CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76075

DRAFT FINAL PRINTED LABELING

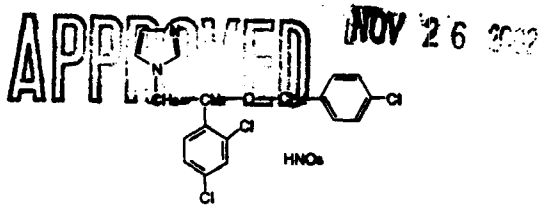
fougera®

ECONAZOLE NITRATE CREAM, 1%

FOR TOPICAL USE ONLY ℞ only **NOT FOR OPHTHALMIC USE**

DESCRIPTION: Econazole Nitrate Cream, 1% contains the antifungal agent, econazole nitrate 1%, in a water-miscible base consisting of pegoxyl 7 stearate, peglicol 5 oleate, mineral oil, benzoic acid, butylated hydroxyanisole, and purified water. The white to off-white soft cream is for topical use only.

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



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, 1% 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.

(over)

CONTRAINDICATIONS: Econazole Nitrate Cream, 1% is contraindicated in individuals who have shown hypersensitivity to any of its ingredients.

WARNINGS: Econazole Nitrate Cream, 1% 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.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: 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: ***Teratogenic effects*** - *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 know 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.

OVERDOSAGE: 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 1% 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 as follows:

NDC 0168-0312-15 15 gram tube
NDC 0168-0312-30 30 gram tube
NDC 0168-0312-85 85 gram tube

Store Econazole Nitrate 1% Cream below 86°F (30°C).

