

OXISTAT- oxiconazole nitrate lotion
ANI Pharmaceuticals, Inc.

OXISTAT® (oxiconazole nitrate) Lotion, 1%*

***Potency expressed as oxiconazole**

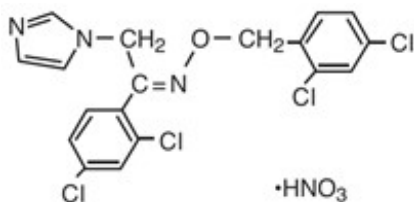
Rx only

**FOR TOPICAL DERMATOLOGIC USE ONLY—
NOT FOR ORAL, OPHTHALMIC OR INTRAVAGINAL USE**

DESCRIPTION

OXISTAT® (oxiconazole nitrate) Lotion, 1% contains the antifungal active compound oxiconazole nitrate. This formulation is for topical dermatologic use only.

Chemically, oxiconazole nitrate is 2',4'-dichloro-2-imidazol-1-ylacetophenone (Z)-[O-(2,4-dichlorobenzyl)oxime], mononitrate. The compound has the molecular formula $C_{18}H_{13}ON_3Cl_4 \cdot HNO_3$, a molecular weight of 492.15, and the following structural formula:



Oxiconazole nitrate is a nearly white crystalline powder, soluble in methanol; sparingly soluble in ethanol, chloroform, and acetone; and very slightly soluble in water.

OXISTAT Lotion contains 10 mg of oxiconazole per gram of lotion in a white to off-white, opaque lotion base of purified water, white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60, cetyl alcohol, and benzoic acid 0.2% as a preservative.

CLINICAL PHARMACOLOGY

Pharmacokinetics

The penetration of oxiconazole nitrate into different layers of the skin was assessed using an in vitro permeation technique with human skin. Five hours after application of 2.5 mg/cm^2 of oxiconazole nitrate cream onto human skin, the concentration of oxiconazole nitrate was demonstrated to be $16.2 \text{ } \mu\text{mol}$ in the epidermis, $3.64 \text{ } \mu\text{mol}$ in the upper corium, and $1.29 \text{ } \mu\text{mol}$ in the deeper corium. Systemic absorption of oxiconazole nitrate is low. Using radiolabeled drug, less than 0.3% of the applied dose of oxiconazole nitrate was recovered in the urine of volunteer subjects up to 5 days after application of

the cream formulation.

Neither in vitro nor in vivo studies have been conducted to establish relative activity between the lotion and cream formulations.

Microbiology

Oxiconazole nitrate is an imidazole derivative whose antifungal activity is derived primarily from the inhibition of ergosterol biosynthesis, which is critical for cellular membrane integrity. It has in vitro activity against a wide range of pathogenic fungi.

Oxiconazole has been shown to be active against most strains of the following organisms both in vitro and in clinical infections at indicated body sites (see INDICATIONS AND USAGE):

Epidermophyton floccosum
Trichophyton mentagrophytes
Trichophyton rubrum
Malassezia furfur

The following in vitro data are available; however, their clinical significance is unknown. Oxiconazole exhibits satisfactory in vitro minimum inhibitory concentrations (MICs) against most strains of the following organisms; however, the safety and efficacy of oxiconazole in treating clinical infections due to these organisms have not been established in adequate and well-controlled clinical trials:

Candida albicans
Microsporum audouini
Microsporum canis
Microsporum gypseum
Trichophyton tonsurans
Trichophyton violaceum

INDICATIONS AND USAGE

OXISTAT Lotion is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, or *Epidermophyton floccosum* (see DOSAGE AND ADMINISTRATION and CLINICAL STUDIES).

CONTRAINDICATIONS

OXISTAT Lotion is contraindicated in individuals who have shown hypersensitivity to any of their components.

WARNINGS

OXISTAT (oxiconazole nitrate) Lotion, 1% is for topical use only and not for oral, ophthalmic or intravaginal use.

PRECAUTIONS

General

OXISTAT Lotion is for external dermal use only. Avoid introduction of OXISTAT Lotion into the mouth, eyes, or vagina. If a reaction suggesting sensitivity or chemical irritation should occur with the use of OXISTAT Lotion, treatment should be discontinued and appropriate therapy instituted. If signs of epidermal irritation should occur, the drug should be discontinued.

