

LOPROX[®] Gel
(ciclopirox)
0.77%

FOR DERMATOLOGIC USE ONLY
NOT FOR USE IN EYES

Rx Only

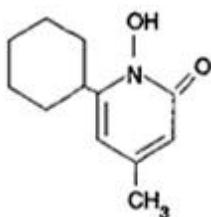
DESCRIPTION

LOPROX[®] Gel (ciclopirox) 0.77% contains a synthetic antifungal agent, ciclopirox. It is intended for topical dermatologic use only.

Each gram of LOPROX[®] Gel contains 7.70 mg of ciclopirox in a gel consisting of Purified Water USP, Isopropyl Alcohol USP, Octyldodecanol NF, Dimethicone Copolyol 190, Carbomer 980, Sodium Hydroxide NF, and Docusate Sodium USP.

LOPROX[®] Gel is a white, slightly fluid gel.

The chemical name for ciclopirox is 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridinone, with the empirical formula C₁₂H₁₇NO₂ and a molecular weight of 207.27. The CAS Registry Number is [29342-05-0]. The chemical structure is:



CLINICAL PHARMACOLOGY

Mechanism of Action

Ciclopirox acts by chelation of polyvalent cations (Fe³⁺ or Al³⁺) resulting in the inhibition of the metal-dependent enzymes that are responsible for the degradation of peroxides within the fungal cell.

In vitro studies showed that ciclopirox inhibited the formation of 5-lipoxygenase inflammatory mediators (5-HETE and LTB₄) and also inhibited PGE₂ release in a cell culture model. *In vivo*, ciclopirox inhibited inflammation in an arachidonic acid-induced murine ear edema model. The clinical significance of these findings is unknown.

Pharmacokinetics

A comparative study of the pharmacokinetics of LOPROX[®] Gel and LOPROX[®] Cream (ciclopirox olamine) 0.77% in 18 healthy males indicated that systemic absorption of ciclopirox from LOPROX[®] Gel was higher than that of LOPROX[®]

Cream. A 5 gm dose of LOPROX[®] Gel produced a mean (\pm SD) peak serum concentration of 25.02 (\pm 20.6) ng/mL total ciclopirox and 5 gm of LOPROX[®] Cream produced 18.62 (\pm 13.56) ng/mL total ciclopirox. Approximately 3% of the applied ciclopirox was excreted in the urine within 48 hours after application, with a renal elimination half-life of about 5.5 hours.

In a study of LOPROX[®] Gel, 16 men with moderate to severe tinea cruris applied approximately 15 grams/day of the gel for 14.5 days. The mean (\pm SD) dose-normalized values of C_{max} for total ciclopirox in serum were 100 (\pm 42) ng/mL on Day 1 and 238 (\pm 144) ng/mL on Day 15. During the 10 hours after dosing on Day 1, approximately 10% of the administered dose was excreted in the urine.

Microbiology

Ciclopirox is a hydroxypyridinone antifungal agent that inhibits the growth of pathogenic dermatophytes. Ciclopirox has been shown to be active against most strains of the following microorganisms both *in vitro* and in clinical infections as described in the INDICATIONS AND USAGE section:

Trichophyton rubrum, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*.

INDICATIONS AND USAGE

Superficial Dermatophyte Infections

LOPROX[®] Gel is indicated for the topical treatment of interdigital tinea pedis and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum*.

Seborrheic Dermatitis

LOPROX[®] Gel is indicated for the topical treatment of seborrheic dermatitis of the scalp.

CONTRAINDICATIONS

LOPROX[®] Gel is contraindicated in individuals who have shown hypersensitivity to any of its components.

WARNINGS

LOPROX[®] Gel is not for ophthalmic, oral, or intravaginal use.

Keep out of reach of children.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation should occur with the use of LOPROX[®] Gel, treatment should be discontinued and appropriate therapy instituted. A transient burning sensation may occur, especially after application to sensitive

areas. Avoid contact with eyes. Efficacy of LOPROX[®] Gel in immunosuppressed individuals has not been studied. Seborrheic dermatitis in association with acne, atopic dermatitis, Parkinsonism, psoriasis and rosacea has not been studied with LOPROX[®] Gel. Efficacy in the treatment of plantar and vesicular types of tinea pedis has not been established.

