CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76005

DRAFT FINAL PRINTED LABELING

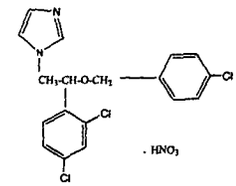
Econazole Nitrate Cream 1%

For Topical Use Only

Rx Only

DESCRIPTION:
Econazole nitrate cream contains the antifungal agent, econazole nitrate USP 1%, in a water-miscible base consisting of apricot kernel oil/PEG-6, benzoic acid, butylated hydroxytoluene, mineral oil, PEG-6-32 stearate/glycol stearate and purified water. The white to off-white soft cream is for topical use only.

Chemically, econazole nitrate is 1-[2-[(4-chlorophenyl) methoxy]-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole mononitrate. Its structure is as follows:



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CLINICAL PHARMACOLOGY:
After topical application to the skin of normal subjects, systemic absorption of econazole nitrate is extremely low. Although most of the applied drug remains on the skin surface, drug concentrations were found in the stratum corneum which, by far, exceeded the minimum inhibitory concentration for dermatophytes. Inhibitory concentrations were achieved in the epidermis and as deep as the middle region of the dermis. Less than 1% of the applied dose was recovered in the urine and feces.

Microbiology: Econazole nitrate has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as described in the **INDICATIONS AND USAGE** section.

Dermatophytes	**Yeasts**
Epidermophyton floccosum	*Candida albicans*
Microsporum audouini	*Malassezia furfur*
Microsporum canis	
Microsporum gypseum	
Trichophyton mentagrophytes	
Trichophyton rubrum	
Trichophyton tonsurans	

Econazole nitrate exhibits broad-spectrum antifungal activity against the following organisms *in vitro*, but the clinical significance of these data is unknown:

Dermatophytes	**Yeasts**
Trichophyton verrucosum	*Candida guillermondii*
	Candida parapsilosis
	Candida tropicalis

INDICATIONS AND USAGE:
Econazole nitrate cream is indicated for topical application in the treatment of tinea pedis, tinea cruris, and tinea corporis caused by *Trichophyton rubrum, Trichophyton mentagrophytes, Trichophyton tonsurans, Microsporum canis, Microsporum audouini, Microsporum gypseum,* and *Epidermophyton floccosum,* in the treatment of cutaneous candidiasis, and in the treatment of tinea versicolor.

CONTRAINDICATIONS:
Econazole nitrate cream is contraindicated in individuals who have shown hypersensitivity to any of its ingredients.

WARNINGS:
Econazole nitrate cream is not for ophthalmic use.

PRECAUTIONS:
General: If a reaction suggesting sensitivity or chemical irritation should occur, use of the medication should be discontinued.

For external use only. Avoid introduction of econazole nitrate cream into the eyes.

Carcinogenicity Studies: Long-term animal studies to determine carcinogenic potential have not been performed.

Fertility (Reproduction): Oral administration of econazole nitrate in rats has been reported to produce prolonged gestation. Intravaginal administration in humans has not shown prolonged gestation or other adverse reproductive effects attributable to econazole nitrate therapy.

Pregnancy: Pregnancy Category C. Econazole nitrate has not been shown to be teratogenic when administered orally to mice, rabbits or rats. Fetotoxic or embryotoxic effects were observed in Segment I oral studies with rats receiving 10 to 40 times the human dermal dose. Similar effects were observed in Segment II or Segment III studies with mice, rabbits and/or rats receiving oral doses 80 or 40 times the human dermal dose.

Econazole nitrate should be used in the first trimester of pregnancy only when the physician considers it essential to the welfare of the patient. The drug should be used during the second and third trimesters of pregnancy only if clearly needed.

Nursing Mothers: It is not known whether econazole nitrate is excreted in human milk. Following oral administration of econazole nitrate to lactating rats, econazole and/or metabolites were excreted in milk and were found in nursing pups. Also, in lactating rats receiving large oral doses (40 or 80 times the human dermal dose), there was a reduction in post partum viability of pups and survival to weaning; however, at these high doses, maternal toxicity was present and may have been a contributing factor. Caution should be exercised when econazole nitrate is administered to a nursing woman.

ADVERSE REACTIONS:
During clinical trials, approximately 3% of patients treated with econazole nitrate 1% cream reported side effects thought possibly to be due to the drug, consisting mainly of burning, itching, stinging and erythema. One case of pruritic rash has also been reported.

OVERDOSE:
Overdosage of econazole nitrate in humans has not been reported to date. In mice, rats, guinea pigs and dogs, the oral LD 50 values were found to be 462, 668, 272, and >160 mg/kg, respectively.

DOSAGE AND ADMINISTRATION:
Sufficient econazole nitrate cream should be applied to cover affected areas once daily in patients with tinea pedis, tinea cruris, tinea corporis, and tinea versicolor, and twice daily (morning and evening) in patients with cutaneous candidiasis.

