NAFTIN (naftifine hydrochloride) Cream, 2% is an allylamine antifungal indicated for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum* in adult patients ≥18 years of age. (1)

**DOSAGE AND ADMINISTRATION**

For topical use only. NAFTIN (naftifine hydrochloride) Cream, 2% is not for ophthalmic, oral, or intravaginal use. (2)

Apply a thin layer of NAFTIN (naftifine hydrochloride) Cream, 2% once-daily to the affected areas plus a ½ inch margin of healthy surrounding skin for 2 weeks. (2)

**INDICATIONS AND USAGE**

NAFTIN (naftifine hydrochloride) Cream, 2% is indicated for the treatment of: interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum* in adult patients ≥18 years of age. (1)

**CONTRAINDICATIONS**

None (4)

**WARNINGS AND PRECAUTIONS**

If redness or irritation develops with the use of NAFTIN Cream, 2% treatment should be discontinued. (5.1)

The most common adverse reaction (≥1%) is pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merz Pharmaceuticals, LLC at 877-743-8454 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 01/2012

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**ADVERSE REACTIONS**

redness/irritation, inflammation, maceration, swelling, burning, blister, erosive drainage, crustling, headache, dizziness, leukopenia, agranulocytosis. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

**HOW SUPPLIED/STORAGE AND HANDLING**

- Cream: 2%, white to off-white cream

**PUBLICATION INFORMATION: CONTENTS**

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2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
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7 CLINICAL PHARMAOCOLOGY
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11 DESCRIPTION
12 CLINICAL PHARMAOCOLOGY
13 NONCLINICAL TOXICOLOGY
14 CLINICAL STUDIES
15 HOW SUPPLIED/STORAGE AND HANDLING
16 PATIENT COUNSELING INFORMATION

Sections or subsections omitted from the full prescribing information are not listed

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**INDICATIONS AND USAGE**

NAFTIN (naftifine hydrochloride) Cream, 2% is indicated for the treatment of: interdigital tinea pedis, tinea cruris, and tinea corporis caused by the organism *Trichophyton rubrum* in adult patients ≥18 years of age. (1)

**CONTRAINDICATIONS**

None (4)

**WARNINGS AND PRECAUTIONS**

If redness or irritation develops with the use of NAFTIN Cream, 2% treatment should be discontinued. (5.1)

The most common adverse reaction (≥1%) is pruritus. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merz Pharmaceuticals, LLC at 877-743-8454 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 01/2012
11 DESCRIPTION
NAFTIN (naftifine hydrochloride) Cream, 2% is a white to off-white cream for topical use only. Each gram of (naftifine hydrochloride) Cream contains 20 mg of naftifine hydrochloride, a synthetic allylamine antifungal compound.

Chemically, naftifine HCl is (E)-N-Cinnamyl-N-methyl-1-napthalenemethylamine hydrochloride. The molecular formula is C_{21}H_{26}N•HCl with a molecular weight of 323.86.

The structural formula of naftifine hydrochloride is:

\[
\text{Chemically, naftifine HCl is (E)-N-Cinnamyl-N-methyl-1-napthalenemethylamine hydrochloride.}
\]

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
NAFTIN (naftifine hydrochloride) Cream, 2% is a topical antifungal drug [see Clinical Pharmacology(12.4)].

12.2 Pharmacodynamics
The pharmacodynamics of NAFTIN (naftifine hydrochloride) Cream, 2% have not been established.

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

The pharmacokinetics of NAFTIN Cream, 2% was evaluated following once-daily topical application for 2 weeks to twenty one adult subjects, both males and females, with both tinea pedis and tinea cruris. The mean total amount of cream applied was 6.4 g (range 5.3-7.5 g) per day. The results showed that the systemic exposure (i.e. maximum concentration (Cmax) and area under the curve (AUC)) to naftifine increased over the 2 week treatment period in all the 21 subjects. Geometric Mean (CV %) AUCo-24 was 117 (41.2) ng•hr/mL on Day 1, and 204 (28.5) ng•hr/mL on Day 14. Geometric Mean (CV %) Cmax was 7 ng/mL (55.6) on Day 1 and 11 ng/mL (29.3) on day 14. Median Tmax was 8.0 hours on Day 1 (range: 4 to 24) and 6.0 hours on Day 14 (range: 0 to 16). Accumulation after 14 days of topical application was less than two fold. Trough concentrations generally increased throughout the 14 day study period. Naftifine continued to be detected in plasma in 13/21 (62%) subjects on day 28, the mean (SD) plasma concentrations were 1.6 ± 0.5 ng/mL (range below limit of quantitation (BLQ) to 3 ng/mL).

