

1 **HIGHLIGHTS OF PRESCRIBING INFORMATION**

2 These highlights do not include all the information needed to
3 use LOPROX® Shampoo safely and effectively. See full
4 prescribing information for LOPROX® Shampoo.

5 **LOPROX® (ciclopirox) Shampoo 1% for topical use**
6 **Initial U.S. Approval: 1982**

8 -----INDICATIONS AND USAGE-----

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

11 -----DOSAGE AND ADMINISTRATION-----

12 • Apply approximately 1 teaspoon of LOPROX Shampoo to
13 the scalp twice per week for 4 weeks. (2)

14 • For topical use only. Not for ophthalmic, oral, or
15 intravaginal use. (2)

16 -----DOSAGE FORM AND STRENGTHS-----

17 • Shampoo, 1% (3)

18 -----CONTRAINDICATIONS-----

19 None (4)

20 -----WARNINGS AND PRECAUTIONS-----

21 • If signs of irritation occur, discontinue use. (5.1)

22 • Avoid contact with eyes. (5.1)

23 • Hair discoloration has been reported with LOPROX use.
24 (5.1)

25 -----ADVERSE REACTIONS-----

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

28 **To report SUSPECTED ADVERSE REACTIONS, contact**
29 **Medicis, The Dermatology Company at 1-800-900-6389 or**
30 **FDA at 1-800-FDA-1088 or <http://www.fda.gov/medwatch>.**

31 **See 17 for PATIENT COUNSELING INFORMATION and**
32 **FDA-approved patient labeling**

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Revised: 11/2012

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

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATION AND USAGE**

3 LOPROX Shampoo is indicated for the topical treatment of seborrheic dermatitis of the scalp in adults.

4 **2 DOSAGE AND ADMINISTRATION**

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

6 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.
7 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
8 per week for 4 weeks, with a minimum of 3 days between applications.

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

11 **3 DOSAGE FORMS AND STRENGTHS**

12 Loprox is a shampoo containing 1% ciclopirox.

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

14 **4 CONTRAINDICATIONS**

15 None.

16 **5 WARNINGS AND PRECAUTIONS**

17 **5.1 Local Effects**

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

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

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

22 **6 ADVERSE REACTIONS**

23 **6.1 Clinical Trials Experience**

24 Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be
25 directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

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

28 **6.2 Post Marketing Experience**

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

32 **8 USE IN SPECIFIC POPULATIONS**

33 **8.1 Pregnancy**

34 Teratogenic Effects: Pregnancy Category B

35 There are no adequate or well-controlled studies in pregnant women. Therefore, LOPROX Shampoo should be used during pregnancy only if the
36 potential benefit justifies the potential risk to the fetus.

37 Oral embryofetal developmental studies were conducted in mice, rats, rabbits and monkeys. Ciclopirox or ciclopirox olamine was orally
38 administered during the period of organogenesis. No maternal toxicity, embryotoxicity or teratogenicity were noted at the highest doses of 77,
39 125, 80 and 38.5 mg/kg/day ciclopirox in mice, rats, rabbits and monkeys, respectively (approximately 13, 42, 54 and 26 times the maximum
40 recommended human dose based on body surface area comparisons, respectively).

41 Dermal embryofetal developmental studies were conducted in rats and rabbits with ciclopirox olamine dissolved in PEG 400. Ciclopirox olamine
42 was topically administered during the period of organogenesis. No maternal toxicity, embryotoxicity or teratogenicity were noted at the highest
43 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
44 human dose based on body surface area comparisons, respectively).

45 **8.3 Nursing Mothers**

46 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
47 LOPROX Shampoo is administered to a nursing woman.

48 **8.4 Pediatric Use**

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

50 **8.5 Geriatric Use**

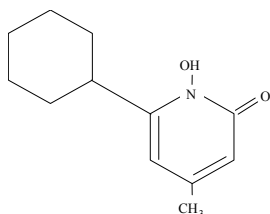
51 In clinical trials, the safety and tolerability of LOPROX Shampoo in the population 65 years and older was comparable to that of younger
52 subjects. Results of the efficacy analysis in those subjects 65 years and older showed effectiveness in 25 of 85 (29%) subjects treated with
53 LOPROX Shampoo, and in 15 of 61 (25%) subjects treated with the vehicle; due to the small sample size, a statistically significant difference
54 was not demonstrated. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects, but
55 greater sensitivity to adverse effects in some older individuals cannot be ruled out.

56 **11 DESCRIPTION**

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

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

60 LOPROX Shampoo is a colorless, translucent solution. The chemical name for ciclopirox is 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone,
61 with the empirical formula C₁₂H₁₇NO₂ and a molecular weight of 207.27. The CAS Registry Number is [29342-05-0]. The chemical structure is:
62



63

64 **12 CLINICAL PHARMACOLOGY**

65 **12.1 Mechanism of Action**

66 Ciclopirox is a hydroxypyridone antifungal agent although the relevance of this property for the indication of seborrheic dermatitis is not known.
67 Ciclopirox acts by chelation of polyvalent cations (Fe³⁺ or Al³⁺), resulting in the inhibition of the metal-dependent enzymes that are responsible
68 for the degradation of peroxides within the fungal cell.

69 **12.2 Pharmacodynamics**

70 The pharmacodynamics of LOPROX Shampoo are unknown.

71 **12.3 Pharmacokinetics**

72 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
73 exposure time of 3 minutes per application, resulted in detectable serum concentrations of ciclopirox in 6 out of 18 patients. The serum
74 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
75 ciclopirox was less than 0.5% of the administered dose.

