CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40386

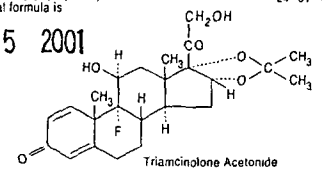
DRAFT FINAL PRINTED LABELING

TRIAMCINOLONE ACETONIDE LOTION USP, TRIAMCINOLONE ACETONIDE CREAM USP AND TRIAMCINOLONE ACETONIDE OINTMENT USP (TOPICAL)

R300

DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and antipruritic agents. The steroids in this class include Triamcinolone Acetonide. Triamcinolone Acetonide is designated chemically as Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-,(11β,16α)- With molecular formula as $C_{24}H_{31}FO_6$ and molecular weight 434.51 Structural formula is



Triamcinolone Acetonide

Triamcinolone Acetonide Lotion 0.1% (each mL contains 1 mg Triamcinolone Acetonide) in a base containing propylene glycol, cetyl alcohol, stearyl alcohol, sorbitan monopalmitate, polysorbate 20, simethicone and purified water.

Triamcinolone Acetonide Creams 0.025% (each gram contains 0.25 mg Triamcinolone Acetonide)· 0.1% (each gram contains 1 mg Triamcinolone Acetonide)· 0.5% (each gram contains 5 mg Triamcinolone Acetonide) in a base containing purified water, propylene glycol, propylene glycol stearate, sorbic acid, mineral oil and lanolin alcohol, isopropyl palmitate, polysorbate 60, cetyl alcohol, sorbitan monostearate, polyoxyl 40 stearate, methylparaben and propylparaben. Triamcinolone Acetonide Ointment 0.1% (each gram contains 1 mg Triamcinolone Acetonide) in a base containing white petrolatum and mineral oil: Triamcinolone Acetonide Ointment 0.025% (each gram contains 0.25 mg Triamcinolone Acetonide): Triamcinolone Acetonide Ointment 0.5% (each gram contains 5 mg Triamcinolone Acetonide) in a base containing white petrolatum and light mineral oil.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, antipruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See **DOSAGE AND ADMINISTRATION**).

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS

General

Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (See **PRECAUTIONS—Pediatric Use**).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests

The following tests may be helpful in evaluating the HPA axis suppression:
Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy, Teratogenic Effects, Pregnancy Category C

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities *not* likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in pediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in pediatric patients include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to pediatric patients should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of pediatric patients.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin Atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	Miliaria

OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (See **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION

Cream (0.025%): Apply to affected area two to four times daily. Rub in gently.
Cream (0.1% and 0.5%); Lotion (0.1%). Apply to affected area two or three times daily. Rub in gently.
Ointment (0.025%): Apply a thin film to affected area two to four times daily.
Ointment (0.1% and 0.5%): Apply a thin film to affected area two or three times daily.

Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED

Lotion, 0.1% in 15 mL (NDC 49158-211-42), 60 mL (NDC 49158-211-32) plastic squeeze bottles. Cream, 0.025% in 15 g (NDC 49158-139-20), 1 oz (28.35 g) (NDC 49158-139-08), 80 g (NDC 49158-139-21) tubes, one lb (453.6 g) (NDC 49158-139-16), and 5 lb (2268 g) (NDC 49158-139-22) jars. Cream, 0.1% in 15 g (NDC 49158-140-20), 20 g (NDC 49158-140-07), 1 oz (28.35 g) (NDC 49158-140-08), 80 g (NDC 49158-140-21) tubes, one lb (453.6 g) (NDC 49158-140-16), and 5 lb (2268 g) (NDC 49158-140-22) jars. Cream, 0.5% in 15 g (NDC 49158-141-20) tubes. Ointment, 0.025% in 15 g (NDC 49158-355-20), 1 oz (28.35 g) (NDC 49158-355-08), 80 g (NDC 49158-355-21) tubes and 1 lb (453.6 g) (NDC 49158-355-16) jars. Ointment, 0.1% in 15 g (NDC 49158-160-20), 1 oz (28.35 g) (NDC 49158-160-08), and 80 g (NDC 49158-160-21) tubes and one lb (453.6 g) (NDC 49158-160-16) jars. Ointment, 0.5% in 15 g (NDC 49158-356-20), 1 oz (28.35 g) (NDC 49158-356-08), 80 g (NDC 49158-356-21) tubes and 1 lb (453.6 g) (NDC 49158-356-16) jars.

