CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40310

DRAFT FINAL PRINTED LABELING

Approval

40-310

12/29/00

USUAL DOSAGE: Apply to affected area two to four times daily.
See insert for complete information.
For External Use Only. Not for Ophthalmic Use.
Keep this and all medications out of the reach of children.
Keep away from eyes.

NDC 49158-347-08

HYDROCORTISONE
OINTMENT USP, 2.5%

℞ only

NET WT 1 OZ (28.35 g)

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

Each gram contains: 25 mg of Hydrocortisone in a base containing white petrolatum and 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.

R1198

USUAL DOSAGE: Apply to affected area two to four times daily.
See insert for complete information.
For External Use Only. Not for Ophthalmic Use.
Keep this and all medications out of the reach of children.
Keep away from eyes.

NDC 49158-347-07

HYDROCORTISONE
OINTMENT USP, 2.5%

℞ only

NET WT 20 g

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

Each gram contains: 25 mg of Hydrocortisone in a base containing white petrolatum and 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.

R1198

NDC 49158-347-16

HYDROCORTISONE
OINTMENT
USP, 2.5%

For Hospital and/or Institutional Use Only.

℞ only

NET WT 16 OZ (453.6 g)

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

Each gram contains: 25 mg of Hydrocortisone in a base containing white petrolatum and 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.

R1198

USUAL DOSAGE: Apply to affected area two to four times daily. See insert for complete information.
For External Use Only. 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 the USP.

N 3 49158-347-16 3

(Approval) 40-310

HYDROCORTISONE CREAM USP, HYDROCORTISONE OINTMENT USP AND HYDROCORTISONE LOTION USP

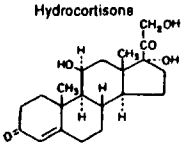
R398

FOR TOPICAL USE ONLY

DESCRIPTION

The topical steroids constitute a class of primarily synthetic steroids used as anti-inflammatory and antipruritic agents. Hydrocortisone is a member of this class. Hydrocortisone has the chemical name Pregn-4-ene-3,20-dione, 11,17,21- trihydroxy-, (11β)-. Its molecular formula is $C_{21}H_{30}O_5$ and molecular weight 362.47. Structural formula is

Hydrocortisone



Hydrocortisone Cream USP, 1% (Each gram contains 10 mg of Hydrocortisone) 2.5% (Each gram contains 25 mg of Hydrocortisone) Hydrocortisone Lotion USP, 2.5% (Each gram contains 25 mg of Hydrocortisone) in a base containing Purified Water, Propylene Glycol, Propylene Glycol Monostearate, Mineral Oil and Lanolin Alcohol, Isopropyl Palmitate, Polysorbate 60, Cetyl Alcohol, Sorbitan Monostearate, Polyoxyl 40 Stearate, Sorbic Acid, Methylparaben and Propylparaben.

Hydrocortisone Ointment USP, 1% (Each gram contains 10 mg of Hydrocortisone) 2.5% (Each gram contains 25 mg of Hydrocortisone) in a base containing White Petrolatum and 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 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 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 dressings.
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

12/29

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

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

Topical corticosteroids are generally applied to the affected area as a thin film from two to four times daily depending on the severity of the condition.

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.

Lotion - Shake well before use.

HOW SUPPLIED

Hydrocortisone Cream USP, 1% in
20 g tubes NDC 49158-101-07,
1 oz (28.35 g) tubes NDC 49158-101-08,
4 oz (113.4 g) jars NDC 49158-101-12,
16 oz (453.6 g) jars NDC 49158-101-16.

Hydrocortisone Cream USP, 2.5% in
20 g tubes NDC 49158-200-07,
1 oz (28.35 g) tubes NDC 49158-200-08,
16 oz (453.6 g) jars NDC 49158-200-16.

Hydrocortisone Lotion USP, 2.5% in
2 fl oz (59.2 mL) bottles NDC 49158-348-32,
4 fl oz (118.3 mL) bottles NDC 49158-348-34.

Hydrocortisone Ointment USP, 1% in
20 g tubes NDC 49158-103-07,
1 oz (28.35 g) tubes NDC 49158-103-08,
16 oz (453.6 g) jars NDC 49158-103-16.

Hydrocortisone Ointment USP, 2.5% in
20 g tubes NDC 49158-347-07,
1 oz (28.35 g) tubes NDC 49158-347-08,
16 oz (453.6 g) jars NDC 49158-347-16.

