STZC:R1

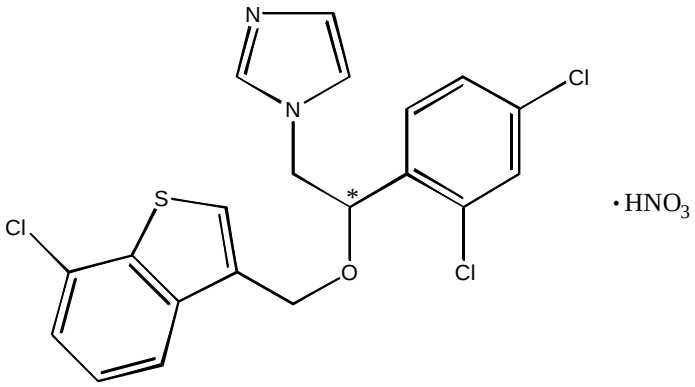
ERTACZO™ (SERTACONAZOLE NITRATE) CREAM, 2%

Rx only

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

DESCRIPTION: ERTACZO™ (sertaconazole nitrate) Cream, 2%, contains the imidazole antifungal, sertaconazole nitrate. Sertaconazole nitrate contains one asymmetric carbon atom and exists as a racemic mixture of equal amounts of R and S enantiomers.

Sertaconazole nitrate is designated chemically as (±)-1-[2,4-dichloro-ß-[(7-chlorobenzo[*b*]thien-3-yl)methoxy]phenethyl]imidazole nitrate. It has a molecular weight of 500.8. The molecular formula is $C_{20}H_{15}Cl_3N_2OS \cdot HNO_3$, and the structural formula is as follows:



Sertaconazole nitrate is a white or almost white powder. It is practically insoluble in water, soluble in methanol, sparingly soluble in alcohol and in methylene chloride. Each gram of ERTACZO™ Cream, 2%, contains 17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg) in

a white cream base of ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

CLINICAL PHARMACOLOGY: Pharmacokinetics: In a multiple dose pharmacokinetic study that included 5 male patients with interdigital tinea pedis (range of diseased area, 42 – 140 cm^2; mean, 93 cm^2), ERTACZO™ Cream, 2%, was topically applied every 12 hours for a total of 13 doses to the diseased skin (0.5 grams sertaconazole nitrate per 100 cm^2). Sertaconazole concentrations in plasma measured by serial blood sampling for 72 hours after the thirteenth dose were below the limit of quantitation (2.5 ng/mL) of the analytical method used.

Microbiology: Sertaconazole is an antifungal that belongs to the imidazole class of antifungals. While the exact mechanism of action of this class of antifungals is not known, it is believed that they act primarily by inhibiting the cytochrome P450-dependent synthesis of ergosterol. Ergosterol is a key component of the cell membrane of fungi, and lack of this component leads to fungal cell injury primarily by leakage of key constituents in the cytoplasm from the cell.

Activity *In Vivo*: Sertaconazole nitrate has been shown to be active against isolates of the following microorganisms in clinical infections as described in the INDICATIONS AND USAGE section:

Trichophyton rubrum

Trichophyton mentagrophytes

Epidermophyton floccosum

CLINICAL STUDIES: In two randomized, double-blind, clinical trials, patients 12 years and older with interdigital tinea pedis applied either ERTACZO™ Cream, 2%, or vehicle, twice daily for four weeks. Patients with moccasin-type (plantar) tinea pedis and/or onychomycosis were excluded from the study. Two weeks after completion of therapy (six weeks after beginning therapy), patients were evaluated for signs and symptoms related to interdigital tinea pedis.

Treatment outcomes are summarized in the table below.