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

APPROVED

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R10/01
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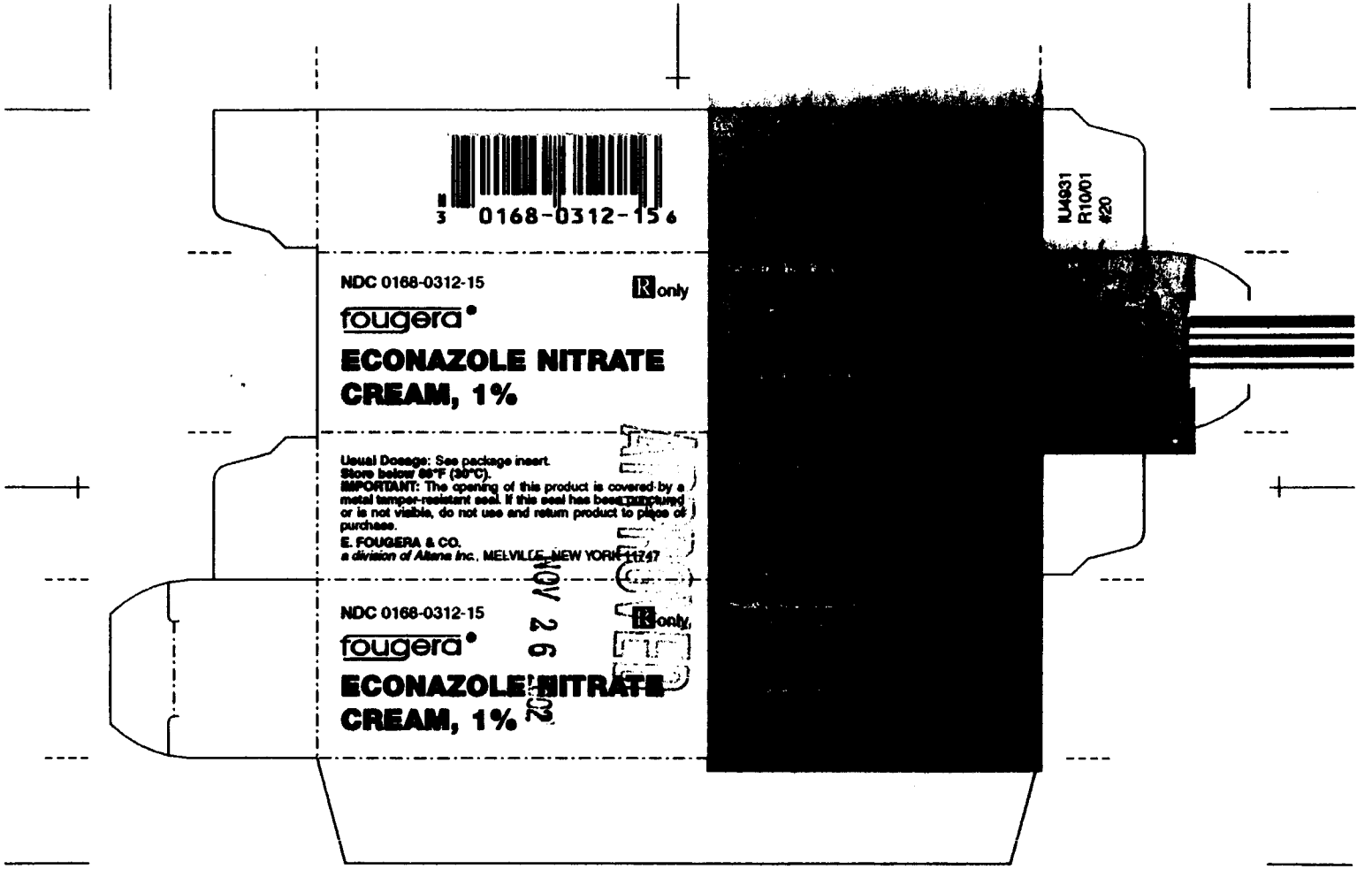
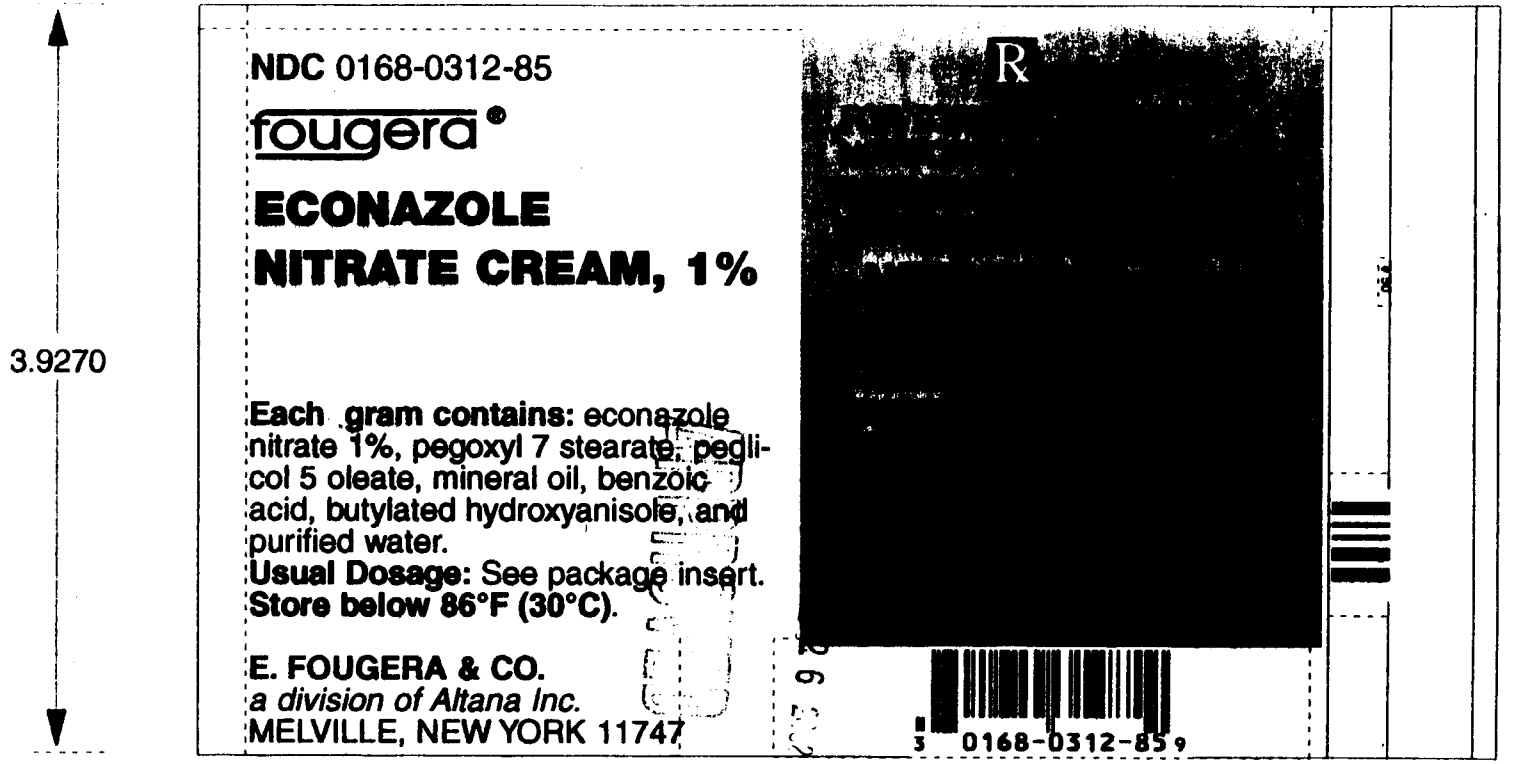


