

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-422

APPROVED LABELING

76-422

ENLARGED TO 110%
BY FOIA STAFF



fougera®

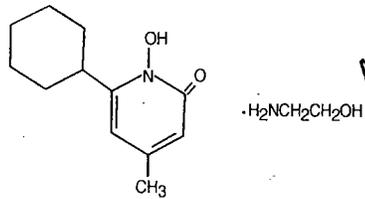
CICLOPIROX TOPICAL SUSPENSION, USP 0.77% (w/w) (LOTION)

FOR DERMATOLOGIC USE ONLY

R only

NOT FOR OPHTHALMIC USE

DESCRIPTION: Ciclopirox Topical Suspension, USP 0.77% (Lotion) is for topical use. Each gram of Ciclopirox Topical Suspension, USP 0.77% (Lotion) contains 7.7 mg of ciclopirox (as ciclopirox olamine) in a water miscible lotion base consisting of purified water USP, cocamide DEA, octyl-dodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as a preservative. Ciclopirox Topical Suspension, USP 0.77% (Lotion) contains a synthetic, broad-spectrum, antifungal agent ciclopirox (as ciclopirox olamine). The chemical name is 6-cyclohexyl-1-hydroxy-4-methyl-2(1*H*)-pyridone, 2-aminoethanol salt. The CAS Registry Number is 41621-49-2. The chemical structure is:



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Ciclopirox Topical Suspension, USP 0.77% (Lotion) has a pH of 7.
CLINICAL PHARMACOLOGY: Ciclopirox is a broad-spectrum, antifungal agent that inhibits the growth of pathogenic dermatophytes, yeasts, and *Malassezia furfur*. Ciclopirox exhibits fungicidal activity *in vitro* against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, *Microsporum canis*, and *Candida albicans*. Pharmacokinetic studies in men with radiolabeled ciclopirox solution in polyethylene glycol 400, showed an average of 1.3% absorption of the dose when it was applied topically to 750 cm² on the back followed by occlusion for 6 hours. The biological half-life was 1.7 hours and excretion occurred via the kidney. Two days after application only 0.01% of the dose applied could be found in the urine. Fecal excretion was negligible. Autoradiographic studies with human cadaver skin showed that ciclopirox penetrates into the hair and through the epidermis and hair follicles into the sebaceous glands and dermis, while a portion of the drug remains in the stratum corneum. *In vitro* penetration studies in frozen or fresh excised human cadaver and pig skin indicated that the penetration of Ciclopirox Topical Suspension, USP 0.77% (Lotion) is equivalent to that of Ciclopirox Cream 0.77%. Therapeutic equivalence of cream and lotion formulations also was indicated by studies of experimentally induced guinea pig and human trichophytosis.
INDICATIONS AND USAGE: Ciclopirox Topical Suspension, USP 0.77% (Lotion) is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; cutaneous candidiasis (moniliasis) due to *Candida albicans*; and tinea (pityriasis) versicolor due to *Malassezia furfur*.
CONTRAINDICATIONS: Ciclopirox Topical Suspension, USP 0.77% (Lotion) is contraindicated in individuals who have shown hypersensitivity to any of its components.
WARNINGS: General: Ciclopirox Topical Suspension, USP 0.77% (Lotion) is not for ophthalmic use. **Keep out of reach of children.**

(over)

PRECAUTIONS: If a reaction suggesting sensitivity or chemical irritation should occur with the use of Ciclopirox Topical Suspension, USP 0.77% (Lotion), treatment should be discontinued and appropriate therapy instituted.

Information for Patients

The patient should be told to:

1. Use the medication for the full treatment time even though signs/symptoms may have improved and notify the physician if there is no improvement after four weeks.
2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, oozing) indicative of possible sensitization.
3. Avoid the use of occlusive wrappings or dressings.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A carcinogenicity study in female mice dosed cutaneously twice per week for 50 weeks followed by a 6-month drug free observation period prior to necropsy revealed no evidence of tumors at the application site. The following *in vitro* and *in vivo* genotoxicity tests have been conducted with ciclopirox olamine: studies to evaluate gene mutation in the Ames *Salmonella* / Mammalian Microsome Assay (negative) and Yeast *Saccharomyces Cerevisiae* Assay (negative); and studies to evaluate chromosome aberrations *in vivo* in the Mouse Dominant Lethal Assay, and in the Mouse Micronucleus Assay at 500 mg/kg (negative). The following battery of *in vitro* genotoxicity tests were conducted with ciclopirox: a chromosome aberration assay in V79 Chinese Hamster Cells, with and without metabolic activation (positive); a gene mutation assay in the HGPRT - test with V79 Chinese Hamster Cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA Synthesis Assay in A549 Human Cells (negative)). An *in vitro* Cell Transformation Assay in BALB/C3T3 Cells was negative for cell transformation. In an *in vivo* Chinese Hamster Bone Marrow Cytogenetic Assay, ciclopirox was negative for chromosome aberrations at 5000 mg/kg.

Pregnancy Category B. Reproduction studies have been performed in the mouse, rat, rabbit, and monkey, via various routes of administration, at doses 10 times or more the topical human dose and have revealed no significant evidence of impaired fertility or harm to the fetus due to ciclopirox. There are, however, no adequate or 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. Caution should be exercised when Ciclopirox Topical Suspension, USP 0.77% (Lotion) is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 10 years have not been established.