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, New York 11779

MG #12424 R398

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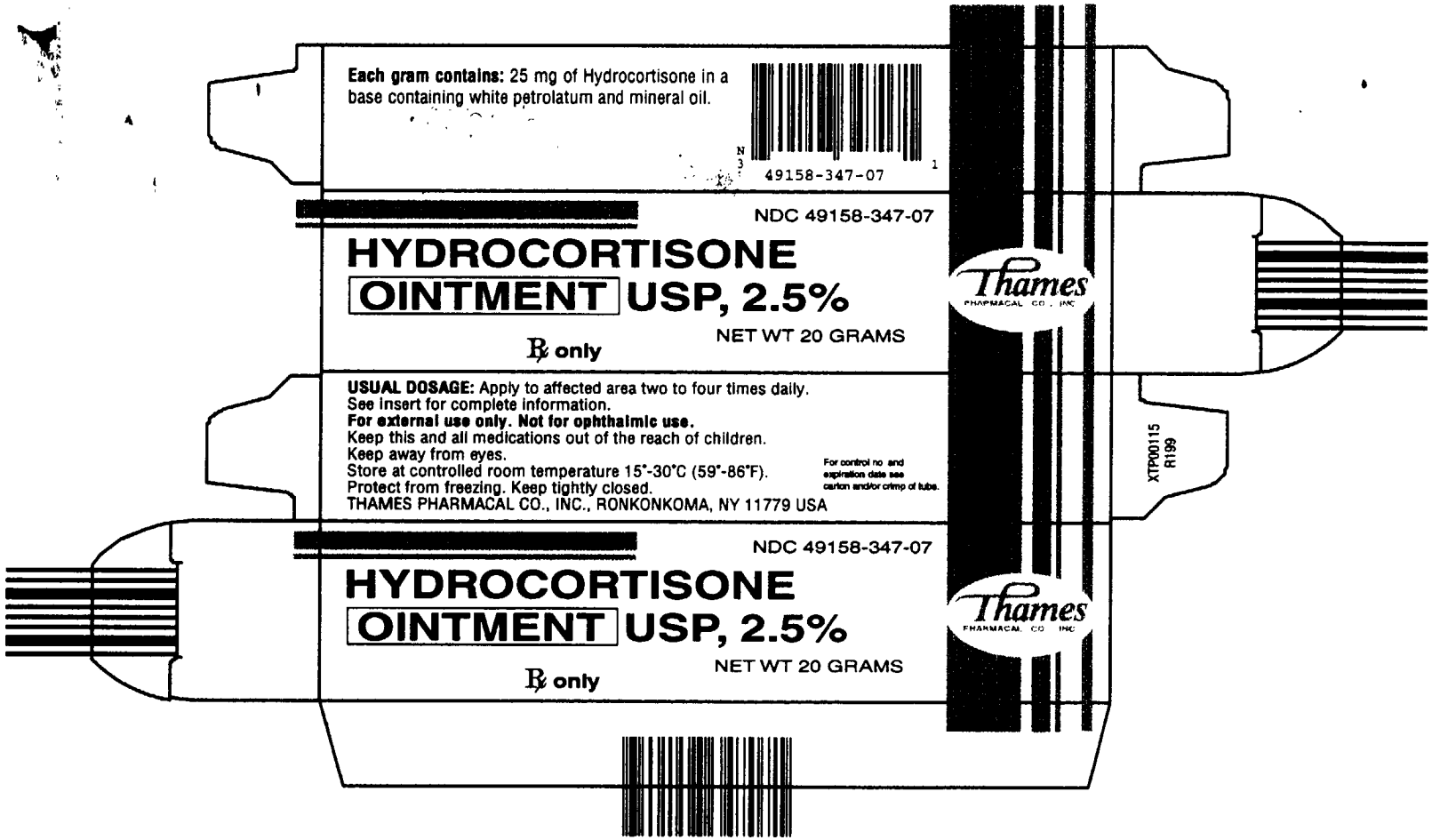
Each gram contains: 25 mg of Hydrocortisone in a base containing white petrolatum and mineral oil.
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OINTMENT USP, 2.5%
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NET WT 20 GRAMS
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Keep away from eyes.
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Protect from freezing. Keep tightly closed.
THAMES PHARMACAL CO., INC., RONKONKOMA, NY 11779 USA
For control no. and expiration date see carton and/or crimp of tube.
Thames
PHARMACAL CO., INC.
XTP00115
R199
NDC 49158-347-07
HYDROCORTISONE
OINTMENT USP, 2.5%
℞ only
NET WT 20 GRAMS
Thames
PHARMACAL CO., INC.