HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Extina® (ketoconazole) Foam, 2%
For topical use only
Initial U.S. Approval: 1981

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

Extina Foam is indicated for topical treatment of seborrheic dermatitis in immunocompetent patients 12 years of age and older (1).

Safety and efficacy of Extina Foam for treatment of fungal infections have not been established.

---DOSAGE AND ADMINISTRATION---

- Extina Foam should be applied to the affected area(s) twice daily for four weeks (2).
- Extina Foam is not for ophthalmic, oral, or intravaginal use (2).

-DOSAGE FORMS AND STRENGTHS-

Extina Foam contains 2% ketoconazole in a thermolabile hydroethanolic foam in 50 g and 100 g containers (3).

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

None

---WARNINGS AND PRECAUTIONS----

- Extina Foam may result in contact sensitization, including photoallergenicity (5.1, 6.2).
- The contents of Extina Foam are flammable (5.2).

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

The most common adverse reactions observed in clinical studies (incidence >1%) were application site burning and application site reaction (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Stiefel Laboratories, Inc. at 1-888-500-DERM or adverse.event@stiefel.com and FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-APPROVED PATIENT LABELING.

Revised: 06/2007

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Extina® (ketoconazole) Foam, 2% is indicated for the topical treatment of seborrheic dermatitis in immunocompetent patients 12 years of age and older. Safety and efficacy of Extina Foam for treatment of fungal infections have not been established.

2 DOSAGE AND ADMINISTRATION

Extina Foam should be applied to the affected area(s) twice daily for four weeks.

Hold the container upright, and dispense Extina Foam into the cap of the can or other cool surface in an amount sufficient to cover the affected area(s). Dispensing directly onto hands is not recommended, as the foam will begin to melt immediately upon contact with warm skin. Pick up small amounts of Extina Foam with the fingertips, and gently massage into the affected area(s) until the foam disappears. For hair-bearing areas, part the hair, so that Extina Foam may be applied directly to the skin (rather than on the hair).

Avoid contact with the eyes and other mucous membranes. Extina Foam is not for ophthalmic, oral or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Extina Foam contains 2% ketoconazole in a thermolabile hydroethanolic foam, and is provided in 50 g and 100 g aluminum containers.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Contact Sensitization

Extina Foam may result in contact sensitization, including photoallergenicity. *[See Adverse Reactions (6.2)]*

5.2 Flammable Contents

The contents of Extina Foam include alcohol and propane/butane, which are flammable. Avoid fire, flame and/or smoking during and immediately following application. Do not puncture and/or incinerate the containers. Do not expose containers to heat and/or store at temperatures above 120°F (49°C).

5.3 Systemic Effects

Hepatitis has been seen with orally administered ketoconazole (1:10,000 reported incidence). Lowered testosterone and ACTH–induced corticosteroid serum levels have been seen with high doses of orally administered ketoconazole. These effects have not been seen with topical ketoconazole.

Extina® (ketoconazole) Foam, 2%

6 ADVERSE REACTIONS

6.1 Adverse Reactions in Clinical Trials

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. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse reactions that appear to be related to drug use and for approximating rates.

The safety data presented in Table 1 (below) reflect exposure to Extina Foam in 672 subjects, 12 years and older with seborrheic dermatitis. Subjects applied Extina Foam or vehicle foam twice daily for 4 weeks to affected areas on the face, scalp, and/or chest. Adverse reactions occurring in > 1% of subjects are presented in Table 1.

Table 1: Adverse Reactions Reported by > 1% Subjects in Clinical Trials

Adverse Reactions	Extina Foam N = 672 n (%)	Vehicle Foam N = 497 n (%)
Subjects with an Adverse Reaction	**188 (28%)**	**122 (25%)**
Application site burning	67 (10%)	49 (10%)
Application site reaction	41 (6%)	24 (5%)

Application site reactions that were reported in ≤ 1% of subjects were dryness, erythema, irritation, paresthesia, pruritus, rash and warmth.

6.2 Dermal Safety Studies

In a photoallergenicity study, 9 of 53 subjects (17%) had reactions during the challenge period at both the irradiated and non-irradiated sites treated with Extina Foam. Extina Foam may cause contact sensitization.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects, Pregnancy Category C: Ketoconazole has been shown to be teratogenic (syndactylia and oligodactylia) in the rat when given orally in the diet at 80 mg/kg/day (4.8 times the maximum expected human topical dose based on a mg/m^2 comparison, assuming 100% absorption from 8 g of foam). However, these effects may be partly related to maternal toxicity, which was also observed at this dose level. *[See Pharmacokinetics (12.3)]*

No reproductive studies in animals have been performed with Extina Foam. There are no adequate and well-controlled studies of Extina Foam in pregnant women.

Extina Foam should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Extina® (ketoconazole) Foam, 2%

8.3 Nursing Mothers

It is not known whether Extina Foam administered topically could result in sufficient systemic absorption to produce detectable quantities in breast milk. Because many drugs are excreted in human milk, caution should be exercised when Extina Foam is administered to women who are breastfeeding.