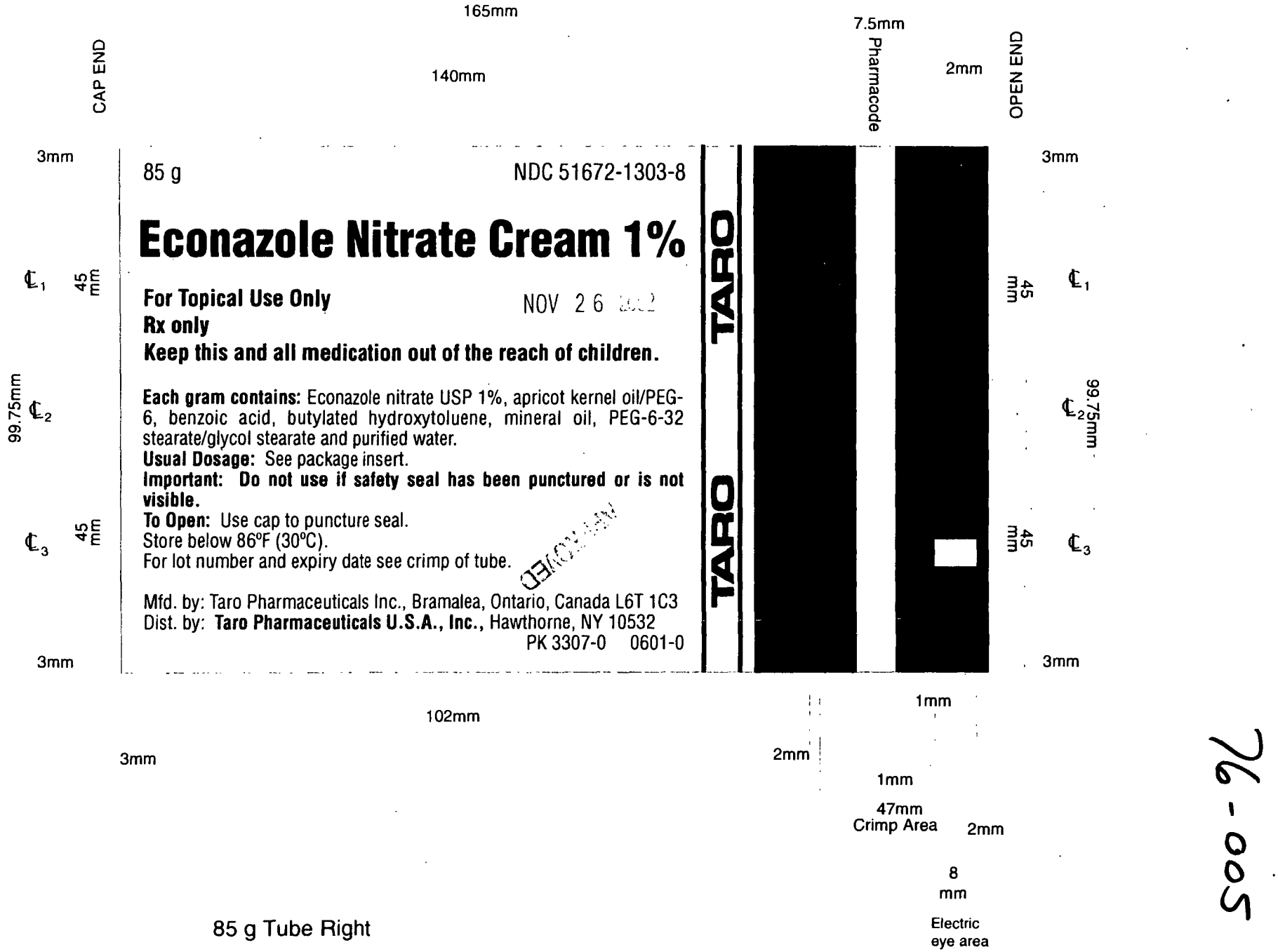
Early relief of symptoms is experienced by the majority of patients and clinical improvement may be seen fairly soon after treatment is begun; however, candidal infections and tinea cruris and corporis should be treated for two weeks and tinea pedis for one month in order to reduce the possibility of recurrence. If a patient shows no clinical improvement after the treatment period, the diagnosis should be redetermined. Patients with tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

HOW SUPPLIED:
Econazole Nitrate Cream 1% is supplied in tubes of 15 grams, 30 grams, 85 grams and 120 grams.

Store Econazole Nitrate Cream below 86°F (30°).

Mfd. by: Taro Pharmaceuticals Inc., Brampton, Ontario, Canada L6T 1C1

Issued: September 2001 PK-3310-0 0901-0



85 g Tube Right

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Each gram contains: Econazole nitrate USP 1%, apricot kernel oil/PEG-6, benzoic acid, butylated hydroxytoluene, mineral oil, PEG-6-32 stearate/glycol stearate and purified water.
Usual Dosage: See package insert.
Important: The opening of this product is covered by a safety seal. If this seal has been punctured or is not visible, do not use and return to place of purchase.
To Open: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open. To close, screw the cap back onto the tube.
Store below 86°F (30°C).
For lot number and expiry date see flap of carton or crimp of tube.

30 g

NDC 51672-1303-2

Econazole Nitrate Cream 1%

For Topical Use Only

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Rx only

Keep this and all medication out of the reach of children.