Treatment Outcomes as Percent (%) of Total Subjects				
	Study 1		**Study 2**	
	Sertaconazole	Vehicle	Sertaconazole	Vehicle
Complete Cure* (Primary Efficacy Variable)	13/99 (13.1%)	3/92 (3.3%)	28/103 (27.2%)	5/103 (4.9%)
Effective Treatment**	32/99 (32.3%)	11/92 (12.0%)	52/103 (50.5%)	16/103 (15.5%)
Mycological Cure***	49/99 (49.5%)	18/92 (19.6%)	71/103 (68.9%)	20/103 (19.4%)

* Complete Cure – Patients who had complete clearing of signs and symptoms and Mycological Cure

** Effective Treatment – Patients who had minimal residual signs and symptoms of interdigitial tinea pedis and Mycological Cure

*** Mycological Cure – Patients who had both negative microscopic KOH preparation and a negative fungal culture.

In clinical trials, complete cure in sertaconazole treated patients was achieved in 32 of 160 (20%) patients with *Trichophyton rubrum,* in 7 of 28 (25%) patients with *Trichophyton mentagrophytes* and in 2 of 13 (15%) patients with *Epidermophyton floccosum*.

INDICATIONS AND USAGE: ERTACZO™ (sertaconazole nitrate) Cream, 2%, is indicated for the topical treatment of interdigital tinea pedis in immunocompetent patients 12 years of age and older, caused by *Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum* (See Clinical Studies Section).

CONTRAINDICATIONS: ERTACZO™ Cream, 2%, is contraindicated in patients who have a known or suspected sensitivity to sertaconazole nitrate or any of its components or to other imidazoles.

WARNINGS: ERTACZO™ Cream, 2%, is not indicated for ophthalmic, oral or intravaginal use.

PRECAUTIONS: General: ERTACZO™ Cream, 2%, is for use on the skin only. If irritation or sensitivity develops with the use of ERTACZO™ Cream, 2%, treatment should be discontinued and appropriate therapy instituted.

Diagnosis of the disease should be confirmed either by direct microscopic examination of infected superficial epidermal tissue in a solution of potassium hydroxide or by culture on an appropriate medium.

Physicians should exercise caution when prescribing ERTACZO™ Cream, 2%, to patients known to be sensitive to imidazole antifungals, since cross-reactivity may occur.

Information for Patients: The patient should be instructed to:

1. Use ERTACZO™ Cream, 2%, 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. ERTACZO™ Cream, 2%, is for external use only.

2. Dry the affected area(s) thoroughly before application, if you wish to use ERTACZO™ Cream, 2%, after bathing.

3. 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 the end of the prescribed treatment period, or sooner, if the condition worsens.

4. Inform the physician if the area of application shows signs of increased irritation, redness, itching, burning, blistering, swelling or oozing.

5. Avoid the use of occlusive dressings unless otherwise directed by the physician.

6. Do not use this medication for any disorder other than that for which it was prescribed.

Drug/Laboratory Test Interactions: Potential interactions between ERTACZO™ Cream, 2%, and other drugs or laboratory tests have not been systematically evaluated.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies to evaluate the carcinogenic potential of sertaconazole nitrate have not been conducted. No clastogenic potential was observed in a mouse micronucleus test. Sertaconazole nitrate was considered negative for sister chromatid exchange (SCE) in the *in vivo* mouse bone marrow SCE assay. There was no evidence that sertaconazole nitrate induced unscheduled DNA synthesis in rat primary hepatocyte cultures. Sertaconazole nitrate exhibited no toxicity or adverse effects on

reproductive performance or fertility of male or female rats given up to 60 mg/kg/day orally by gastric intubation (16 times the maximum recommended human dose based on a body surface area comparison).

Pregnancy: ***Teratogenic Effects. Pregnancy Category C:*** Oral reproduction studies in rats and rabbits did not produce any evidence of maternal toxicity, embryotoxicity or teratogenicity of sertaconazole nitrate at an oral dose of 160 mg/kg/day (40 times (rats) and 80 times (rabbits) the maximum recommended human dose on a body surface area comparison). In an oral peri-postnatal study in rats, a reduction in live birth indices and an increase in the number of still-born pups was seen at 80 and 160 mg/kg/day.