8.4 Pediatric Use

The safety and effectiveness of Extina Foam in pediatric patients less than 12 years of age have not been established.

Of the 672 subjects treated with Extina Foam in the clinical trials, 44 (7%) were from 12 to 17 years of age. ***[See Clinical Studies (14)]***

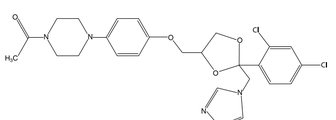
8.5 Geriatric Use

Of the 672 subjects treated with Extina Foam in the clinical trials, 107 (16%) were 65 years and over.

11 DESCRIPTION

Extina Foam contains 2% ketoconazole USP, an antifungal agent, in a thermolabile hydroethanolic foam for topical application.

The chemical name for ketoconazole is piperazine, 1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, *cis*- with the molecular formula $C_{26}H_{28}Cl_2N_4O_4$ and a molecular weight of 531.43. The following is the chemical structure:



Extina® (ketoconazole) Foam, 2%

Extina Foam contains 20 mg ketoconazole USP per gram in a thermolabile hydroethanolic foam vehicle consisting of cetyl alcohol NF, citric acid USP, ethanol (denatured with *tert*-butyl alcohol and brucine sulfate) 58%, polysorbate 60 NF, potassium citrate USP, propylene glycol USP, purified water USP, and stearyl alcohol NF pressurized with a hydrocarbon (propane/butane) propellant.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of ketoconazole in the treatment of seborrheic dermatitis is not known.

12.2 Pharmacodynamics

The pharmacodynamics of Extina Foam has not been established.

12.3 Pharmacokinetics

In a bioavailability study, 12 subjects with moderate to severe seborrheic dermatitis applied 3 g of Extina Foam twice daily for 4 weeks. Circulating plasma levels of ketoconazole were < 6 ng/mL for a majority of subjects (75%), with a maximum level of 11 ng/mL observed in one subject.

12.4 Microbiology

Ketoconazole is an antifungal agent which inhibits the *in vitro* synthesis of ergosterol, a key sterol in the cell membrane of *Malassezia furfur*. The clinical significance of antifungal activity in the treatment of seborrheic dermatitis is not known.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic or photo-carcinogenic potential of Extina Foam.

In oral carcinogenicity studies in mice (18-months) and rats (24-months) at dose levels of 5, 20 and 80 mg/kg/day ketoconazole was not carcinogenic. The high dose in these studies was approximately 2.4 to 4.8 times the expected topical dose in humans based on a mg/m^2 comparison. In a bacterial reverse mutation assay, ketoconazole did not express any mutagenic potential. In three *in vivo* assays (sister chromatid exchange in humans, dominant lethal and micronucleus tests in mice), ketoconazole did not exhibit any genotoxic potential.

At oral dose levels of 75 mg/kg/day (4.5 times the expected topical human dose in mg/m^2), ketoconazole impaired reproductive performance and fertility when administered to male rats (increased abnormal sperm, decreased sperm mobility and decreased pregnancy in mated females).

FPO
Pharma Code

extina® (ketoconazole) Foam, 2%

14 CLINICAL STUDIES

The safety and efficacy of Extina Foam were evaluated in a randomized, double-blind, vehicle-controlled study in subjects 12 years and older with mild to severe seborrheic dermatitis. In the study, 427 subjects received Extina Foam and 420 subjects received vehicle foam. Subjects applied Extina Foam or vehicle foam twice daily for 4 weeks to affected areas on the face, scalp, and/or chest. The overall disease severity in terms of erythema, scaling, and induration was assessed at Baseline and week 4 on a 5-point Investigator's Static Global Assessment (ISGA) scale.

Treatment success was defined as achieving a Week 4 (end of treatment) ISGA score of 0 (clear) or 1 (majority of lesions have individual scores for scaling, erythema, and induration that averages 1 [minimal or faint]) and at least two grades of improvement from baseline. The results are presented in Table 2. The database was not large enough to assess whether there were differences in effects in age, gender, or race subgroups.

Table 2: Efficacy Results

Number of Subjects	Extina Foam N = 427 n (%)	Vehicle Foam N = 420 n (%)
Subjects Achieving Treatment Success	239 (56%)	176 (42%)

16 HOW SUPPLIED/STORAGE AND HANDLING

Extina Foam, 2% is supplied in 50 g (NDC 63032-051-50) and 100 g (NDC 63032-051-00) aluminum containers.

Store at controlled room temperature 68° - 77°F (20° - 25°C). Do not store under refrigerated conditions. **Do not expose containers to heat, and/or store at temperatures above 120°F (49°C).** Do not store in direct sunlight.

Contents are flammable.

Contents under pressure. Do not puncture and/or incinerate container.

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling. (17.3)

17.1 Instructions for Use

- **Avoid fire, flame and/or smoking during and immediately following application.**

Extina® (ketoconazole) Foam, 2%

- Do not apply Extina Foam directly to hands. Dispense onto a cool surface, and apply to the affected areas using the fingertips.