Pharmacist: Dispense in tight containers, as specified in USP.

Store at controlled room temperature 15° - 30°C (59° - 86°F). Protect from freezing.

℞ only

Manufactured by
THAMES PHARMACAL CO., INC.
Ronkonkoma, N.Y. 11779 USA

MG# 14169

R300

USUAL DOSAGE: Apply a thin film to the affected area two or three times daily. See insert for complete information.
Keep this and all medications out of the reach of children.
Keep away from eyes. Not for ophthalmic use.

NDC 49158-356-20

TRIAMCINOLONE ACETONIDE OINTMENT USP, 0.5%

℞ only
For external use only.

NET WT 15 g

Thames PHARMACAL CO., INC.
Ronkonkoma, NY 11779 USA

Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.
For Control No. and Expiration Date See Crimp of Tube.
Store at controlled room temperature 15°-30°C (59°-86°F).
Protect from freezing.
Keep tightly closed.

R300

USUAL DOSAGE: Apply a thin film to the affected area two or three times daily. See insert for complete information
Keep this and all medications out of the reach of children
Keep away from eyes Not for ophthalmic use.

NDC 49158-356-21

TRIAMCINOLONE ACETONIDE OINTMENT USP, 0.5%

℞ only
For external use only.

NET WT 80 g

Thames PHARMACAL CO., INC.
Ronkonkoma, NY 11779 USA

Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.

For Control No. and Expiration Date
See Crimp of Tube.

Store at controlled room temperature 15°-30°C (59°-86°F).
Protect from freezing. Keep tightly closed.
Pharmacist: Dispense in tight containers, as specified in USP.

R300

USUAL DOSAGE: Apply a thin film to the affected area two or three times daily. See insert for complete information.
Keep this and all medications out of the reach of children
Keep away from eyes. Not for ophthalmic use.

NDC 49158-356-08

TRIAMCINOLONE ACETONIDE OINTMENT USP, 0.5%

℞ only
For external use only.

NET WT 1 OZ (28.35 g)

Thames PHARMACAL CO., INC.
Ronkonkoma, NY 11779 USA

Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.
For Control No. and Expiration Date See Crimp of Tube.
Store at controlled room temperature 15°-30°C (59°-86°F).
Protect from freezing. Keep tightly closed. R300

USUAL DOSAGE: Apply a thin film to the affected area two or three times daily. See insert for complete information.
Not for ophthalmic use.
Keep this and all medications out of the reach of children
Keep away from eyes.
PHARMACIST: Dispense in tight containers, as specified in USP.