In the same pharmacokinetic study conducted in patients with tinea pedis and tinea cruris, median fraction of the dose excreted in urine during the treatment period was 0.0016% on Day 1 versus 0.0020% on Day 14.

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

Naftifine has been shown to be active against most isolates of the following fungi, both in vitro and in clinical infections, as described in the INDICATIONS AND USAGE section:

Trichophyton rubrum

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies to evaluate the carcinogenic potential of NAFTIN (naftifine hydrochloride) Cream, 2% have not been performed.

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 (59-86°F).

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 (59-86°F).

14 CLINICAL STUDIES
14.1 Tinea Cruris
NAFTIN (naftifine hydrochloride) Cream, 2% has been investigated for efficacy in a randomized, double-blind, vehicle-controlled, multi-center study in 217 subjects with symptomatic and dermatophyte culture positive tinea cruris. Subjects were randomized to receive NAFTIN (naftifine hydrochloride) Cream, 2% or vehicle. Subjects applied the study agent (naftifine hydrochloride) Cream or vehicle) to the affected area plus a ½-inch margin of healthy skin surrounding the affected area once-daily for 2 weeks. Signs and symptoms of tinea cruris (presence or absence of erythema, pruritus, and scaling) were assessed, and KOH examination and dermatophyte culture were performed at the primary efficacy endpoint at week 4.

The mean age of the study population was 47 years and 87% were male and 43% were white. At baseline, subjects were confirmed to have signs and symptoms of tinea cruris, positive KOH exam, and confirmed dermatophyte presence based on culture results from a central mycology laboratory. The analysis of the intent-to-treat population was a comparison of the proportions of subjects with a complete cure at the week 4 visit (see Table 1). Complete cure was defined as both clinical cure (absence of erythema, pruritus, and scaling) and mycological cure (negative KOH and dermatophyte culture).

The percentage of subjects experiencing clinical cure and the percentage of subjects experiencing mycological cure at week 4 are presented individually in Table 1 below.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>NAFTIN (naftifine hydrochloride)</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cream, 2%</td>
<td>N=75</td>
<td>N=71</td>
</tr>
<tr>
<td>Complete Cure</td>
<td>19(25%)</td>
<td>2(3%)</td>
</tr>
<tr>
<td>Effective Treatment</td>
<td>45(60%)</td>
<td>7(10%)</td>
</tr>
<tr>
<td>Mycological Cure</td>
<td>54(72%)</td>
<td>11(16%)</td>
</tr>
</tbody>
</table>

a. Complete cure is a composite endpoint of both mycological cure and clinical cure. Clinical cure is defined as the absence of erythema, pruritus, and scaling (grade of 0).

b. Effective treatment is a negative KOH preparation and negative dermatophyte culture, erythema, scaling, and pruritus grades of 0 or 1 (absent or nearly absent).

c. Mycological cure is defined as negative KOH and dermatophyte culture.

14.2 Interdigital Tinea Pedis
NAFTIN (naftifine hydrochloride) Cream, 2% has been investigated for efficacy in a randomized, double-blind, vehicle-controlled, multi-center study in 217 subjects with symptomatic and dermatophyte culture positive tinea pedis. Subjects were randomized to receive NAFTIN (naftifine hydrochloride) Cream, 2% or vehicle. Subjects applied the study agent (naftifine hydrochloride) Cream or vehicle) to the affected area of the foot plus a ½-inch margin of healthy skin surrounding the affected area once-daily for 2 weeks. Signs and symptoms of tinea pedis (presence or absence of erythema, pruritus, and scaling) were assessed and KOH examination and dermatophyte culture was performed at the primary efficacy endpoint at week 6.

The mean age of the study population was 42 years and 71% were male and 57% were white. At baseline, subjects were confirmed to have signs and symptoms of tinea pedis, positive KOH exam, and confirmed dermatophyte culture. The primary efficacy endpoint was the proportions of subjects with a complete cure at the week 6 visit (see Table 2). Complete cure was defined as both a clinical cure (absence of erythema, pruritus, and scaling) and mycological cure (negative KOH and dermatophyte culture).