Mfd. by: Taro Pharmaceuticals Inc.
Bramalea, Ontario, Canada L6T 1C3
Dist. by: **Taro Pharmaceuticals U.S.A., Inc.**
Hawthorne, NY 10532

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30 g
Econazole Nitrate Cream 1%

30 g

NDC 51672-1303-2

Econazole Nitrate Cream 1%

For Topical Use Only
Rx only
Keep this and all medication out of the reach of children.

TARO

261

Each gram contains: Econazole nitrate USP 1%, apricot kernel oil/PEG-6, benzoic acid, butylated hydroxytoluene, mineral oil, PEG-6-32 stearate/glycol stearate and purified water.
Usual Dosage: See package insert.
Important: The opening of this product is covered by a safety seal. If this seal has been punctured or is not visible, do not use and return to place of purchase.
To Open: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open. To close, screw the cap back onto the tube.
Store below 86°F (30°C).
For lot number and expiry date see flap of carton or crimp of tube.

120 g NDC 51672-1303-4

Econazole Nitrate Cream 1%

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120 g
Econazole Nitrate Cream 1%

120 g NDC 51672-1303-4

Econazole Nitrate Cream 1%

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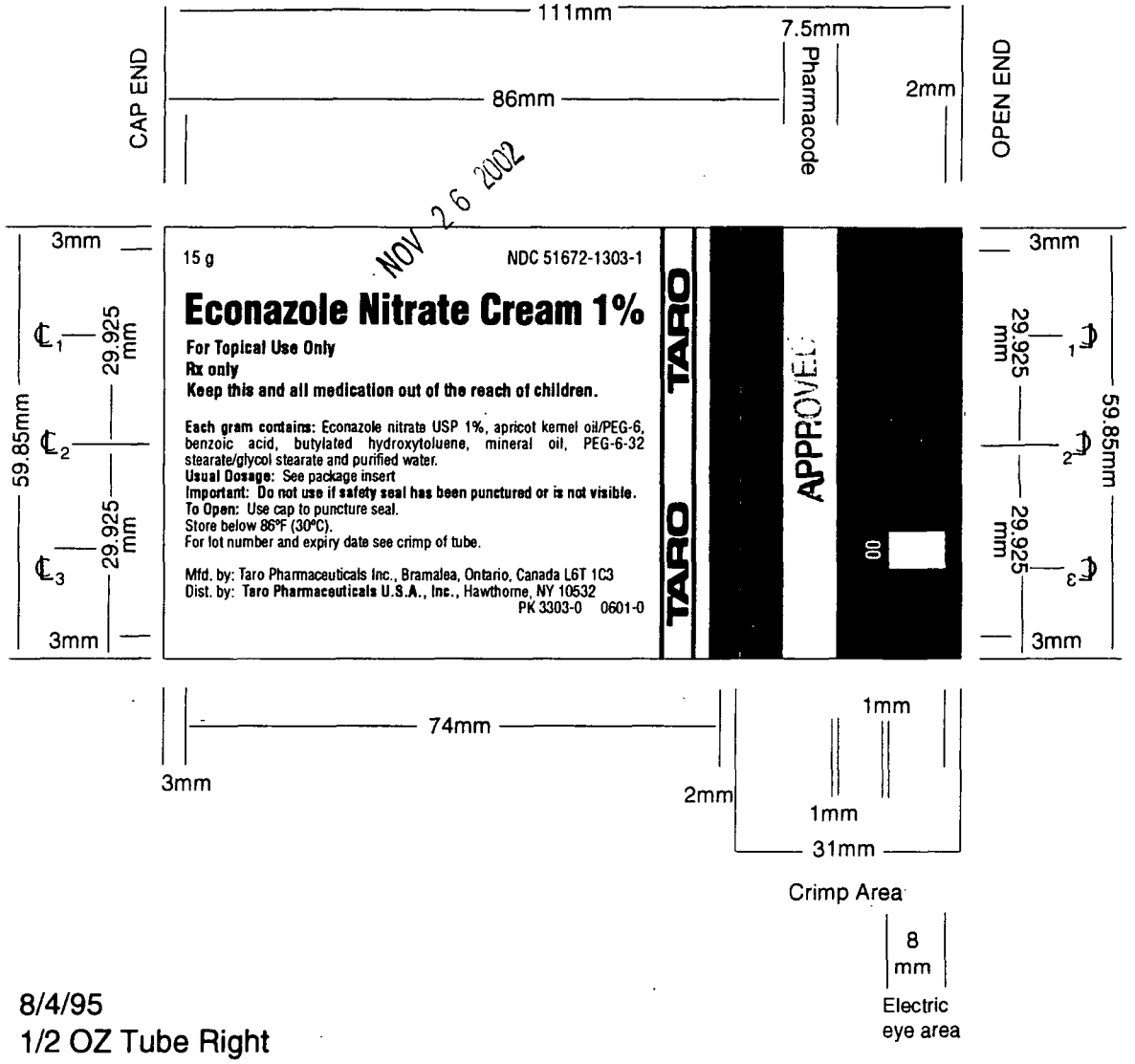
TARO

SCALED 90%



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1/2 OZ Tube Right