LOPROX- ciclopirox shampoo
Bausch Health US, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOPROX Shampoo safely and effectively. See full prescribing information for LOPROX Shampoo.

LOPROX® (ciclopirox) Shampoo, for topical use
Initial U.S. Approval: 1982

INDICATIONS AND USAGE

- LOPROX Shampoo is an antifungal indicated for the topical treatment of seborrheic dermatitis of the scalp in adults. (1)

DOSAGE AND ADMINISTRATION

- Apply approximately 1 teaspoon of LOPROX Shampoo to the scalp twice per week for 4 weeks. (2)
- For topical use only. Not for ophthalmic, oral, or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS

- Shampoo, 1% (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- If signs of irritation occur, discontinue use. (5.1)
- Avoid contact with eyes. (5.1)
- Hair discoloration has been reported with LOPROX use. (5.1)

ADVERSE REACTIONS

- The most frequently reported adverse reactions are pruritus, burning, and erythema. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch Health US, LLC at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 5/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LOPROX® (ciclopirox) Shampoo, 1% is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

2 DOSAGE AND ADMINISTRATION

LOPROX Shampoo is not for ophthalmic, oral, or intravaginal use.

Wet hair and apply approximately 1 teaspoon (5 mL) of LOPROX Shampoo to the scalp. Up to 2 teaspoons (10 mL) may be used for long hair. Lather and leave on hair and scalp for 3 minutes. A timer may be used. Avoid contact with eyes. Rinse off. Treatment should be repeated twice per week for 4 weeks, with a minimum of 3 days between applications.

If a patient with seborrheic dermatitis shows no clinical improvement after 4 weeks of treatment with LOPROX Shampoo, the diagnosis should be reviewed.

3 DOSAGE FORMS AND STRENGTHS

LOPROX is a shampoo containing 1% ciclopirox.

Each gram (equivalent to 0.96 mL) of LOPROX Shampoo contains 10 mg ciclopirox in a colorless and translucent shampoo base.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Local Effects

If a reaction suggesting sensitivity or irritation occurs with the use of LOPROX Shampoo, treatment should be discontinued and appropriate therapy instituted.

Contact of LOPROX Shampoo with the eyes should be avoided. If contact occurs, rinse thoroughly with water.

In patients with lighter hair color, hair discoloration has been reported.

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 clinical practice.

In 626 subjects treated with LOPROX Shampoo twice weekly in the two pivotal clinical trials, the most frequent adverse events were increased itching in 1% of subjects, and application site reactions, such as burning, erythema, and itching, also in 1% of subjects.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of LOPROX Shampoo: hair discoloration and abnormal hair texture, alopecia, irritation, and rash. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category B

There are no adequate or well-controlled studies in pregnant women. Therefore, LOPROX Shampoo 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 13, 42, 54, and 26 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 31 and 54 times the maximum recommended human dose based on body surface area comparisons, respectively).

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 LOPROX Shampoo is administered to a nursing woman.

8.4 Pediatric Use

No clinical trials have been conducted in subjects younger than 16 years.

8.5 Geriatric Use

In clinical trials, the safety and tolerability of LOPROX Shampoo in the population 65 years and older was comparable to that of younger subjects. Results of the efficacy analysis in those subjects 65 years and older showed effectiveness in 25 of 85 (29%) subjects treated with LOPROX Shampoo, and in 15

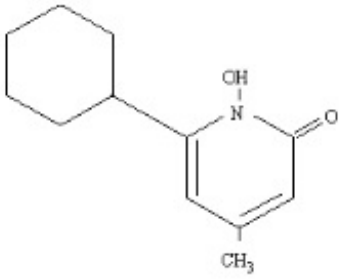
of 61 (25%) subjects treated with the vehicle; due to the small sample size, a statistically significant difference was not demonstrated. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects, but greater sensitivity to adverse effects in some older individuals cannot be ruled out.

11 DESCRIPTION

LOPROX (ciclopirox) Shampoo, 1% contains the synthetic antifungal agent ciclopirox for topical use.

Each gram (equivalent to 0.96 mL) of LOPROX Shampoo contains 10 mg ciclopirox in a shampoo base consisting of disodium laureth sulfosuccinate, laureth-2, purified water, sodium chloride, and sodium laureth sulfate.