The efficacy results at week 6, four weeks following the end of treatment, are presented in Table 2 below. Naftin Cream demonstrated complete cure in subjects with interdigital tinea pedis, but complete cure in subjects with only moccasin type tinea pedis was not demonstrated.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>NAFTIN (naftifine hydrochloride)</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cream, 2%</td>
<td>N=147</td>
<td>N=70</td>
</tr>
<tr>
<td>Complete Cure</td>
<td>26(18%)</td>
<td>5(7%)</td>
</tr>
<tr>
<td>Effective Treatment</td>
<td>83(57%)</td>
<td>14(20%)</td>
</tr>
<tr>
<td>Mycological Cure</td>
<td>99(67%)</td>
<td>15(21%)</td>
</tr>
</tbody>
</table>

a. Complete cure is a composite endpoint of both mycological cure and clinical cure. Clinical cure is defined as absence of erythema, pruritus, and scaling (grade of 0).

b. Effective treatment is a negative KOH preparation and negative dermatophyte culture, erythema, scaling, and pruritus grades of 0 or 1 (absent or nearly absent).

c. Mycological cure is defined as negative KOH and dermatophyte culture.

16 HOW SUPPLIED/STORAGE AND HANDLING
How Supplied
NAFTIN (naftifine hydrochloride) Cream, 2% is a white to off-white cream supplied in collapsible tubes in the following sizes:

30g – NDC 0259-1102-30
45g – NDC 0259-1102-45
60g – NDC 0259-1102-60

Storage
Store NAFTIN (naftifine hydrochloride) Cream, 2% at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION
• Inform patients that NAFTIN (naftifine hydrochloride) Cream, 2% is for topical use only. NAFTIN (naftifine hydrochloride) Cream, 2% is not intended for intravaginal or ophthalmic use.

• If irritation or sensitivity develops with the use of NAFTIN (naftifine hydrochloride) Cream, 2% treatment should be discontinued and appropriate therapy instituted. Patients should be directed to contact their physician if these conditions develop following use of NAFTIN (naftifine hydrochloride) Cream, 2%.

NAFTIN (naftifine hydrochloride) Cream, 2% is manufactured for Merz Pharmaceuticals, LLC, Greensboro, NC 27410
NAFTIN (naftifine hydrochloride) Cream, 2% is a registered trademark of Merz Pharmaceuticals, LLC

5011727
Rev. 01/2012
NAFTIN (naftifine hydrochloride) Gel, 2% for topical use
Initial U.S. Approval: 1988

INDICATIONS AND USAGE
NAFTIN (naftifine hydrochloride) Gel, 2% is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum in patients 18 years of age and older. (1)

DOSAGE AND ADMINISTRATION
Apply a thin layer of NAFTIN (naftifine hydrochloride) Gel, 2% once daily to the affected areas plus an approximate 1/2 inch margin of healthy surrounding skin for 2 weeks. (2)

For topical use only. NAFTIN (naftifine hydrochloride) Gel, 2% is not for ophthalmic, oral, or intravaginal use. (2)

ADVERSE REACTIONS
The most common adverse reactions are application site reactions (2%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merz Pharmaceuticals, LLC at 877-743-8454 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 06/2013
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
NAFTIN (naftifine hydrochloride) Gel, 2% is an allylamine antifungal indicated for the treatment of interdigital tinea pedis caused by the organisms Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum in patients 18 years of age and older.

2 DOSAGE AND ADMINISTRATION
Apply a thin layer of NAFTIN (naftifine hydrochloride) Gel, 2% once daily to the affected areas plus an approximate ½ inch margin of healthy surrounding skin for 2 weeks.

For topical use only. NAFTIN (naftifine hydrochloride) Gel, 2% is not for ophthalmic, oral, or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS
Gel, 2%. Each gram contains 20 mg of naftifine hydrochloride in a colorless to yellow gel.

4 CONTRAINDICATIONS
None

5 WARNINGS AND PRECAUTIONS
5.1 Local Adverse Reactions
If irritation or sensitivity develops with the use of NAFTIN (naftifine hydrochloride) Gel, 2%, treatment should be discontinued.

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In two randomized, vehicle-controlled trials, 1143 subjects were treated with NAFTIN (naftifine hydrochloride) Gel, 2% versus 571 subjects treated with the vehicle. The trial subjects were 12 to 92 years old, were primarily male (76%), and were 59% Caucasian, 38% Black or African American, and 23% Hispanic or Latino. Subjects received doses once daily, topically, for 2 weeks to cover the affected skin areas plus a ½-inch margin of surrounding healthy skin. The most common adverse reactions were application site reactions which occurred at the rate of 2% in NAFTIN (naftifine hydrochloride) Gel, 2% arm versus 1% in vehicle arm. Most adverse reactions were mild in severity.