There are no adequate and well-controlled studies that have been conducted on topically applied ERTACZO™ Cream, 2%, in pregnant women. Because animal reproduction studies are not always predictive of human response, ERTACZO™ Cream, 2%, should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known if sertaconazole is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when prescribing ERTACZO™ Cream, 2%, to a nursing woman.

Pediatric Use: The efficacy and safety of ERTACZO™ Cream, 2%, have not been established in pediatric patients below the age of 12 years.

Geriatric Use: Clinical studies of ERTACZO™ Cream, 2%, did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ADVERSE EVENTS: In clinical trials, cutaneous adverse events occurred in 7 of 297 (2%) patients (2 of them severe) receiving ERTACZO™ Cream, 2%, and in 7 of 291 (2%) patients (2 of them severe) receiving vehicle. These reported cutaneous adverse events included contact dermatitis, dry skin, burning skin, application site reaction and skin tenderness.

In a dermal sensitization study, 8 of 202 evaluable patients tested with ERTACZO™ Cream, 2%, and 4 of 202 evaluable patients tested with vehicle, exhibited a slight erythematous reaction in the challenge phase. There was no evidence of cumulative irritation or contact sensitization in a repeated insult patch test involving 202 healthy volunteers. In non-US post-marketing surveillance for ERTACZO™ Cream, 2%, the following cutaneous adverse events were reported: contact dermatitis, erythema, pruritus, vesiculation, desquamation, and hyperpigmentation.

OVERDOSAGE: Overdosage with ERTACZO™ Cream, 2%, has not been reported to date. ERTACZO™ Cream, 2%, is intended for topical dermatologic use only. It is not for oral, ophthalmic, or intravaginal use.

DOSAGE AND ADMINISTRATION: In the treatment of interdigital tinea pedis, ERTACZO™ Cream, 2%, should be applied twice daily for 4 weeks. Sufficient ERTACZO™ Cream, 2%, should be applied to cover both the affected areas between the toes and the

immediately surrounding healthy skin of patients with interdigital tinea pedis. If a patient shows no clinical improvement 2 weeks after the treatment period, the diagnosis should be reviewed.

HOW SUPPLIED: ERTACZO™ Cream, 2%, is supplied in tubes in the following sizes:

15-gram tube	NDC 62794-170-46
30-gram tube	NDC 62794-170-43

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

Manufactured By: DPT Laboratories Inc.
San Antonio, TX 78215

Distributed By: Bertek Pharmaceuticals Inc.
Research Triangle Park, NC 27709

BERTEK®

Bertek Pharmaceuticals Inc.

Research Triangle Park, NC 27709

Revised December 9, 2003 **STZC:R1**

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
2g

FRONT PANEL

***Ertaczo*™** (sertaconazole nitrate) Cream 2%	
	BERTEK PHARMACEUTICALS INC
Distributed By: Bertek Pharmaceuticals Inc., Research Triangle Park, NC 27709	

BACK PANEL

Each gram contains 17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

Usual Dosage: See accompanying package insert for full prescribing information.

Distributed By: Bertek Pharmaceuticals Inc., Research Triangle Park, NC 27709

Manufactured by: DPT Laboratories Inc. San Antonio, TX 78215

BK170-47-12C:R1S LOT:
EXP:

SIDE PANEL (1)

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

SIDE PANEL (2)

Available for prescription in 15g and 30g tubes

Box Contains 12, 2g tubes

Rx only

For Topical Dermatologic Use Only – Not For Oral, Ophthalmic or Intravaginal Use

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

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
2g

END FLAPS (2)

NDC 62794-170-47

Physician Sample

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
15g

SIDE PANEL (1)

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

15g

FRONT PANEL

NDC 62974-170-46

Rx only

15g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

For Topical Dermatologic Use Only-
Not for Oral, Ophthalmic or Intravaginal Use

Distributed by:
Bertek Pharmaceuticals Inc.
Research Triangle Park, NC 27709

SIDE PANEL (2)

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

15g

Usual Dosage: See accompanying package insert for full prescribing information.