Information for Patients

The patient should be instructed to:

1. Use OXISTAT as directed by the physician. The hands should be washed after applying the medication to the affected area(s). Avoid contact with the eyes, nose, mouth, and other mucous membranes. OXISTAT is for external use only.
2. Use the medication for the **full** treatment time recommended by the physician, even though symptoms may have improved. Notify the physician if there is no improvement after 2 to 4 weeks, or sooner if the condition worsens (see below).
3. Inform the physician if the area of application shows signs of increased irritation, itching, burning, blistering, swelling, or oozing.
4. Avoid the use of occlusive dressings unless otherwise directed by the physician.
5. Do not use this medication for any disorder other than that for which it was prescribed.

Drug Interactions

Potential drug interactions between OXISTAT and other drugs have not been systematically evaluated.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no evidence of mutagenic effect was found in 2 mutation assays (Ames test and Chinese hamster V79 in vitro cell mutation assay) or in 2 cytogenetic assays (human peripheral blood lymphocyte in vitro chromosome aberration assay and in vivo micronucleus assay in mice).

Reproductive studies revealed no impairment of fertility in rats at oral doses of 3 mg/kg/day in females (1 time the human dose based on mg/m²) and 15 mg/kg/day in males (4 times the human dose based on mg/m²). However, at doses above this level, the following effects were observed: a reduction in the fertility parameters of males and females, a reduction in the number of sperm in vaginal smears, extended estrous cycle, and a decrease in mating frequency.

Pregnancy

Teratogenic Effects

Reproduction studies have been performed in rabbits, rats, and mice at oral doses up to 100, 150, and 200 mg/kg/day (57, 40, and 27 times the human dose based on mg/m²), respectively, and revealed no evidence of harm to the fetus due to oxiconazole nitrate. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this

drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Because oxiconazole is excreted in human milk, caution should be exercised when the drug is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

A limited number of patients at or above 60 years of age (n ~ 396) have been treated with oxiconazole nitrate cream in US and non-US clinical trials, and a limited number (n = 43) have been treated with OXISTAT Lotion in US clinical trials. The number of patients is too small to permit separate analysis of efficacy and safety. No adverse events were reported with OXISTAT Lotion in geriatric patients, and the adverse reactions reported with oxiconazole nitrate cream in this population were similar to those reported by younger patients. Based on available data, no adjustment of dosage of OXISTAT Lotion in geriatric patients is warranted.

ADVERSE REACTIONS

In a controlled, multicenter clinical trial of 269 patients treated with oxiconazole nitrate lotion, 1%, 7 (2.6%) reported adverse reactions thought to be related to drug therapy. These reactions included burning and stinging (0.7% each) and pruritus, scaling, tingling, pain, and dyshidrotic eczema (0.4% each).

The following additional adverse experiences have been reported with the topical use of oxiconazole nitrate: irritation and allergic contact dermatitis, folliculitis, erythema, papules, fissure, maceration, rash, and nodules.

To report SUSPECTED ADVERSE REACTIONS, contact ANI Pharmaceuticals, Inc. at 1-800-308-6755 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

When 5% oxiconazole cream (5 times the concentration of the marketed product) was applied at a rate of 1 g/kg to approximately 10% of body surface area of a group of 40 male and female rats for 35 days, 3 deaths and severe dermal inflammation were reported. No overdoses in humans have been reported with use of oxiconazole nitrate cream or lotion.

DOSAGE AND ADMINISTRATION

OXISTAT Lotion should be applied to affected and immediately surrounding areas once to twice daily in patients with tinea pedis, tinea corporis, or tinea cruris. Tinea corporis and tinea cruris should be treated for 2 weeks and tinea pedis for 1 month to reduce the possibility of recurrence. If a patient shows no clinical improvement after the treatment period, the diagnosis should be reviewed.

CLINICAL STUDIES

The following definitions were applied to the clinical and microbiological outcomes in patients enrolled in the clinical trial that form the basis for the approval of OXISTAT Lotion.

Definitions

1. Mycological Cure: No evidence (culture and KOH preparation) of the baseline (original) pathogen in a specimen from the affected area taken at the 2-week post-treatment visit (for tinea [pityriasis] versicolor, mycological cure was limited to KOH only).
2. Treatment Success: Both a global evaluation of 90% clinical improvement and a microbiologic eradication (see above) at the 2-week post-treatment visit.