Cumulative irritancy testing revealed the potential for NAFTIN (naftifine hydrochloride) Gel, 2% to cause irritation. There was no evidence that NAFTIN (naftifine hydrochloride) Gel, 2% causes contact sensitization, phototoxicity, or photoallergenicity in healthy skin.

6.2 Postmarketing Experience
Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse reactions have been identified during postmarketing use of naftifine hydrochloride: blisters, burning sensation, crusty, dryness, erythema/redness, inflammation, irritation, maceration, pain, pruritus [mild]/itching, rash and swelling.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category B. There are no adequate and well-controlled trials of NAFTIN (naftifine hydrochloride) Gel, 2% in pregnant women. Because animal reproduction studies are not always predictive of human response, NAFTIN (naftifine hydrochloride) Gel, 2% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The animal multiples of human exposure calculations were based on daily dose body surface area comparison (mg/m²) for the reproductive toxicology studies described in this section and in Section 13.1. The Maximum Recommended Human Dose (MRHD) was set at 4 g 2% gel per day (1.33 mg/kg/day for a 60 kg individual).

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 30, 100, and 300 mg/kg/day naftifine hydrochloride were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. No treatment-related effects on embryofetal toxicity or teratogenicity were noted at 30 mg/kg/day (3.7X MRHD). Subcutaneous doses of 10 and 30 mg/kg/day naftifine hydrochloride were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. No treatment-related effects on embryofetal toxicity or teratogenicity were noted at 30 mg/kg/day (36.5X MRHD). Subcutaneous doses of 3, 10, and 30 mg/kg/day naftifine hydrochloride were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment-related effects on embryofetal toxicity or teratogenicity were noted at 30 mg/kg/day (7.3X MRHD).

A peri- and post-natal development study was conducted in rats. Oral doses of 30, 100, and 300 mg/kg/day naftifine hydrochloride were administered to female rats from gestational day 14 to lactation day 21. Reduced body weight gain of females during gestation and of the offspring during lactation was noted at 300 mg/kg/day (36.5X MRHD). No developmental toxicity was noted at 100 mg/kg/day (12.2X MRHD).

8.3 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 (naftifine hydrochloride) Gel, 2% is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established. The number of pediatric subjects ≤ 12 years of age studied was too small to adequately assess safety and efficacy.
8.5 Geriatric Use
During clinical trials, 99 subjects (9%) aged 65 years and over were exposed to NAFTIN Gel, 2%. Safety and effectiveness were similar to those reported by younger patients.

11 DESCRIPTION
NAFTIN (naftifine hydrochloride) Gel, 2% is a clear to yellow gel for topical use only. Each gram of NAFTIN (naftifine hydrochloride) Gel, 2% contains 20 mg of naftifine hydrochloride, a synthetic allylamine antifungal compound.

Chemically, naftifine HCl is (E)-N-Cinnamyl-N-methyl-1-naphthalenemethylamine hydrochloride.

The molecular formula is $C_{21}H_{21}N\cdot HCl$ with a molecular weight of 323.86.

The structural formula of naftifine hydrochloride is:

NAFTIN (naftifine hydrochloride) Gel, 2% contains the following inactive ingredients: alcohol, benzyl alcohol, edentate disodium, hydroxyethyl cellulose, purified water, propylene glycol, polysorbate 20 and trolamine.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
NAFTIN (naftifine hydrochloride) Gel, 2% is a topical antifungal drug [see Clinical Pharmacology (12.4)].

12.2 Pharmacodynamics
The pharmacodynamics of NAFTIN (naftifine hydrochloride) Gel, 2% have not been established.

12.3 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.

Pharmacokinetic analysis of plasma samples from 32 tinea pedis subjects treated with a mean dose of 3.9 grams NAFTIN (naftifine hydrochloride) Gel, 2% applied once daily to both feet for 14 days showed increased exposure over the treatment period, with a geometric mean (CV%) $AUC_{0-24}$ (area under plasma concentration-versus-time curve from time 0 to 24 hours) of 10.5 (118) ng•hr/mL on Day 1 and an $AUC_{0-24}$ of 70 (59) ng•hr/mL on Day 14. The accumulation ratio based on $AUC$ was approximately 6.