LOPROX Shampoo is a colorless, translucent solution. The chemical name for ciclopirox is 6-cyclohexyl-1-hydroxy-4-methyl-2(1*H*)-pyridone, with the empirical formula $C_{12}H_{17}NO_2$ and a molecular weight of 207.27. The CAS Registry Number is [29342-05-0]. The chemical structure is:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ciclopirox is a hydroxypyridone antifungal agent although the relevance of this property for the indication of seborrheic dermatitis is not known. Ciclopirox acts by chelation of polyvalent cations (Fe^{3+} or Al^{3+}), resulting in the inhibition of the metal-dependent enzymes that are responsible for the degradation of peroxides within the fungal cell.

12.2 Pharmacodynamics

The pharmacodynamics of LOPROX Shampoo are unknown.

12.3 Pharmacokinetics

In a study in patients with seborrheic dermatitis of the scalp, application of 5 mL ciclopirox shampoo, 1% twice weekly for 4 weeks, with an exposure time of 3 minutes per application, resulted in detectable serum concentrations of ciclopirox in 6 out of 18 patients. The serum concentrations measured throughout the dosing interval on Days 1 and 29 ranged from 10.3 ng/mL to 13.2 ng/mL. Total urinary excretion of ciclopirox was less than 0.5% of the administered dose.

12.4 Microbiology

Ciclopirox is fungicidal *in vitro* against *Malassezia furfur* (*Pityrosporum* spp.), *P. ovale*, and *P. orbiculare*.

The clinical significance of antifungal activity in the treatment of seborrheic dermatitis is not known.

13 NONCLINICAL TOXICOLOGY

13.1 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/m^2/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 Fe^{3+}, 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 5,000 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 1.3 times the maximum recommended human dose based on body surface area comparisons).

14 CLINICAL STUDIES

In two randomized, double-blind clinical trials, subjects 16 years and older with seborrheic dermatitis of the scalp applied LOPROX Shampoo or its vehicle twice weekly for 4 weeks. Subjects who were immunocompromised, those with psoriasis or atopic dermatitis, women of childbearing potential not using adequate contraception, and pregnant or lactating women were excluded from the clinical trials. An evaluation of the overall status of the seborrheic dermatitis, the presence and severity of erythema or inflammation, and scaling was made at Week 4, using a scale of 0=none, 1=slight, 2=mild, 3=moderate, 4=pronounced, and 5=severe. Effective treatment was defined as achieving a score of 0 (or a score of 1 if the baseline score was ≥3) simultaneously for status of the seborrheic dermatitis, erythema or inflammation, and scaling at Week 4. Ciclopirox shampoo was shown to be statistically significantly more effective than vehicle in both trials. Efficacy results for the two trials are presented in Table 1 below.

Table 1. Effective Treatment Rates at Week 4 in Trials 1 and 2

	Ciclopirox Shampoo	**Vehicle**
Study 1	220/380 (58%)	60/192 (31%)
Study 2	65/250 (26%)	32/249 (13%)

Efficacy for African American subjects was not demonstrated, although only 53 African American subjects were enrolled in the two pivotal trials.

16 HOW SUPPLIED/STORAGE AND HANDLING

LOPROX (ciclopirox) Shampoo, 1% is colorless and translucent, and supplied in 120 mL plastic bottles (NDC 99207-010-10).

Discard unused product after initial treatment duration.

Store between 15° to 30°C (59° to 86°F).

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

The patient should be instructed to:

- Use LOPROX Shampoo as directed by the physician. Avoid contact with the eyes. If contact occurs, rinse thoroughly with water. LOPROX Shampoo is for external use on the scalp only. Do not swallow.
- Use LOPROX Shampoo for seborrheic dermatitis for the full treatment time even though symptoms may have improved. Notify the physician if there is no improvement after 4 weeks.
- Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, or oozing).

Manufactured for:
Bausch Health US, LLC
Bridgewater, NJ 08807 USA

Manufactured by:
Bausch Health Companies Inc.
Laval, Quebec H7L 4A8, Canada

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Patient Information
LOPROX® (loh-proks)
(ciclopirox)
Shampoo

Important: For use on the scalp only. Do not get LOPROX Shampoo in your eyes, mouth, or vagina.

What is LOPROX Shampoo?

LOPROX Shampoo is a prescription medicine used on the scalp to treat adults with a skin condition called seborrheic dermatitis.

It is not known if LOPROX Shampoo is safe and effective in children under 16 years of age.

What should I tell my doctor before using LOPROX Shampoo?

