

LOPROX- ciclopirox olamine suspension

LOPROX- ciclopirox olamine

Medimetriks Pharmaceuticals, Inc.

LOPROX® (ciclopirox)

Topical Suspension, 0.77%

For Topical Use Only

Not for use in eyes

Rx Only

DESCRIPTION

LOPROX® (ciclopirox) Topical Suspension, 0.77% is for topical use.

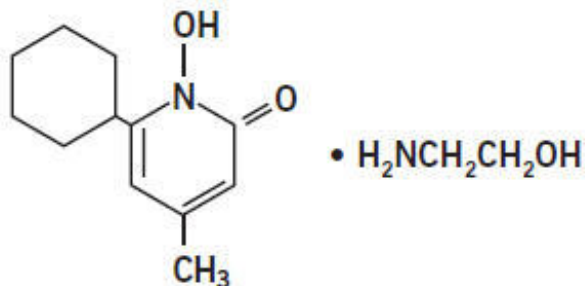
Each gram of LOPROX® Topical Suspension contains 7.70 mg of ciclopirox (as ciclopirox olamine) in a water miscible suspension base consisting of purified water USP, cocamide DEA, octyldodecanol NF, mineral oil USP, stearyl alcohol NF, cetyl alcohol NF, polysorbate 60 NF, myristyl alcohol NF, lactic acid USP, sorbitan monostearate NF, and benzyl alcohol NF (1%) as preservative.

LOPROX® Topical Suspension 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.

LOPROX® Topical Suspension has a pH of 7.

The chemical structure is:



CLINICAL PHARMACOLOGY

Mechanism of Action

Ciclopirox is a hydroxypyridone antifungal agent that 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.

Pharmacokinetics

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 LOPROX[®] Topical Suspension is equivalent to that of LOPROX[®] (ciclopirox) Cream, 0.77%. Therapeutic equivalence of cream and suspension formulations also was indicated by studies of experimentally induced guinea pig and human trichophytosis.

INDICATIONS AND USAGE

LOPROX[®] Topical Suspension 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

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

WARNINGS

General

LOPROX[®] Topical Suspension is not for ophthalmic use.

Keep out of reach of children.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation should occur with the use of LOPROX[®] Topical Suspension, 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 104-week dermal carcinogenicity study in mice was conducted with ciclopirox cream applied at doses up to 1.93% (100 mg/kg/day or 300 mg/m²/day). No increase in drug related neoplasms was noted when compared to control.

The following *in vitro* genotoxicity tests have been conducted with ciclopirox: evaluation of gene mutation in the Ames Salmonella and E. coli assays (negative); chromosome aberration assays in V79 Chinese hamster lung fibroblast cells, with and without metabolic activation (positive); chromosome aberration assays in V79 Chinese hamster lung fibroblast cells in the presence of supplemental Fe³⁺, with and without metabolic activation (negative); gene mutation assays in the HGPRT-test with V79 Chinese hamster lung fibroblast 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 a dosage of 5000 mg/kg body weight.

A combined oral fertility and embryofetal developmental study was conducted in rats with ciclopirox olamine. No effect on fertility or reproductive performance was noted at the highest dose tested of 3.85 mg/kg/day ciclopirox (approximately 1.2 times the maximum recommended human dose based on body surface area comparisons).

Pregnancy

Teratogenic Effects

Pregnancy Category B

There are no adequate or well-controlled studies in pregnant women. Therefore, LOPROX[®] Topical Suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Oral embryofetal developmental studies were conducted in mice, rats, rabbits and monkeys. Ciclopirox or ciclopirox olamine was orally administered during the period of organogenesis. No maternal toxicity, embryotoxicity or teratogenicity were noted at the highest doses of 77, 125, 80 and 38.5 mg/kg/day ciclopirox in mice, rats, rabbits and monkeys, respectively (approximately 11, 37, 51 and 24 times the maximum recommended human dose based on body surface area comparisons, respectively).

Dermal embryofetal developmental studies were conducted in rats and rabbits with ciclopirox olamine dissolved in PEG 400. Ciclopirox olamine was topically administered during the period of organogenesis. No maternal toxicity, embryotoxicity or teratogenicity were noted at the highest doses of 92 mg/kg/day and 77 mg/kg/day ciclopirox in rats and rabbits, respectively (approximately 27 and 49 times the maximum recommended human dose based on body surface area comparisons, respectively).