Maximum concentration ($C_{max}$) also increased over the treatment period; geometric mean (CV%) $C_{max}$ after a single dose was 0.9 (92) ng/mL on Day 1; $C_{max}$ on Day 14 was 3.7 (64) ng/mL. Median $T_{max}$ was 20.0 hours (range: 8, 20 hours) after a single application on Day 1 and 8.0 hours (range: 0, 24 hours) on Day 14. Trough plasma concentrations increased during the trial period and reached steady state after 11 days.

In the same pharmacokinetic trial the fraction of dose excreted in urine was less than or equal to 0.01% of the applied dose.

12.4 Microbiology
Mechanism of Action
Naftifine is an antifungal that belongs to the allylamine class. 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. The inhibition of enzyme activity by this allylamine results in decreased amounts of sterols, especially ergosterol, and a corresponding accumulation of squalene in the cells.

Mechanism of Resistance
To date, a mechanism of resistance to naftifine has not been described.

Naftifine has been shown to be active against most isolates of the following fungi, both in vitro and in clinical infections, as described in the INDICATIONS AND USAGE section:

- *Trichophyton rubrum*
- *Trichophyton mentagrophytes*
- *Epidermophyton floccosum*

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies to evaluate the carcinogenic potential of NAFTIN (naftifine hydrochloride) Gel, 2% have not been performed.

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 (12.2X MRHD).


14 CLINICAL STUDIES

NAFTIN (naftifine hydrochloride) Gel, 2% has been evaluated for efficacy in two randomized, double-blind, vehicle-controlled, multicenter trials that included 1175 subjects with symptomatic and dermatophyte culture-positive tinea pedis. Subjects were randomized to receive NAFTIN (naftifine hydrochloride) Gel, 2% or vehicle. Subjects applied naftifine hydrochloride gel 2% or vehicle to the affected area of the foot once daily for 2 weeks. Signs and symptoms of tinea pedis (presence or absence of erythema, pruritus, and scaling) were assessed and potassium hydroxide (KOH) examination and dermatophyte culture were performed 6 weeks after the first treatment.

The mean age of the study population was 45 years; 77% were male; and 60% were Caucasian, 35% were Black or African American, and 26% were Hispanic or Latino. At baseline, subjects were confirmed to have signs and symptoms of tinea pedis, positive KOH exam, and confirmed dermatophyte culture. The primary efficacy endpoint was the proportion of subjects with a complete cure at 6 weeks after the start of treatment (4 weeks after the last treatment). Complete cure was defined as both a clinical cure (absence of erythema, pruritus, and scaling) and mycological cure (negative KOH and dermatophyte culture).

The efficacy results at week 6, four weeks following the end of treatment, are presented in Table 1 below. Naftin Gel demonstrated complete cure in subjects with interdigital type tinea pedis.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Trial 1</th>
<th>Trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NAFTIN Gel, 2% N=382 n (%)</td>
<td>Vehicle N=179 n (%)</td>
</tr>
<tr>
<td></td>
<td>N=400 n (%)</td>
<td></td>
</tr>
<tr>
<td>Complete Cure</td>
<td>64 (17%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Treatment Effectiveness</td>
<td>207 (54%)</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Mycological Cure</td>
<td>250 (65%)</td>
<td>25 (14%)</td>
</tr>
</tbody>
</table>

a. Complete cure is a composite endpoint of both mycological cure and clinical cure. Clinical cure is defined as the absence of erythema, pruritus, and scaling (grade of 0).

b. Effective treatment is a negative KOH preparation and negative dermatophyte culture, erythema, scaling, and pruritus grades of 0 or 1 (absent or nearly absent).

c. Mycological cure is defined as negative KOH and dermatophyte culture.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

NAFTIN (naftifine hydrochloride) Gel, 2% is a colorless to yellow gel supplied in collapsible tubes in the following size:

45g – NDC 0259-1202-45

Storage

Store NAFTIN (naftifine hydrochloride) Gel, 2% at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

- Inform patients that NAFTIN (naftifine hydrochloride) Gel, 2% is for topical use only. NAFTIN (naftifine hydrochloride) Gel, 2% is not intended for ophthalmic, oral, or intravaginal use.
- Patients should be directed to contact their physician if irritation develops with the use of NAFTIN (naftifine hydrochloride) Gel, 2%.

NAFTIN (naftifine hydrochloride) Gel, 2% is manufactured for Merz Pharmaceuticals, LLC, Greensboro, NC 27410. NAFTIN (naftifine hydrochloride) is a registered trademark of Merz Pharmaceuticals, LLC.