NAFTIN- naftifine hydrochloride gel
Sebela Pharmaceuticals Inc.

NAFTIN ®

NAFTIFINE HCl 1%

Rx ONLY

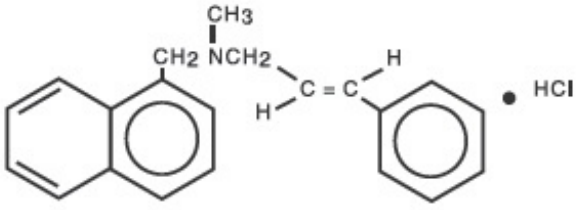
DESCRIPTION

Naftin ® Gel, 1% contains the synthetic, broad-spectrum, antifungal agent naftifine hydrochloride. Naftin ® Gel, 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

Naftin ® Gel, 1% contains polysorbate 80, carbomer 934P, diisopropanolamine, edetate disodium, alcohol (52%v/v), 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.* Naftin ® 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

Naftin ® 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].

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

CONTRAINDICATIONS

Naftin ® Gel, 1% is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS

Naftin ® Gel, 1% is for topical use only and not for ophthalmic use.

PRECAUTIONS

General

Naftin ® Gel, 1%, is for external use only. If irritation or sensitivity develops with the use of Naftin ® 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 Naftin ® 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/m2 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 Naftin ® 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 Naftin ® 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%).

DOSAGE AND ADMINISTRATION

A sufficient quantity of Naftin ® 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 Naftin ® Gel, 1%, the patient should be re-evaluated.

HOW SUPPLIED

Naftin ® (naftifine hydrochloride) Gel, 1% is supplied in collapsible tubes in the following sizes

- 40g – NDC 54766-770-40
- 60g – NDC 54766-770-60
- 90g – NDC 54766-770-90

Note: Store Naftin ® Gel, 1% at room temperature.

Distributed by Sebela Pharmaceuticals Inc.

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Roswell, Georgia 30076

www.sebelapharma.com

Toll Free 1-844-732-3521

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PI 77040001

PRINCIPAL DISPLAY PANEL - 40g Tube Carton

NDC 54766-770-40

NAFTIN ®

40g gel

NAFTIFINE HCl 1% GEL

Rx Only

PRINCIPAL DISPLAY PANEL - 60g Tube Carton

NDC 54766-770-60

NAFTIN ®

60g gel

NAFTIFINE HCl 1% GEL

Rx Only

PRINCIPAL DISPLAY PANEL - 90g Tube Carton

NDC 54766-770-90

NAFTIN ®

90g gel

NAFTIFINE HCl 1% GEL

Rx Only

NAFTIN

naftifine hydrochloride gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54766-770
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)	
WATER (UNII: 059QF0KO0R)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
CARBOMER HOMOPOLYMER TYPE B (ALLYL SUCROSE CROSSLINKED) (UNII: Z135WT9208)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
DIISOPROPANOLAMINE (UNII: 0W44HYL8T5)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54766-770-40	1 in 1 CARTON	01/22/2018	
1		40 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:54766-770-60	1 in 1 CARTON	01/22/2018	
2		60 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:54766-770-90	1 in 1 CARTON	01/22/2018	
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
NDA	NDA019356	01/22/2018	

Labeler - Sebela Pharmaceuticals Inc. (079104574)

Establishment

Name	Address	ID/FEI	Business Operations
DPT Laboratories, Ltd.		832224526	manufacture(54766-770) , analysis(54766-770) , pack(54766-770)

Revised: 12/2018 Sebela Pharmaceuticals Inc.