17.2 Local Reactions

- Extina Foam may cause skin irritation (application site burning and/or reactions)
- Extina Foam may cause contact sensitization.
- As with any topical medication, patients should wash their hands after application.
- Inform a physician if the area of application shows signs of increased irritation and report any signs of adverse reactions.

17.3 Patient Package Insert

- See below-

Extina® (ketoconazole) Foam, 2%

PATIENT INFORMATION

Extina (ex-TEEN-ah) Foam (ketoconazole, 2%)

IMPORTANT: For skin use only. Do not use in the eyes, mouth or vagina.

Read the Patient Information that comes with Extina Foam before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment.

What is Extina Foam?

Extina Foam is used on the skin (topical) to treat a skin condition called seborrheic dermatitis in patients 12 years and older. Seborrheic dermatitis can cause areas of flaky skin (scales) on the scalp, face, ears, chest or upper back.

Extina Foam has not been studied in children less than 12 years old.

What should I tell my doctor before using Extina Foam?

For female patients, tell your doctor if you:

- **are pregnant or become pregnant.** It is not known if Extina Foam can harm a fetus (unborn baby).
- **breastfeeding.** It is not known if Extina Foam passes into breast milk.

How should I use Extina Foam?

- **Apply Extina Foam exactly as prescribed.** Extina Foam is usually applied to the affected skin areas two times a day (once in the morning and once at night) for 4 weeks. Talk to your doctor if your skin does not improve after 4 weeks of treatment with Extina Foam.
- **Keep the Extina Foam can away from and do not spray it near fire, open flame, or direct heat. Extina Foam is flammable. Never throw the Extina Foam can into a fire, even if the can is empty.**

Extina® (ketoconazole) Foam, 2%

Instructions for applying Extina Foam

1. Hold the can at an upright angle.
2. Push the button to spray Extina Foam directly into the cap of the can or other cool surface. Spray only the amount of Extina Foam that you will need to cover your affected skin.

   Do not spray Extina Foam directly onto your affected skin or your hands because the foam will begin to melt right away when it touches your skin.
3. If your fingers are warm, rinse them in cold water first. Be sure to dry them well before handling the Extina Foam. If the Extina Foam can seems warm or the foam seems runny, place the can under cool running water for a few minutes.
4. Using your fingertips, gently massage Extina Foam into the affected areas until the foam disappears.
5. If you are treating skin areas with hair such as your scalp, move any hair away so that the foam can be applied to the affected skin.
6. **Do not get Extina Foam in your eyes, mouth or vagina. If any Extina Foam gets in your eyes, mouth or vagina, rinse areas well with water.**
7. Wash your hands well after applying Extina Foam.

What are the possible side effects of Extina Foam?

The most common side effects of Extina Foam are reaction or burning on treated skin areas. Tell your doctor if you have any reaction on your treated skin such as redness, itching, or a rash. These are not all the side effects of Extina Foam. Ask your doctor or pharmacist for more information.

How should I store Extina Foam?

- **Extina Foam is flammable.**
- **Do not spray Extina Foam near fire or direct heat. Never throw the can into a fire, even if the can is empty.**
- **Store the can of Extina Foam at room temperature,** 68° to 77°F (20°-25°C). Do not place the Extina Foam can in the refrigerator or freezer.
- **Keep the Extina Foam can away from all sources of fire and heat. Do not leave the Extina Foam can in direct sunlight.**
- **Do not smoke while holding the Extina Foam can** or while spraying or applying the foam.
- **Do not pierce or burn the Extina Foam can.**
- **Keep Extina Foam and all medicines out of the reach of children.**

General information about Extina Foam

Medicines are sometimes prescribed for conditions that are not mentioned in Patient Information leaflets. Do not use Extina Foam for any other condition for which it was not prescribed. Do not give Extina Foam to other people, even if they have the same condition that you have. It may harm them.

This leaflet summarizes the most important information about Extina Foam. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Extina Foam that is written for health professionals.

If you have questions about Extina Foam you can also call: 1-888-500-DERM (this is a toll-free number) between 6:00 a.m. and 4:00 p.m. Pacific Standard Time, Monday through Friday.

Extina® (ketoconazole) Foam, 2%

What are the ingredients in Extina Foam?

Active ingredients:	ketoconazole, USP
Inactive Ingredients:	cetyl alcohol NF, citric acid USP, ethanol (denatured with *tert*-butyl alcohol and brucine sulfate) 58%, polysorbate 60 NF, potassium citrate USP, propylene glycol USP, purified water USP, and stearyl alcohol NF pressurized with a hydrocarbon (propane/butane) propellant.

Rx Only

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

The Patient Information leaflet was last revised: June 2007

Manufactured for

Stiefel Laboratories, Inc., Coral Gables, FL 33134 USA

DELIVERED IN VersaFoam-HF™ HYDROETHANOLIC FORMULATION

U.S. Patent Pending

STIEFEL®

AW No.: AW-0733
P/N: 128118