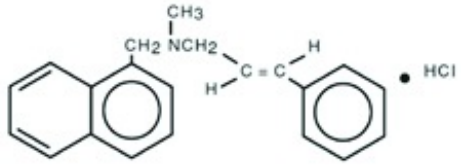
DESCRIPTION

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

CHEMICAL NAME

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

Structural Formula



naftifine hydrochloride, USP

Contains

Active Ingredient
Naftifine hydrochloride, USP 1%.

Inactive Ingredients
Naftifine hydrochloride gel, USP 1% contains alcohol (52%v/v), carbopol 974P, diisopropanolamine, edetate disodium, polysorbate 80, and purified water.

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 gel, 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 single topical applications of ^{3}H- labeled naftifine gel 1% to the skin of healthy subjects, up to 4.2% of the applied dose was absorbed. 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 gel, 1% is indicated for the topical treatment of tinea pedis, tinea cruris, and tinea corporis caused by the organisms *Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans*[1]*, Epidermophyton floccosum*[1].

[1] Efficacy for this organism in this organ system was studied in fewer than 10 infections.

CONTRAINDICATIONS

Naftifine hydrochloride gel, 1% is contraindicated in individuals who have shown hypersensitivity to any of their components.

WARNINGS

Naftifine hydrochloride gel, 1% is for topical use only and not for ophthalmic use.

PRECAUTIONS

General

Naftifine hydrochloride gel, 1%, is for external use only. If irritation or sensitivity develops with the use of naftifine hydrochloride gel, 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 gel, 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, 20, 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 gel, 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 gel, 1%. The incidence of adverse reactions was as follows: burning/stinging (5.0%), itching (1.0%), erythema (0.5%), rash (0.5%), skin tenderness (0.5%).

To report SUSPECTED ADVERSE REACTIONS contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

A sufficient quantity of naftifine hydrochloride gel, 1% should be gently massaged into the affected and surrounding skin areas twice a day, in the morning and evening. The hands should be washed after application. If no clinical improvement is seen after four weeks of treatment with naftifine hydrochloride gel, 1%, the patient should be re-

evaluated.

HOW SUPPLIED

Naftifine hydrochloride gel, USP 1% is supplied in collapsible tubes in the following sizes:

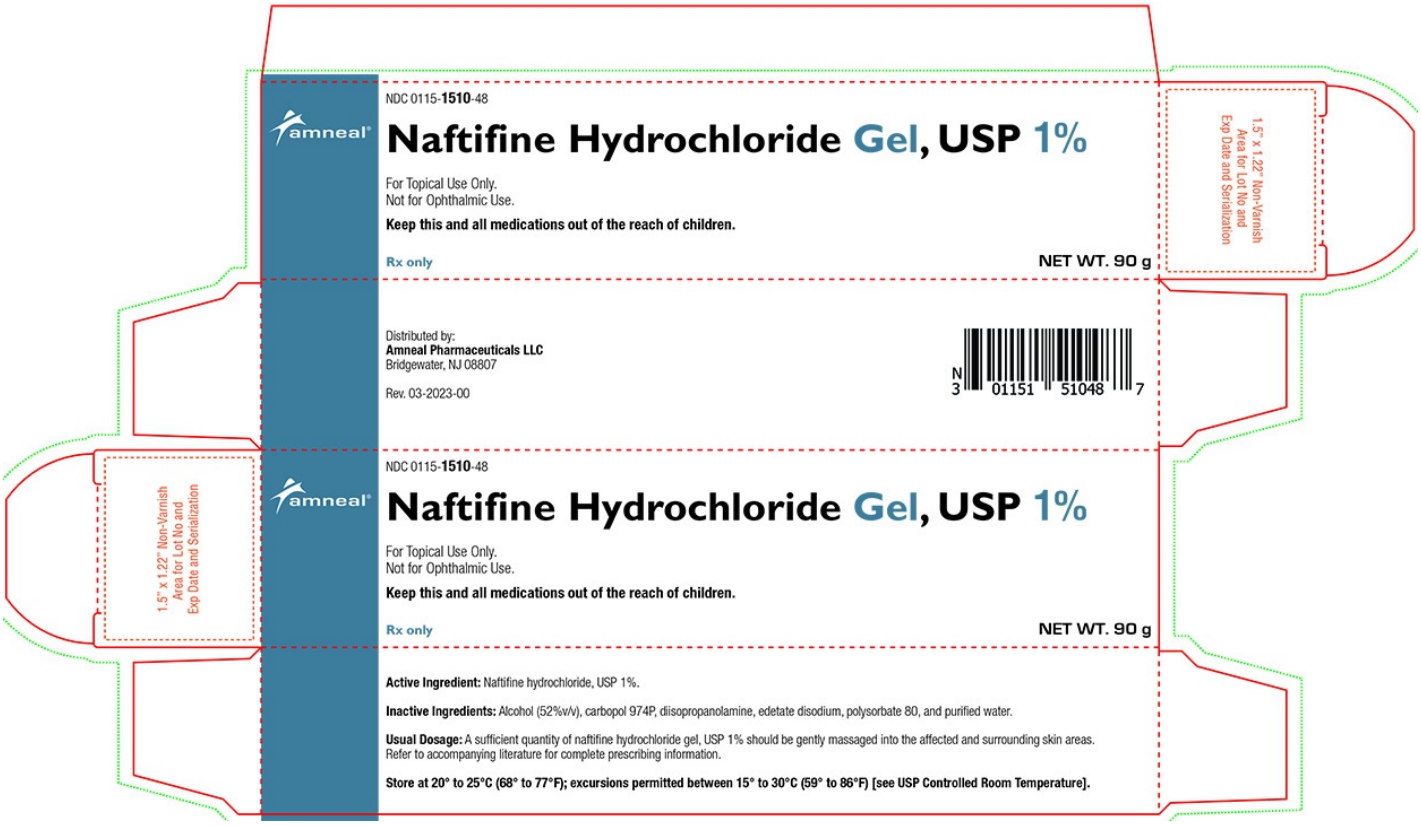
40g – NDC 0115-1510-63
60g – NDC 0115-1510-58
90g – NDC 0115-1510-48

Note: Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Distributed by:
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

Rev. 03-2023-00

PACKAGE LABEL PRINCIPAL DISPLAY PANEL



NAFTIFINE HYDROCHLORIDE

naftifine hydrochloride gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0115-1510
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
ALCOHOL (UNII: 3K9958V90M)	
CARBOMER HOMOPOLYMER TYPE B (ALLYL PENTAERYTHRITOL CROSSLINKED) (UNII: HHT01ZNK31)	
DIISOPROPANOLAMINE (UNII: 0W44HYL8T5)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	white (colorless to yellow clear to slightly hazy)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0115-1510-63	1 in 1 CARTON	03/20/2019	
1		40 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:0115-1510-58	1 in 1 CARTON	03/20/2019	
2		60 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:0115-1510-48	1 in 1 CARTON	03/20/2019	
3		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	ANDA206165	03/20/2019	

Labeler - Amneal Pharmaceuticals of New York LLC (123797875)

Establishment

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals, LLC		079389286	analysis(0115-1510) , label(0115-1510) , manufacture(0115-1510) , pack(0115-1510)

Revised: 3/2023

Amneal Pharmaceuticals of New York LLC