HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ECOZA safely and effectively. See full prescribing information for ECOZA.

ECOZA® (econazole nitrate) topical foam
Initial U.S. Approval: 1982

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

Ecoza is an azole antifungal indicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum* in patients 12 years of age and older. (1)

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

- For topical use only; not for oral, ophthalmic, or intravaginal use. (2)
- Apply once daily for 4 weeks. (2)

----------DOSAGE FORMS AND STRENGTHS----------

Topical foam, 1%. (3)

----------CONTRAINDICATIONS----------

None. (4)

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

Contents are flammable. Instruct the patient to avoid heat, flame, and/or smoking during and immediately following application. (5.1)

----------ADVERSE REACTIONS----------

The most common adverse reactions were application site reactions which occurred in less than 1% of subjects in both the Ecoza and vehicle arms. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Glenmark Therapeutics Inc., at 1-888-721-7115 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised 11/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ecoza isindicated for the treatment of interdigital tinea pedis caused by *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum* in patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

Ecoza is for topical use only. It is not for oral, ophthalmic, or intravaginal use.

Ecoza should be applied to cover affected areas once daily for 4 weeks.

3 DOSAGE FORMS AND STRENGTHS

Topical foam, 1%. Each gram contains 10 mg of econazole nitrate in a white to off-white foam.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Flammability

Ecoza is flammable. Avoid heat, flame, and smoking during and immediately following application. Contents under pressure. Do not puncture and/or incinerate the containers. Do not expose containers to heat and/or store at temperatures above 120°F (49°C) even when empty. Do not store in direct sunlight.

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 practice.

In two double-blind, vehicle-controlled clinical trials, 495 subjects with interdigital tinea pedis applied Ecoza or vehicle once daily for approximately 28 days (246 subjects were exposed to Ecoza and 249 were exposed to vehicle). During clinical trials with Ecoza, the most common adverse reactions were application site reactions which occurred in less than 1% of subjects in both the Ecoza and vehicle arms.

7 DRUG INTERACTIONS

7.1 Warfarin

Concomitant administration of econazole and warfarin has resulted in enhancement of anticoagulant effect. Most cases reported product application with use under occlusion, genital application, or application to a large body surface area which may increase the systemic absorption of econazole nitrate. Monitoring of International Normalized Ratio (INR) and/or prothrombin time may be indicated especially for patients who apply econazole to large body surface areas, in the genital area, or under occlusion.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Ecoza use in pregnant women to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

In animal reproduction studies, econazole nitrate did not cause malformation in mice, rabbits and/or rats at oral doses 80 or 40 times the human dermal dose *(see Data)*.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

Econazole nitrate did not cause malformation in mice, rabbits and/or rats. Fetotoxic or embryotoxic effects were observed in oral fertility studies in rats receiving 10 to 40 times the human dermal dose. Similar effects were observed in embryofetal and pre- and postnatal developmental studies in mice, rabbits and/or rats receiving oral doses 80 or 40 times the human dermal dose.

8.2 Lactation

Risk Summary

There is no information available on the presence of econazole nitrate in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production after topical application of Ecoza to women who are breastfeeding. It is not known whether econazole nitrate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when econazole nitrate is administered to a nursing woman. Following oral administration of econazole nitrate to lactating rats, econazole and/or metabolites were excreted in milk and were found in nursing pups.

The lack of clinical data during lactation precludes a clear determination of the risk Ecoza to an infant during lactation. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Ecoza and any potential adverse effects on the breastfed infant from Ecoza or from the underlying maternal condition.

8.4 Pediatric Use

Of the 173 subjects treated with Ecoza in the clinical trials, 2 subjects were 12-17 years old. In a pediatric maximal use trial, Ecoza was applied once daily to eighteen subjects aged 12 to 17 years with interdigital tinea pedis for 28 days [*see Clinical Pharmacology (12.3)*]. The safety findings for subjects 12 to 17 years were similar to those in adult population.

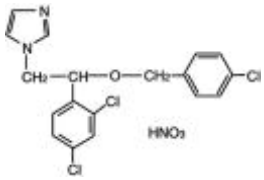
8.5 Geriatric Use

Of the 173 subjects treated with Ecoza in the adult clinical trials, 6 subjects were 65 years or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

11 DESCRIPTION

Ecoza (econazole nitrate) topical foam, 1% contains the azole antifungal agent, econazole nitrate in an oil-in-water emulsion base. Each gram of Ecoza topical foam, 1% contains 10 mg of econazole nitrate, USP, in a white to off-white foam. Ecoza topical foam, 1% is alcohol (ethanol)-free and for topical use only.

Chemically, econazole nitrate is 1-[2-{(4-chloro-phenyl)methoxy}-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole mononitrate. Econazole nitrate has the molecular formula $C_{18}H_{15}Cl_3N_2O.HNO_3$ and a molecular weight of 444.70. Its molecular structure is as follows:



Ecoza (econazole nitrate) topical foam contains the following inactive ingredients: dimethicone, glycerin, polysorbate 20, povidone, propylene glycol, stearic acid, trolamine, purified water and butane as a propellant.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ecoza is an azole antifungal [*see Clinical Pharmacology (12.4)*].