Nursing Mothers

It is not known whether this drug is excreted in human milk. Caution should be exercised when LOPROX[®] Topical Suspension 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 LOPROX[®] Topical Suspension and 89 patients using the 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 suspension and one patient using the suspension vehicle, and burning, which occurred in one patient using ciclopirox suspension.

DOSAGE AND ADMINISTRATION

Gently massage LOPROX[®] Topical Suspension 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 LOPROX[®] Topical Suspension, the diagnosis should be redetermined. Patients with tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

HOW SUPPLIED

LOPROX[®] (ciclopirox) Topical Suspension, 0.77% is supplied in 60 mL bottles (NDC 43538-550-60)

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

Store between 5° - 25°C (41° - 77°F).

To report SUSPECTED ADVERSE REACTIONS, contact Medimetriks Pharmaceuticals, Inc., at 1-973-882-7512 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured for:

MEDIMETRIKS

PHARMACEUTICALS, INC.

383 Route 46 West, Fairfield, NJ 07004-2402 USA

www.medimetriks.com

Manufactured by: Teligent Pharma, Inc., Buena, NJ 08310

Rev. 03/2016

IP043-R1

PRINCIPAL DISPLAY PANEL - 60 mL Bottle Carton

NDC 43538-550-60

For Topical Use Only

Not for use in eyes

60 mL

LOPROX[®]

(ciclopirox)

Topical

Suspension,

0.77%

R_x Only

MEDIMETRIKS

PHARMACEUTICALS, INC.



PRINCIPAL DISPLAY PANEL - Kit Carton

NDC 43538-551-60

For Topical Use Only

Not for use in eyes

60mL

R_x Only

LOPROX[®]
(ciclopirox)
Topical
Suspension,
0.77%
KIT

KIT CONTAINS:

- 1 - LOPROX[®] (ciclopirox) Topical Suspension, 0.77%
60 mL Bottle
- 1 - Rehyla[®] Hair + Body Cleanser
Net wt. 16 oz. (454 g) Bottle

MEDIMETRIKS
PHARMACEUTICALS, INC.

NDC 43538-551-60

For Topical Use Only
Not for use in eyes

60 mL

Rx Only



LOPROX[®]
(ciclopirox)
**Topical
Suspension,
0.77%**
KIT

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Topical Suspension, 0.77%
60 mL Bottle
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Net wt. 16 oz. (454 g) Bottle



NDC 43538-551-60

60 mL
Rx Only

LOPROX[®] (ciclopirox)
Topical Suspension, 0.77%
KIT



Medimetrix Pharmaceuticals guarantees that this product was manufactured with the highest pharmaceutical control standards, the most desirable ingredients, under strict demands for quality and safety, ensuring batch-to-batch quality and use-to-use consistency.

CAUTION: For external use only. Avoid contact with eyes, lips and mucous membranes. If contact occurs, rinse well with water. If rash or irritation develops, discontinue use.
DIRECTIONS: Wet skin and hair and pump Rehya® Hair & Body Cleanser into hands. Gently massage into hair and skin and work into a lather. Rinse thoroughly and pat dry with a soft towel.
Keep out of reach of children.
Store at room temperature between 15°-30°C (59°-86°F).



For Topical Use Only
Not for use in eyes
Keep out of reach of children.
Shake well before use.
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.



Topical Suspension, 0.77%

60 mL

Rx Only

NDC 43538-551-60

For Topical Use Only
Not for use in eyes



LOPROX[®] (ciclopirox)
Topical Suspension,
0.77%
KIT

 **MEDIMETRIKS**
PHARMACEUTICALS, INC.

NDC 43538-551-60



Rx Only

LOPROX[®]
(ciclopirox)
Topical
Suspension,
0.77%

Manufactured for: Medimetriks Pharmaceuticals, Inc.
383 Route 46 West, Fairfield, NJ 07004-2402 USA