ADVERSE REACTIONS: In the controlled clinical trial with 89 patients using Ciclopirox Topical Suspension, USP 0.77% (Lotion) and 89 patients using the lotion vehicle, the incidence of adverse reactions was low. Those considered possibly related to treatment or occurring in more than one patient were pruritus, which occurred in two patients using Ciclopirox Topical Suspension, USP 0.77% (Lotion) and one patient using the lotion vehicle; and burning, which occurred in one patient using Ciclopirox Topical Suspension, USP 0.77% (Lotion).

DOSAGE AND ADMINISTRATION: Gently massage Ciclopirox Topical Suspension, USP 0.77% (Lotion) into the affected and surrounding skin areas twice daily, in the morning and evening. Clinical improvement with relief of pruritus and other symptoms usually occurs within the first week of treatment. If a patient shows no clinical improvement after four weeks of treatment with Ciclopirox Topical Suspension, USP 0.77% (Lotion) the diagnosis should be redetermined. Patients with tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

HOW SUPPLIED: Ciclopirox Topical Suspension, USP 0.77% (Lotion) is supplied in:

30 mL bottles (NDC 0168-0314-30)

60 mL bottles (NDC 0168-0314-60)

Bottle space provided to allow for vigorous shaking before each use.

Store between 5°-25°C (41°-77°F).

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747



I2314
R1/04
#218

76-422

EXP
LOT

This product sealed for your protection.
If the seal is missing or broken return to
place of purchase.

Store at 5°-25° C (41°-77° F).
See package insert for full prescribing
information.
twice daily, in the morning and evening.
the affected and surrounding skin areas
Usual Dosage: Gently massage into

NDC 0168-0314-30
fougera[®]
**CICLOPIROX TOPICAL
SUSPENSION, USP
0.77% (w/w) (LOTION)
30 mL**

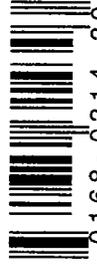
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R only
E. FOUGERA & CO.
a division of *Altana Inc.*
MELVILLE, NEW YORK 11747

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Each gram contains: 7.7 mg of ciclopirox
(as ciclopirox olamine) in a water miscible
lotion base consisting of purified water USP,
cocamide DEA, cetylalcohol NF, mineral
oil USP, stearyl alcohol NF, cetyl alcohol NF,
polyorbate 60 NF, methylparaben NF, sorbitan
monostearate NF, citric acid USP,
and benzyl alcohol NF (0.1%) as a
preservative.
L231430

R1/04



N 0168-0314-303

ENLARGED TO 110%
BY FOIA STAFF

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NDC 0168-0314-30

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**CICLOPIROX
TOPICAL
SUSPENSION,
USP 0.77% (w/w)
(LOTION)**
30 mL

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R only

**E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747**

Usual Dosage: Gently
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and surrounding skin areas
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NDC 0168-0314-30

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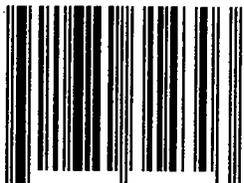
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a division of Altana Inc.
MELVILLE, NEW YORK 11747**

**APPROVED
AUG - 6 2004**

Each gram contains:
7.7 mg of ciclopirox
(as ciclopirox olamine) in a
water miscible lotion base
consisting of purified water
USP, cocamide DEA, octyl-
dodecanol NF, mineral oil
USP, stearyl alcohol NF,
cetyl alcohol NF, polysorbate
60 NF, myristyl alcohol NF,
sorbitan monostearate NF,
lactic acid USP, and benzyl
alcohol NF (1%) as a
preservative.


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76-422

NDC 0168-0314-60

fougera®

**CICLOPIROX TOPICAL
SUSPENSION, USP
0.77% (w/w) (LOTION)**

60 mg **APPROVED**

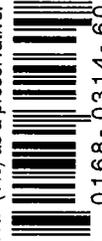
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MELVILLE, NEW YORK 11747

Each gram contains: 7.7 mg ciclopirox (as ciclopirox olamine) in a water miscible lotion base consisting of purified water USP, cocamide DEA, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, polysorbate 60 NF, myristyl alcohol NF, sorbitan monostearate NF, lactic acid USP, and benzyl alcohol NF (1%) as a preservative.



N 0168-0314-60 0

Usual Dosage: Gently massage into the affected and surrounding skin areas twice daily, in the morning and evening. See package insert for full prescribing information.
Store at 5°-25° C (41°-77° F).
This product sealed for your protection. If the seal is missing or broken return to place of purchase.
L231460 R1/04

**LOT
EXP**

76-422

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NDC 0168-0314-60

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**CICLOPIROX
TOPICAL
SUSPENSION,
USP 0.77%
(w/w)
(LOTION)
60 mL**

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TOPICAL
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(w/w)
(LOTION)
60 mL**

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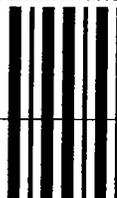
Each gram contains:

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water miscible lotion base
consisting of purified
water USP, cocamide
DEA, octyldodecanol NF,
mineral oil USP, stearyl
alcohol NF, cetyl alcohol
NF, polysorbate 60 NF,
myristyl alcohol NF,
sorbitan monostearate
NF, lactic acid USP, and
benzyl alcohol NF (1%)
as a preservative.

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