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NDC 49158-356-16

TRIAMCINOLONE ACETONIDE OINTMENT USP, 0.5%

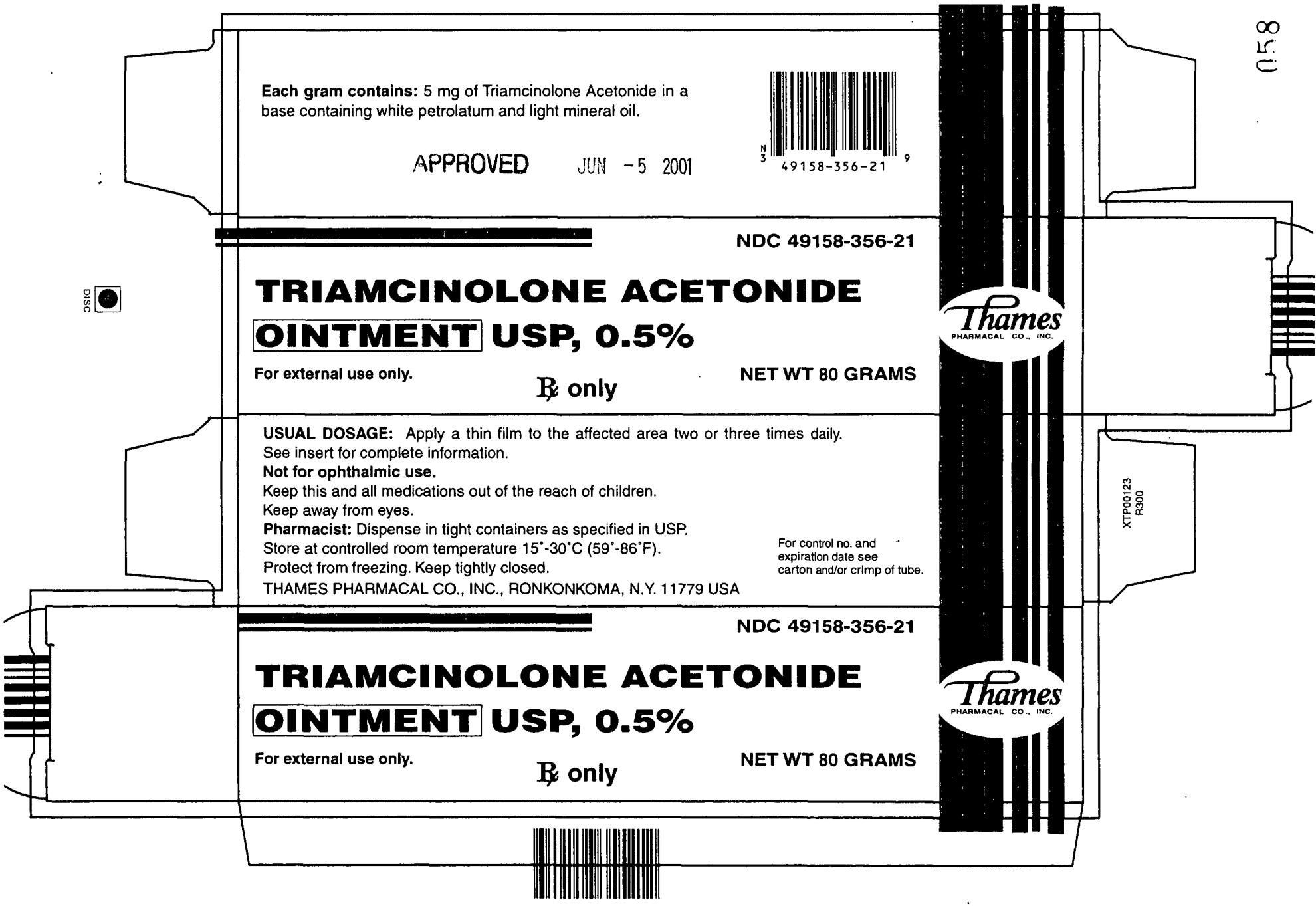
For Hospital and/or Institutional Use Only.

℞ only
For external use only.

NET WT 16 oz (453.6 g)

Thames PHARMACAL CO., INC
Ronkonkoma, NY 11779 USA

Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.
For Control No. and Expiration Date
See Code on Bottom of Jar.
Store at controlled room temperature
15°-30°C (59°-86°F).
Protect from freezing.
Keep tightly closed.
R300



JOB# 140279H-004 3/17/00 RR

4/7/00 ks

DISC

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Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.

JUN -5 2001

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NDC 49158-356-08

TRIAMCINOLONE ACETONIDE

OINTMENT USP, 0.5%

APPROVED

For external use only.

NET WT 1 OZ (28.35 g)

℞ only

USUAL DOSAGE: Apply a thin film to the affected area two or three times daily.
See insert for complete information.
Not for ophthalmic use.
Keep this and all medications out of the reach of children.
Store at controlled room temperature
15°-30°C (59°-86°F).
Protect from freezing. Keep tightly closed.
THAMES PHARMACAL CO., INC., RONKONKOMA, N.Y. 11779 USA

For control no. and expiration date see carton and/or crimp of tube.

Thames PHARMACAL CO., INC.

XTP00122
R300

DISC

NDC 49158-356-08

TRIAMCINOLONE ACETONIDE

OINTMENT USP, 0.5%

For external use only.

NET WT 1 OZ (28.35 g)

℞ only

Thames PHARMACAL CO., INC.