Tinea Pedis

The clinical trial for the lotion formulation line extension involved 332 evaluable patients with clinically and microbiologically established tinea pedis. Of these evaluable patients, 64% were diagnosed with hyperkeratotic plantar tinea pedis and 28% with interdigital tinea pedis. Seventy-seven percent (77%) had disease secondary to infection with *Trichophyton rubrum*, 18% had disease secondary to infection with *Trichophyton mentagrophytes*, and 4% had disease secondary to infection with *Epidermophyton floccosum*.

The results of this clinical trial at the 2-week post-treatment follow-up visit are shown in the following table:

Patient Outcome	OXISTAT Lotion		Vehicle
	b.i.d.	q.d.	
Mycological cure	67%	64%	28%
Treatment success	41%	34%	10%

In this study, the improvement and cure rates of the b.i.d.- and q.d.-treated groups did not differ significantly (95% confidence interval) from each other but were statistically (95% confidence interval) superior to the vehicle-treated group.

HOW SUPPLIED

OXISTAT® (oxiconazole nitrate) Lotion, 1% is supplied in:

30-mL bottle (NDC 62559-285-30)

60-mL bottle (NDC 62559-285-60)

Store at 20° to 25°C (68° to 77°F); excursions permitted at 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Shake well before using.

OXISTAT is a registered trademark of Fougera Pharmaceuticals, Inc. and is licensed to ANI Pharmaceuticals, Inc.

Distributed by:
ANI Pharmaceuticals, Inc.
Baudette, MN 56623



N7000 Rev 05/22

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 62559-285-30

OXISTAT® (oxiconazole nitrate) Lotion, 1%*

*Potency expressed as oxiconazole.

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Rx only

30 mL

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(oxiconazole nitrate)
Lotion
1%*
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OXISTAT®
(oxiconazole nitrate)
Lotion

1%*

*Potency expressed
as oxiconazole.

Rx only



30 mL



GTIN: 00362559000000
SN: A123456789
EXP: MMM YYYY
LOT: A12345



**For Topical
Dermatologic
Use ONLY.**

Not for Oral, Ophthalmic
or Intravaginal Use.

See package insert for
full prescribing information.

Store at 20° to 25°C (68°
to 77°F); excursions
permitted at 15° to 30°C
(59° to 86°F) [see USP
Controlled Room
Temperature].

Shake well before using.

**KEEP OUT OF THE
REACH OF CHILDREN.**

Contains:

Oxiconazole 1%* as
oxiconazole nitrate in a
lotion base composed
of purified water,
white petrolatum,
stearyl alcohol,
propylene glycol,
polysorbate 60, cetyl
alcohol, and benzoic
acid 0.2% as a
preservative.

*Potency expressed as
oxiconazole.

OXISTAT is a registered
trademark of Fougera
Pharmaceuticals, Inc.
and is licensed to
ANI Pharmaceuticals, Inc.

Distributed by:
ANI Pharmaceuticals, Inc.
Baudette, MN 56623

C7030 Rev 05/22

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R05/2022
#270

NDC 62559-285-30

OXISTAT®
(oxiconazole nitrate)
Lotion

1%*

*Potency expressed
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30 mL



OXISTAT

oxiconazole nitrate lotion

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:62559-285
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
oxiconazole nitrate (UNII: RQ8UL4C175) (oxiconazole - UNII:C668Q9I33J)	oxiconazole	10 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
water (UNII: 059QF0KO0R)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
propylene glycol (UNII: 6DC9Q167V3)	
polysorbate 60 (UNII: CAL22UVI4M)	
cetyl alcohol (UNII: 936JST6JCN)	
benzoic acid (UNII: 8SKN0B0MIM)	
WHITE PETROLATUM (UNII: B6E5W8RQJ4)	

Product Characteristics

Color	WHITE (White to off-white)	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62559-285-30	1 in 1 CARTON	09/12/2022	
1		30 mL in 1 BOTTLE; Type 0: Not a Combination Product		
2	NDC:62559-285-60	1 in 1 CARTON	09/12/2022	
2		60 mL in 1 BOTTLE; Type 0: Not a Combination Product		
3	NDC:62559-285-06	6 in 1 CARTON	09/12/2022	
3		7 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing	Application Number or Monograph	Marketing Start	Marketing End

Category	Citation	Date	Date
NDA	NDA020209	09/12/2022	

Labeler - ANI Pharmaceuticals, Inc. (145588013)

Revised: 8/2022

ANI Pharmaceuticals, Inc.