Before using LOPROX Shampoo, tell your doctor if you:

- have any other medical conditions.
- are pregnant or plan to become pregnant. It is not known if LOPROX Shampoo will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if LOPROX Shampoo passes into your breast milk.
- are taking prescription and nonprescription medicines, vitamins, and herbal supplements.

  Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I use LOPROX Shampoo?

- Use LOPROX Shampoo exactly as your doctor tells you to use it.

- Wash your hair using LOPROX Shampoo 2 times each week for 4 weeks. There should be at least 3 days between each time you use LOPROX Shampoo.
- Use LOPROX Shampoo for 4 weeks even if your skin condition improves.
- Tell your doctor if your scalp condition is not getting better after you have used LOPROX Shampoo for 4 weeks.
- Do not swallow LOPROX Shampoo.
- Avoid getting LOPROX Shampoo in your eyes. If LOPROX Shampoo gets into your eyes, rinse them well with water.

How should I apply LOPROX Shampoo?

- Wet your hair and apply approximately 1 teaspoon of LOPROX Shampoo to your scalp. You may use up to 2 teaspoons of LOPROX Shampoo if you have long hair. Lather and leave LOPROX Shampoo on your hair and scalp for 3 minutes. You may use a timer.
- After 3 minutes have passed, rinse your hair and scalp.

What are the possible side effects of LOPROX Shampoo?

The most common side effects of LOPROX Shampoo include: itching, burning, and redness of the scalp. Tell your doctor if you get any of these symptoms and they become worse or do not go away, or if you get blistering, swelling, or oozing in your scalp.

These are not all the possible side effects of LOPROX Shampoo. For more information, ask your doctor.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LOPROX Shampoo?

- Store LOPROX Shampoo at room temperature, between 59° to 86°F (15° to 30°C).
- Safely throw away any unused LOPROX Shampoo after you finish your treatment.

Keep LOPROX Shampoo and all medicines out of reach of children.

General information about LOPROX Shampoo

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LOPROX Shampoo for a condition for which it was not prescribed. Do not give LOPROX Shampoo to other people, even if they have the same symptoms you have. It may harm them.

You can ask your pharmacist or doctor for information about LOPROX Shampoo that is written for health professionals.

For more information about LOPROX Shampoo, call 1-800-321-4576.

What are the ingredients in LOPROX Shampoo?

Active ingredient: ciclopirox

Inactive ingredients: disodium laureth sulfosuccinate, laureth-2, purified water, sodium chloride, and sodium laureth sulfate.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Bausch Health US, LLC
Bridgewater, NJ 08807 USA

Manufactured by:

Bausch Health Companies Inc.
Laval, Quebec H7L 4A8, Canada

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Rev. 05/2019

PRINCIPAL DISPLAY PANEL - 120 mL Bottle Carton

NDC 99207-010-10

Rx only

LOPROX®
SHAMPOO
(ciclopirox) 1%

FOR TOPICAL USE ONLY
NOT FOR OPHTHALMIC, ORAL OR INTRAVAGINAL USE
KEEP OUT OF REACH OF CHILDREN

120 mL

Ortho Dermatologics

LOPROX

ciclopirox shampoo

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:99207-010
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ciclopirox (UNII: 19W019ZDRJ) (ciclopirox - UNII:19W019ZDRJ)	ciclopirox	10 mg in 0.96 mL

Inactive Ingredients	
Ingredient Name	Strength
disodium laureth sulfosuccinate (UNII: D6DH1DTN7E)	
laureth-2 (UNII: D4D38LT1L5)	
water (UNII: 059QF0KO0R)	
sodium chloride (UNII: 451W47IQ8X)	
sodium laureth-3 sulfate (UNII: BPV390UAP0)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:99207-010-10	1 in 1 CARTON	03/20/2003	
1		120 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		
2	NDC:99207-010-01	6 in 1 CARTON	03/20/2003	03/02/2018
2		10 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021159	03/20/2003	

Labeler - Bausch Health US, LLC (831922468)

Establishment

Name	Address	ID/FEI	Business Operations
Contract Pharmaceuticals Limited Canada		248761249	MANUFACTURE(99207-010)

Establishment

Name	Address	ID/FEI	Business Operations
Bausch Health Companies Inc.		245141858	MANUFACTURE(99207-010) , PACK(99207-010) , LABEL(99207-010)

Revised: 5/2019 Bausch Health US, LLC