Information for Patients

The patient should be told the following:

1. Use LOPROX[®] Gel as directed by the physician. Avoid contact with the eyes and mucous membranes. LOPROX[®] Gel is for external use only.
2. Use the medication for fungal infections for the full treatment time even though symptoms may have improved, and notify the physician if there is no improvement after 4 weeks.
3. A transient burning/stinging sensation may be felt. This may occur in approximately 15% to 20% of cases, when LOPROX[®] Gel is used to treat seborrheic dermatitis of the scalp.
4. Inform the physician if the area of application shows signs of increased irritation or possible sensitization (redness with itching, burning, blistering, swelling, and/or oozing).
5. Avoid the use of occlusive dressings.
6. Do not use this medication for any disorder other than that for which it is prescribed.

Carcinogenesis, Mutagenesis, Impairment of Fertility

A carcinogenicity study of ciclopirox (1% and 5% solutions in polyethylene glycol 400) 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 battery of *in vitro* genotoxicity tests was conducted with ciclopirox: evaluation of gene mutation in the Ames *Salmonella* and *E. coli* assays (negative); chromosome aberration assays in V79 Chinese hamster cells, with and without metabolic activation (positive); gene mutation assays 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/c 3T3 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

Teratogenic effects: Pregnancy Category B

Reproduction studies of ciclopirox revealed no significant evidence of impaired fertility in rats exposed orally up to 5 mg/kg body weight (approximately 5 times the

maximum recommended topical human dose based on surface area). No fetotoxicity was shown due to ciclopirox in the mouse, rat, rabbit, and monkey at oral doses up to 100, 30, 30, and 50 mg/kg body weight, respectively (approximately 37.5, 30, 44, and 77 times the maximum recommended topical human dose based on surface area). By the dermal route of administration, no fetotoxicity was shown due to ciclopirox in the rat and rabbit at doses up to 120 and 100 mg/kg body weight, respectively (approximately 121 and 147 times, respectively, the maximum recommended topical human dose based on surface area).

There are no adequate or well-controlled studies of topically applied ciclopirox in pregnant women. LOPROX[®] Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Since many drugs are excreted in human milk, caution should be exercised when LOPROX[®] Gel is administered to a nursing woman.

Pediatric Use

The efficacy and safety of LOPROX[®] Gel in pediatric patients below the age of 16 years have not been established.

ADVERSE REACTIONS

In clinical trials, 140 (39%) of 359 subjects treated with LOPROX[®] Gel reported adverse experiences, irrespective of relationship to test materials, which resulted in 8 subjects discontinuing treatment. The most frequent experience reported was skin burning sensation upon application, which occurred in approximately 34% of seborrheic dermatitis patients and 7% of tinea pedis patients. Adverse experiences occurring between 1% to 5% were contact dermatitis and pruritus. Other reactions that occurred in less than 1% included dry skin, acne, rash, alopecia, pain upon application, eye pain, and facial edema.

DOSAGE AND ADMINISTRATION

Superficial Dermatophyte Infections

Gently massage LOPROX[®] Gel into the affected areas and surrounding skin twice daily, in the morning and evening immediately after cleaning or washing the areas to be treated. Interdigital tinea pedis and tinea corporis should be treated for 4 weeks. If a patient shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.

Seborrheic Dermatitis of the Scalp

Apply LOPROX Gel to affected scalp areas twice daily, in the morning and evening for 4 weeks. Clinical improvement usually occurs within the first week with continuing resolution of signs and symptoms through the fourth week of treatment. If a patient

shows no clinical improvement after 4 weeks of treatment, the diagnosis should be reviewed.

HOW SUPPLIED

LOPROX[®] Gel (ciclopirox) 0.77% is supplied in 30 g tubes (NDC 99207-013-30), and 45 g tubes (NDC 99207-013-45).

Store at 15° - 30°C (59° - 86°F).

Prescribing Information as of September 2001

Manufactured for:

MEDICIS, The Dermatology Company[®]

Scottsdale, AZ 85258

By: Aventis Pharma Deutschland GmbH,

D-65926 Frankfurt am Main

Made in Germany

REG TM THE AVENTIS GROUP

~~01330-08A~~ (New number to be added at final printing.)

NDC 99207-013-30

30g
Rx Only

LOPROX[®] GEL
(ciclopirox) 0.77%

FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.
Keep out of reach of children.

Usual Dosage: Gently massage into the affected areas and surrounding skin twice daily, in the morning and evening. See package insert for full prescribing information.

Each gram contains: 7.70 mg of Ciclopirox in a gel consisting of Purified Water USP, Isopropyl Alcohol USP, Octyldodecanol NF, Dimethicone Copolyol 190, Carbomer 980, Sodium Hydroxide NF, and Docusate Sodium USP.

Lot No.—Exp. Date, see crimp.
Store at 15°-30°C (59°-86°F).