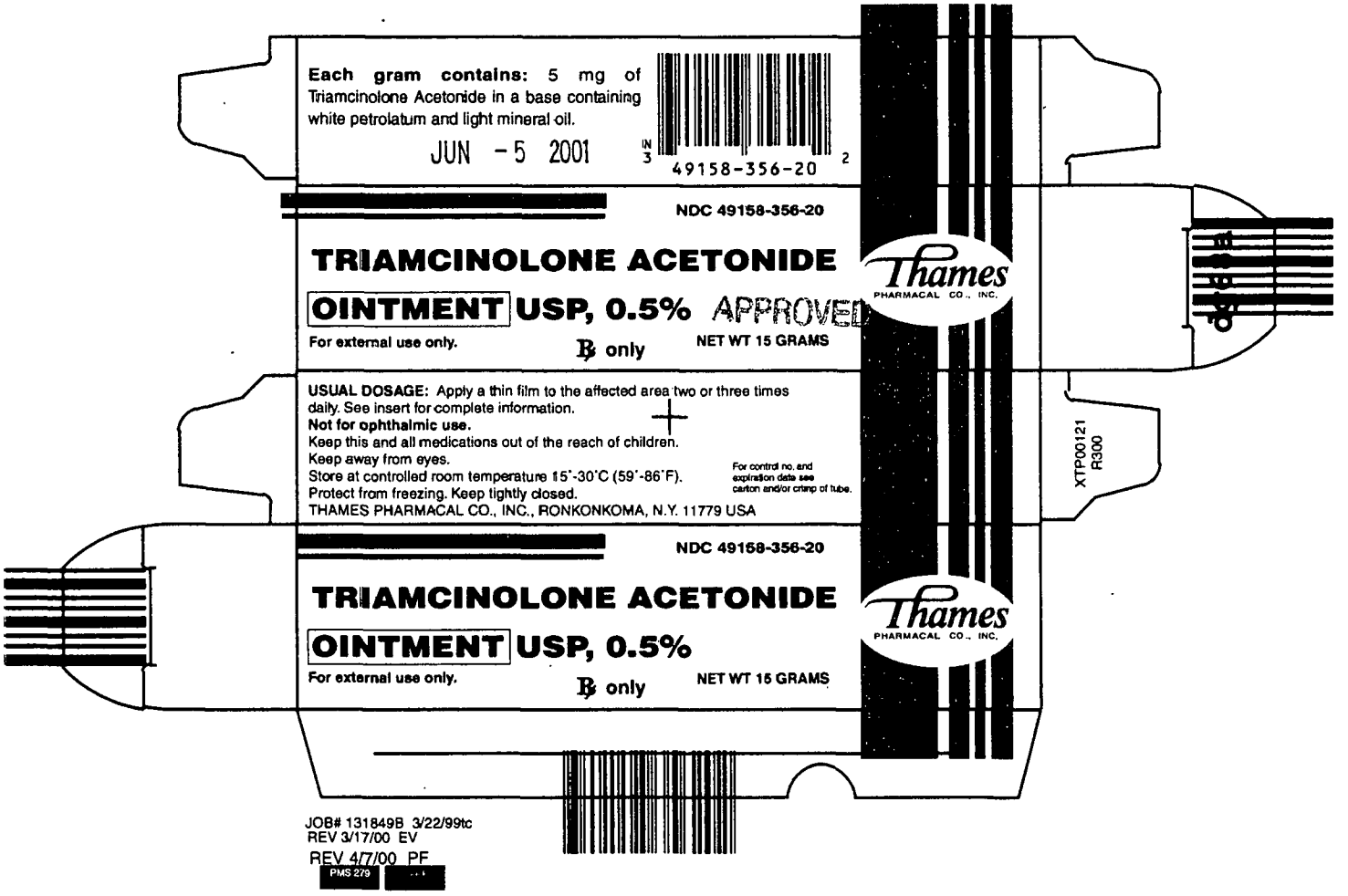
JOB# 131852G 12/1/98tc

PMS 279

131852G-001 4/7/00 ks

DISC

DISC


Each gram contains: 5 mg of Triamcinolone Acetonide in a base containing white petrolatum and light mineral oil.
JUN -5 2001
IN 3
49158-356-20 2
NDC 49158-356-20
TRIAMCINOLONE ACETONIDE
OINTMENT USP, 0.5%
APPROVED
For external use only.
℞ only
NET WT 15 GRAMS
USUAL DOSAGE: Apply a thin film to the affected area two or three times daily. See insert for complete information.
Not for ophthalmic use.
Keep this and all medications out of the reach of children.
Keep away from eyes.
Store at controlled room temperature 15°-30°C (59°-86°F).
Protect from freezing. Keep tightly closed.
THAMES PHARMACAL CO., INC., RONKONKOMA, N.Y. 11779 USA
For control no. and expiration date see carton and/or crimp of tube.
Thames
PHARMACAL CO., INC.
XTP00121
R300
NDC 49158-356-20
TRIAMCINOLONE ACETONIDE
OINTMENT USP, 0.5%
For external use only.
℞ only
NET WT 15 GRAMS
Thames
PHARMACAL CO., INC.
JOB# 131849B 3/22/99tc
REV 3/17/00 EV
REV 4/7/00 PF
PMS 279