76 **12.4 Microbiology**

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

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

79 **13 NONCLINICAL TOXICOLOGY**

80 **13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility**

81 Long-term animal studies have not been performed to evaluate the carcinogenic potential of LOPROX Shampoo or ciclopirox.

82 The following *in vitro* genotoxicity tests have been conducted with ciclopirox: evaluation of gene mutation in the Ames *Salmonella* and *E. coli*
83 assays (negative); chromosome aberration assays in V79 Chinese hamster lung fibroblast cells, with and without metabolic activation (positive);
84 chromosome aberration assays in V79 Chinese hamster lung fibroblast cells in the presence of supplemental Fe³⁺, with and without metabolic
85 activation (negative); gene mutation assays in the HGPRT-test with V79 Chinese hamster lung fibroblast cells (negative); and a primary DNA
86 damage assay (i.e., unscheduled DNA synthesis assay in A549 human cells) (negative). An *in vitro* cell transformation assay in BALB/c 3T3
87 cells was negative for cell transformation. In an *in vivo* Chinese hamster bone marrow cytogenetic assay, ciclopirox was negative for
88 chromosome aberrations at a dosage of 5000 mg/kg body weight.

89 A combined oral fertility and embryofetal developmental study was conducted in rats with ciclopirox olamine. No effect on fertility or
90 reproductive performance was noted at the highest dose tested of 3.85 mg/kg/day ciclopirox (approximately 1.3 times the maximum
91 recommended human dose based on body surface area comparisons).

92 **14 CLINICAL STUDIES**

93 In two randomized, double-blind clinical trials, subjects 16 years and older with seborrheic dermatitis of the scalp applied LOPROX Shampoo or
94 its vehicle twice weekly for 4 weeks. Subjects who were immunocompromised, those with psoriasis or atopic dermatitis, women of childbearing
95 potential not using adequate contraception, and pregnant or lactating women were excluded from the clinical trials. An evaluation of the overall
96 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 =
97 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
98 1 if the baseline score was ≥ 3) simultaneously for status of the seborrheic dermatitis, erythema or inflammation, and scaling at Week 4.
99 Ciclopirox shampoo was shown to be statistically significantly more effective than vehicle in both trials. Efficacy results for the two trials are
100 presented in Table 1 below.

101 **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%)

102

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

104 **16 HOW SUPPLIED/STORAGE AND HANDLING**

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

106 Discard unused product after initial treatment duration.

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

108 Keep out of reach of children.

1 **17 PATIENT COUNSELING INFORMATION**

2 See FDA-approved patient labeling (Patient Information)

3 The patient should be instructed to:

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

14 **Patient Information**
15 **LOPROX® (loh-proks)**
16 **(ciclopirox)**
17 **Shampoo**

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

18

19 **What is LOPROX Shampoo?**

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

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

24 **What should I tell my doctor before using LOPROX Shampoo?**

25 **Before using LOPROX Shampoo, tell your doctor if you:**

- 26 • have any other medical conditions
- 27 • are pregnant or plan to become pregnant. It is not known if LOPROX Shampoo
28 will harm your unborn baby.
- 29 • are breastfeeding or plan to breastfeed. It is not know if LOPROX Shampoo
30 passes into your breast milk.
- 31 • are taking prescription and non-prescription medicines, vitamins, and herbal
32 supplements.

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

35 **How should I use LOPROX Shampoo?**

- 36 • Use LOPROX Shampoo exactly as your doctor tells you to use it.
- 37 • Wash your hair using LOPROX Shampoo 2 times each week for 4 weeks. There
38 should be at least 3 days between each time you use LOPROX Shampoo.
- 39 • Use LOPROX Shampoo for 4 weeks even if your skin condition improves.
- 40 • Tell your doctor if your scalp condition is not getting better after you have used
41 LOPROX Shampoo for 4 weeks.
- 42 • Do not swallow LOPROX Shampoo.
- 43 • Avoid getting LOPROX Shampoo in your eyes. If you LOPROX Shampoo gets
44 into your eyes, rinse them well with water.

45 **How should I apply LOPROX Shampoo**

- 46 • Wet your hair and apply approximately 1 teaspoon of LOPROX Shampoo to your
47 scalp. You may use up to 2 teaspoons of LOPROX Shampoo if you have long

48 hair. Lather and leave LOPROX Shampoo on your hair and scalp for 3 minutes.
49 You may use a timer.

- 50 • After 3 minutes have passed, rinse your hair and scalp.

51 **What are the possible side effects of LOPROX Shampoo?**

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

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

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

60 **How should I store LOPROX Shampoo?**

- 61 • Store LOPROX Shampoo at room temperature, between 59°F to 86°F (15°C to
62 30°C).
- 63 • Safely throw away any unused LOPROX Shampoo after you finish your
64 treatment.

65 **Keep LOPROX Shampoo and all medicines out of the reach of children.**

66 **General information about LOPROX Shampoo**

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

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

73 For more information about LOPROX Shampoo, call 1-800-550-5115.

74 **What are the ingredients in LOPROX Shampoo?**

75 **Active ingredient:** ciclopirox

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

78 Manufactured for: Medicis, The Dermatology Company, Scottsdale, AZ 85256

79 Manufactured by: Contract Pharmaceutical Limited, Mississauga, Ontario L5N 6L6

80 This Patient Information has been approved by the U.S. Food and Drug
81 Administration. ~~Issued: 11/2012~~

82 Product of Italy

83 U.S. Patent 7,981,909 and Patents Pending

84 LOPROX Shampoo is a registered trademark of Medicis Pharmaceutical Corporation.