12.2 Pharmacodynamics

The pharmacodynamics of Ecoza have not been established**.**

12.3 Pharmacokinetics

The systemic absorption of Ecoza following topical application was studied in one clinical trial in adults and one clinical study in pediatric subjects.

In the adult trial, 19 subjects (male and female) with tinea pedis applied Ecoza once daily for 29 days. Subjects applied a mean daily amount of 2.4 g of Ecoza to soles, toes, interdigital spaces and tops of both feet up to the ankles. Blood samples were obtained on Day 29 at pre-dose and 1, 2, 4, 6, 8, and 12 hours after application. Results (mean ± SD) showed the time to reach peak plasma concentrations (T_{max}) was 6.8 ± 5.1 h with maximum concentration (C_{max}) of 417 ± 218 pg/ml. The area under the concentration time curve for the first 12 hours post application on Day 29 ($AUC_{(0-12)}$) was 3440 ± 1920 pg-h/ml.

In the pediatric trial, 18 subjects (male and female ages 12 - 17) with interdigital tinea pedis and positive fungal cultures were treated with Ecoza once daily for 4 weeks. Subjects applied a mean daily amount of 3.2 g of Ecoza to soles, toes, interdigital spaces and tops of both feet up to the ankles. Blood samples were obtained on Day 28 at pre-dose and 7 h and 11 h post-dose. The mean ± SD econazole plasma concentration was 397 ± 289, 534 ± 745 and 575 ± 638 pg/mL at pre-dose and 7 h and 11 h post-dose, respectively.

Drug Interaction Studies

Ecoza is not expected to inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, and 3A4, or induce CYP1A2, 2B6, and 3A4.

12.4 Microbiology

Mechanism of Action

Econazole nitrate, an azole antifungal agent, inhibits fungal cytochrome P-450-mediated 14 alpha-lanosterol demethylase enzyme. This enzyme functions to convert lanosterol to ergosterol. The accumulation of 14 alpha-methyl sterols correlates with the subsequent loss of ergosterol in the fungal cell wall and may be responsible for the fungistatic activity of econazole. Mammalian cell demethylation is less sensitive to econazole inhibition.

Activity in vitro and in clinical infections

Econazole nitrate has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections [*see Indications and Usage (1)*].

Trichophyton rubrum
Epidermophyton floccosum

Trichophyton mentagrophytes

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies to determine the carcinogenic potential of Ecoza have not been performed.

Oral administration of econazole nitrate in rats has been reported to produce prolonged gestation.

14 CLINICAL STUDIES

In two multi-center, randomized, double-blind, vehicle-controlled clinical trials a total of 505 subjects with interdigital tinea pedis were randomized 1:1 to Ecoza or vehicle; subjects applied the assigned medication once daily for 4 weeks. The severity of erythema, scaling, fissuring, maceration, vesiculation, and pruritus were graded using a 4-point scale (none, mild, moderate, severe). Subjects had KOH examination and fungal cultures taken to confirm eligibility. A total of 339 subjects with positive fungal cultures were evaluated for efficacy. Efficacy was evaluated on Day 43, 2 weeks post-treatment with treatment success being defined as complete cure (negative KOH and fungal culture and no evidence of clinical disease). The study population ranged in age from 12 to 71 years with 3 subjects less than 18 years of age at baseline. The subjects were 71% male and 52% Caucasian. Table 1 presents the efficacy results for each trial.

Table 1: Efficacy Results at Two Weeks Post-treatment (Day 43)
Complete Cure, Effective Treatment and Mycological Cure

	Study 1		Study 2	
	Ecoza N = 82 n(%)	**Foam Vehicle N = 83 n(%)**	**Ecoza N = 91 n(%)**	**Foam Vehicle N = 83 n(%)**
Complete cure[a]	19 (23.2%)	2 (2.4%)	23 (25.3%)	4 (4.8%)
Effective treatment[b]	40 (48.8%)	9 (10.8%)	44 (48.4%)	9 (10.8%)
Mycological cure[c]	56 (68.3%)	13 (15.7%)	61 (67.0%)	15 (18.1%)

[a]Mycological cure and an absence of clinical signs and symptoms (erythema, scaling, fissuring, maceration, vesiculation, or pruritus).
[b]Mycological cure and no or mild erythema and/or scaling with all other signs and symptoms absent.
[c]Negative KOH and fungal culture.

16 HOW SUPPLIED/ STORAGE AND HANDLING

Ecoza topical foam, 1% is white to off-white foam supplied in 70 g (NDC 72657-0200-70) aluminum pressurized canister.

Store at controlled room temperature 20°C to 25°C (68°F to 77°F) with excursions permitted between 15°C and 30°C (59°F and 86°F). Do not refrigerate or freeze.

Ecoza topical foam is flammable. Avoid heat, flame, and smoking during and immediately following application.

Contents under pressure. Do not puncture and/or incinerate the containers.

Do not expose containers to heat and/or store at temperatures above 120°F (49°C) even when empty.

Do not store in direct sunlight.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)

The patient should be instructed as follows:

- Inform patients that Ecoza is for topical use only. Ecoza is not intended for oral, intravaginal, or ophthalmic use.
- Ecoza is flammable; avoid heat, flame, and smoking during and immediately following application.
- If a reaction suggesting sensitivity or chemical irritation develops with the use of Ecoza use of the medication should be discontinued.

Marketed by:
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