48

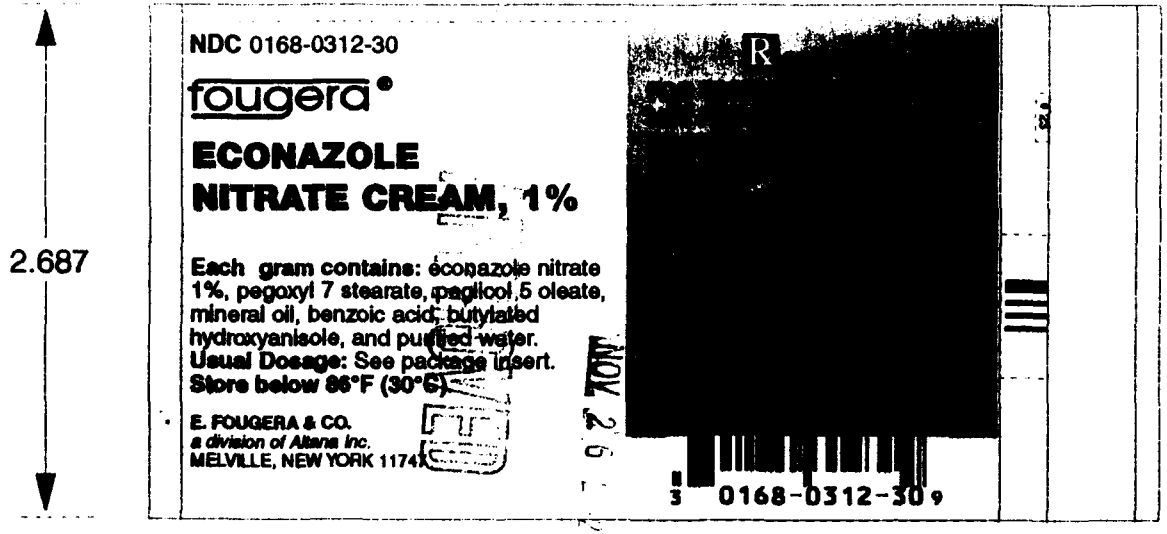
Econazole Nitrate 1% Cream 15 g
IU4931 R7/01
SSC-4
Dimensions: 1.063" x 0.875" x 4.250
Process Yellow & Black
Pharmacode # 20

Prepare DRAFT for FDA submission/Spell checked	- AA-6/13/01
product name in helvetica Nueva Black Italic per DP	- AA-7/25/01
Regulatory Edits	- AA-7/30/01
Research & Development Edit	- AA- 8/6/01
Sales Edit	- AA-8/13/01
FDA comments	-DH10/1501
Sales edit	- AA-11/15/01



Econazole Nitrate 1% Cream 80 g
X4933 R7/01
6.7500" x 1.250" Circ: 3.9270
Process Yellow & Black
Pharmacode # 50

Prepare DRAFT for FDA submission/Spell checked	-AA-6/12/01
Product name Helvetica Nueva Black Italic per DP	-AA-7/25/01
Regulatory Edits	-AA-7/30/01
Research & Development Edit	- AA-8/6/01
Sales Edit	-AA-8/13/01
FDA comments	DH 10/15/01
Regulatory Edit	- AA-10/31/01



23

Econazole Nitrate 1% Cream 30 g
W4932 R7/01
5.250" x .875" , Circ: 2.687
Process Yellow & Black
Pharmacode# 23

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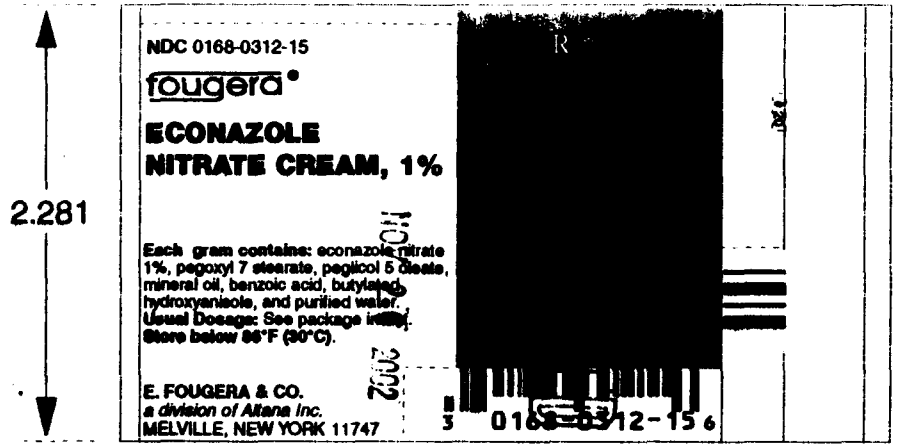
Regulatory Edits	- AA- 7/30/01
Research & Development Edit	-AA-8/6/01
Sales Edit	-AA -8/13/01
FDA comments	DH10/15/01
Regulatory Edit	- AA-10/31/01



CCC 11

Econazole Nitrate 1% Cream 15 g
U4931 R7/01
4.00" x .750" , Circ: 2.281
Process Yellow & Black
Pharmacode# 20

Prepare DRAFT for FDA submission/Spell checked	- AA- 6/12/01
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Regulatory Edits	- AA- 7/30/01
Research & Development Edit	- AA- 8/6/01
Sales Edit	- AA- 8/13/01
FDA Comments	DH 10/15/01
Regulatory Edit	- AA-10/31/01