BACK PANEL

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

See crimp for lot no. and expiration date.

[INSERT UPC CODE]

Manufactured by: DPT Laboratories Inc. San Antonio, TX 78215

BK170-46-1C:R1

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
15g

END FLAP (1)

15g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

(insert bar code)

END FLAP (2)

LOT: [Insert lot number]

EXP: [Insert expiration number]

(insert bar code)

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
30g

SIDE PANEL (1)

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

30g

FRONT PANEL

NDC 62974-170-43

Rx only

30g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

For Topical Dermatologic Use Only-
Not for Oral, Ophthalmic or Intravaginal Use

Distributed by:
Bertek Pharmaceuticals Inc.
Research Triangle Park, NC 27709

SIDE PANEL (2)

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

30g

Usual Dosage: See accompanying package insert for full prescribing information.

BACK PANEL

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

See crimp for lot no. and expiration date.

[INSERT UPC CODE]

Manufactured by: DPT Laboratories Inc. San Antonio, TX 78215

BK170-43-1C:R1

Sertaconazole Nitrate Cream, 2%
CARTON LABELS
30g

END FLAP (1)

30g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

(insert bar code)

END FLAP (2)

LOT: [Insert lot number]

EXP: [Insert expiration number]

(insert bar code)

Sertaconazole Nitrate Cream, 2%
TUBE LABELS
2g

FRONT PANEL

NDC 62794-170-47 **Physician Sample** **2g**

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

For Topical Dermatologic Use Only-
Not For Oral, Ophthalmic or Intravaginal Use

Rx only

[Insert lot number and expiration date].

BACK PANEL

Each gram contains 17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

Usual Dosage: See accompanying package insert for full prescribing information.

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

BK170AB

See crimp for lot no. and expiration date

Distributed By:
Bertek Pharmaceuticals Inc.,
Research Triangle Park, NC 27709

Manufactured by: DPT Laboratories Inc., San Antonio, TX 78215

Sertaconazole Nitrate Cream, 2%
TUBE LABELS
15g

FRONT PANEL

NDC 62794-170-46

Rx only

15g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

For Topical Dermatologic Use Only-
Not For Oral, Ophthalmic or Intravaginal Use

Distributed by:
Bertek Pharmaceuticals Inc.
Research Triangle Park, NC 27709

[Insert lot number and expiration

BACK PANEL

Each gram contains 17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

Usual Dosage: See accompanying package insert for full prescribing information.

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

BK170AG

See crimp for lot no. and expiration date

Manufactured by: DPT Laboratories Inc., San Antonio, TX 78215

Sertaconazole Nitrate Cream, 2%
TUBE LABELS
30g

FRONT PANEL

NDC 62794-170-43

Rx only

30g

***Ertaczo*™**
(sertaconazole nitrate) Cream 2%

For Topical Dermatologic Use Only-
Not For Oral, Ophthalmic or Intravaginal Use

Distributed by:
Bertek Pharmaceuticals Inc.
Research Triangle Park, NC 27709

[Insert lot number and expiration

BACK PANEL

Each gram contains 17.5 mg of sertaconazole (as sertaconazole nitrate, 20 mg), ethylene glycol and polyethylene glycol palmitostearate, glyceryl isostearate, light mineral oil, methylparaben, polyoxyethylened saturated glycerides and glycolized saturated glycerides, sorbic acid and purified water.

Usual Dosage: See accompanying package insert for full prescribing information.

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

BK170AH

See crimp for lot no. and expiration date

Manufactured by: DPT Laboratories Inc., San Antonio, TX 78215