REHYLA[®]
HAIR + BODY
CLEANSER

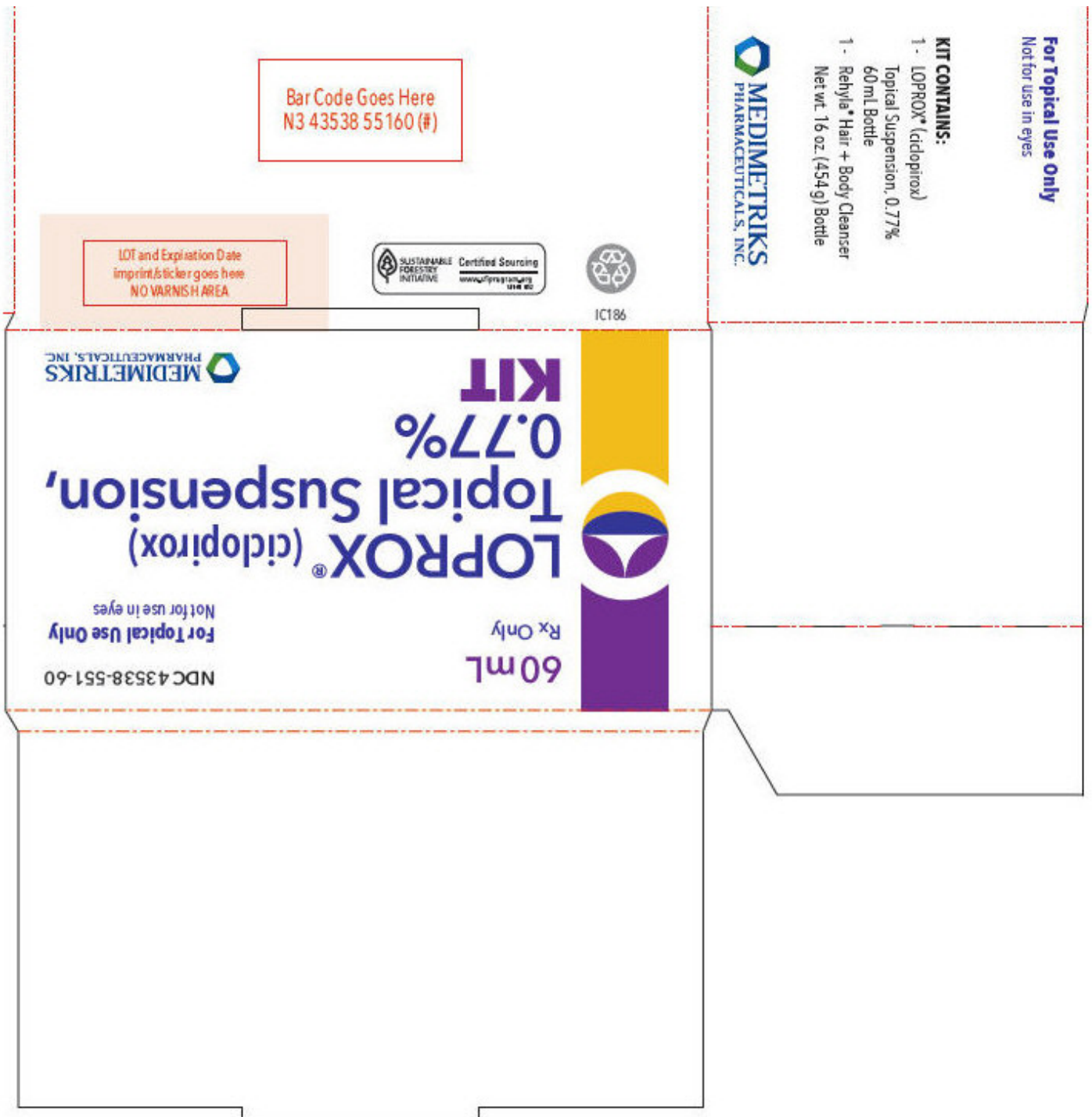
Manufactured for: Medimetriks Pharmaceuticals, Inc.
383 Route 46 West, Fairfield, NJ 07004-2402 USA
MADE IN USA



60 mL
Rx Only

LOPROX[®] (ciclopirox)
Topical Suspension, 0.77%
KIT

NDC 43538-551-60



LOPROX			
ciclopirox olamine suspension			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:43538-550
Route of Administration	TOPICAL		
Active Ingredient/Active Moiety			
	Ingredient Name	Basis of Strength	Strength

ciclopirox olamine (UNII: 50MD4SB4AP) (ciclopirox - UNII:19W019ZDRJ)	ciclopirox	7.7 mg in 1 mL
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Inactive Ingredients

