LOPROX® (ciclopirox) shampoo, for topical use

Initial U.S. Approval: 1982

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

• 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)

Shampoo, 1% (3)

Dosage and Administration

Full Prescribing Information: Contents*

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17. Patient Counseling Information

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For reporting of 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: 05/2019

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)

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

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 for topical use only. Not for ophthalmic, oral, or intravaginal use.

Wet hair and apply approximately 1 teaspoon (5 mL) 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)

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.
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, laueth-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(1H)-pyridone, with the empirical formula C12H17NO2 and a molecular weight of 207.27. The CAS Registry Number is [29342-05-0]. The chemical structure is:


diagram of chemical structure

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 (Fe³⁺ or Al³⁺), 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.), C. 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/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 AS549 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>
<thead>
<tr>
<th>Study</th>
<th>Ciclopirox Shampoo</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>220/380 (58%)</td>
<td>60/192 (31%)</td>
</tr>
<tr>
<td>Study 2</td>
<td>65/250 (26%)</td>
<td>32/249 (13%)</td>
</tr>
</tbody>
</table>

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).

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).

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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.

**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:
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