Manufactured for:
MEDICIS,
The Dermatology Company[®]
Scottsdale, AZ 85258
by: Aventis Pharma
Deutschland GmbH
D-65926 Frankfurt am Main
GERMANY
Made in Germany
REG TM THE AVENTIS GROUP

CAP END

CRIMP END

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.

Keep out of reach of children.

Usual Dosages: Gently massage into the affected area and surrounding skin twice daily, in the morning and evening. See package insert for full prescribing information.

Each gram contains: 7.70 mg of Ciclopirox in a gel consisting of Purified Water USP, Isopropyl Alcohol USP, Cyclohexanediol NF, Dimethylsilyone Copolyol 190, Carbomer 980, Sodium Hydroxide NF, and Decussate Sodium USP.
Store at 15°-30°C (59°-86°F).

NDC 99207-013-30

LOPROX[®] GEL
(ciclopirox) 0.77%

30g
Rx Only

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Scottsdale, AZ 85258
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D-65926 Frankfurt am Main
GERMANY
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MEDICIS
The Dermatology Company[®]

LOT: _____
EXP: _____

NDC 99207-013-30

LOPROX[®] GEL
(ciclopirox) 0.77%

30g
Rx Only

LOPROX GEL
(ciclopirox) 0.77%
30g



NDC 99207-013-45

45g
Rx Only

LOPROX GEL
(ciclopirox) 0.77%

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.

Keep out of reach of children.

Usual Dosage: Gently massage into the affected areas and surrounding skin twice daily, in the morning and evening. See package insert for full prescribing information.

Each gram contains: 7.70 mg of Ciclopirox in a gel consisting of Purified Water USP, Isopropyl Alcohol USP, Octyldodecanol NF, Dimethicone Copolyol 190, Carbomer 980, Sodium Hydroxide NF, and Docosate Sodium USP.

Lot No.—Exp. Date, see crimp.
Store at 15°-30°C (59°-86°F).

Manufactured for:
MEDICIS, The Dermatology Company®
Scottsdale, AZ 85258
by: Aventis Pharma Deutschland GmbH
D-65926 Frankfurt am Main
GERMANY

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CAP END

CRIMP END

FOR DERMATOLOGIC USE ONLY. NOT FOR USE IN EYES.

Keep out of reach of children.

Usual Dosage: Gently massage into the affected areas and surrounding skin twice daily, in the morning and evening. See package insert for full prescribing information.

Each gram contains: 7.70 mg of Cyclopirox in a gel consisting of Purified Water USP, Isopropyl Alcohol USP, Octyldodecanol NF, Dimethicone Copolyol 190, Carbomer 980, Sodium Hydroxide NF, and Docosate Sodium USP.
Store at 15°-30°C (59°-86°F).

NDC 99207-013-45

LOPROX[®] GEL
(ciclopirox) 0.77%

45g
Rx Only

Manufactured for:
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Scottsdale, AZ 85258
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D-65926 Frankfurt am Main
GERMANY
Made in Germany
REG TM THE AVENTIS GROUP



NDC 99207-013-45

LOPROX[®] GEL
(ciclopirox) 0.77%

45g
Rx Only

LOPROX GEL
(ciclopirox) 0.77%

45g



NDC 99207-013-05

4 g
Rx Only

LOPROX GEL
Lidocaine 0.77%

CAP END

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.
Keep out of reach of children.
Lot No. - Exp. Date, see crimp.

Manufactured for:
MEDCIS,
The Dermatology Company®
Scottsdale, AZ 85258
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Deutschland GmbH
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Made in Germany
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CRIMP END





LOPROX GEL
(ciclopirox) 0.77%

PROFESSIONAL SAMPLE - NOT FOR SALE
30 and 45 g tubes available
Net Wt. 4 g

NDC 99207-01305

Rx Only

Manufactured for:
MEDCIS, The Dermatology Company®
Scottsdale, AZ 85258
Medischied GmbH
D-45726 Freiloh am Meer
GERMANY
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REG. IN THE AUSTRIAN GROUP



NDC 99207-01305

Rx Only

LOPROX GEL
(ciclopirox) 0.77%

PROFESSIONAL SAMPLE - NOT FOR SALE
30 and 45 g tubes available
Net Wt. 4 g

FOR DERMATOLOGIC USE ONLY.
NOT FOR USE IN EYES.

Keep out of reach of children.

Usual Dosage: Gently massage into the affected areas and surrounding skin twice daily, in the morning and evening. See package insert for full prescribing information.