Ingredient Name	Strength
benzyl alcohol (UNII: LKG8494WBH)	
cetyl alcohol (UNII: 936JST6JCN)	
lactic acid, unspecified form (UNII: 33X04XA5AT)	
mineral oil (UNII: T5L8T28FGP)	
myristyl alcohol (UNII: V42034O9PU)	
octyldodecanol (UNII: 461N1O614Y)	
water (UNII: 059QF0K00R)	
polysorbate 60 (UNII: CAL22UVI4M)	
sorbitan monostearate (UNII: NVZ4I0H58X)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
Coco Diethanolamide (UNII: 92005F972D)	

Product Characteristics

Color	WHITE	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43538-550-60	1 in 1 CARTON	10/14/2016	
1		60 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019824	10/14/2016	

LOPROX

ciclopirox olamine kit

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:43538-551
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Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43538-551-60	1 in 1 CARTON	10/14/2016	

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 BOTTLE	60 mL
Part 2	1 BOTTLE, PUMP	454 g

Part 1 of 2

LOPROX

ciclopirox olamine suspension

Product Information

Item Code (Source)	NDC:43538-550
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ciclopirox olamine (UNII: 50MD4SB4AP) (ciclopirox - UNII:19W019ZDRJ)	ciclopirox	7.7 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
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myristyl alcohol (UNII: V42034O9PU)	
octyldodecanol (UNII: 461N1O614Y)	
polysorbate 60 (UNII: CAL22UVI4M)	
water (UNII: 059QF0K00R)	
sorbitan monostearate (UNII: NVZ4I0H58X)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
Coco Diethanolamide (UNII: 92005F972D)	

Product Characteristics

Color	WHITE	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1 60 mL in 1 BOTTLE; Type 0: Not a Combination Product

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019824	10/14/2016	

Part 2 of 2

REHYLA HAIR AND BODY CLEANSER

cleansing (cold creams, cleansing lotions, liquids, and pads) lotion/shampoo

Product Information

Route of Administration TOPICAL

Other Ingredients

Ingredient Kind	Ingredient Name	Quantity
INGR	Water (UNII: 059QF0KO0R)	
INGR	glyceryl stearate SE (UNII: FCZ5MH785I)	
INGR	glycerin (UNII: PDC6A3C0OX)	
INGR	SHEA BUTTER (UNII: K49155WL9Y)	
INGR	cetyl alcohol (UNII: 936JST6JCN)	
INGR	cocamidopropyl betaine (UNII: 5OCF3O11KX)	
INGR	DISODIUM OLEAMIDO MIPA-SULFO SUCCINATE (UNII: 0MBZ20845F)	
INGR	sodium lauroyl sarcosinate (UNII: 632GS99618)	
INGR	sodium lauryl sulfoacetate (UNII: D0Y70F2B9J)	
INGR	SOY STEROL (UNII: PL360EPO9J)	
INGR	caprylyl glycol (UNII: 00YIU5438U)	
INGR	phenoxyethanol (UNII: HIE492ZZ3T)	
INGR	sodium chloride (UNII: 451W47IQ8X)	
INGR	propylene glycol (UNII: 6DC9Q167V3)	
INGR	PEG-8 dimethicone (UNII: GIA7T764OD)	
INGR	HYALURONATE SODIUM (UNII: YSE9PPT4TH)	
INGR	CARBOXYPOLYMETHYLENE (UNII: 0A5MM307FC)	
INGR	laureth-12 succinate (UNII: 8W3F9H704N)	
INGR	salicylic acid (UNII: O414PZ4LPZ)	
INGR	C13-14 ISOPARAFFIN (UNII: E4F12ROE70)	
INGR	CHAMAEMELUM NOBILE FLOWER (UNII: O2T154T6OG)	
INGR	hexylene glycol (UNII: KEH0A3F75J)	
INGR	laureth-7 (UNII: Z95S6G8201)	
INGR	edetate disodium (UNII: 7FLD91C86K)	

Product Characteristics

color WHITE C48325

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		454 g in 1 BOTTLE, PUMP; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Cosmetic		07/01/2014	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019824	10/14/2016	

Labeler - Medimetriks Pharmaceuticals, Inc. (019903816)

Establishment

Name	Address	ID/FEI	Business Operations
Teligent		011036910	MANUFACTURE(43538-550, 43538-551), PACK(43538-550, 43538-551)

Revised: 11/2018

Medimetriks Pharmaceuticals, Inc.