CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-489

FINAL PRINTED LABELING

AUG 12 1998

NDC 38245-679-70

HYDROCORTISONE VALERATE CREAM USP, 0.2%

15 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophilic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and water.

See crimp for lot number and expiration date.

Copley Pharmaceutical, Inc., Canton, MA 02021 TUB800700

APPROVED

NDC 38245-679-73

HYDROCORTISONE VALERATE CREAM USP, 0.2%

60 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

For topical use only.

Not for use in eyes.

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See crimp for lot number and expiration date.

Copley Pharmaceutical, Inc., Canton, MA 02021 TUB800900

APPROVED

AUG 12 1998

NDC 38245-679-72

HYDROCORTISONE VALERATE CREAM USP, 0.2%

45 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

For topical use only.

Not for use in eyes.

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Each gram contains: 2 mg Hydrocortisone valerate in a hydrophilic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and water.

See crimp for lot number and expiration date.

Copley Pharmaceutical, Inc., Canton, MA 02021 TUB800800

APPROVED

AUG 12 1998

NDC 38245-679-75

HYDROCORTISONE VALERATE CREAM USP, 0.2%

120 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

For topical use only.

Not for use in eyes.

AUG 12 19

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and water.

See crimp for lot number and expiration date.

Copley Pharmaceutical, Inc., Canton, MA 02021

TUB801000

For topical use only.
Not for use in eyes.
USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily.
Read accompanying information carefully.
Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

NDC 38245-679-70

HYDROCORTISONE VALERATE CREAM USP, 0.2%

15 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

CAR603900

For topical use only.
Not for use in eyes.
USUAL DOSAGE: Apply a small amount to affected areas
2 or 3 times daily. Read accompanying information carefully.
Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

3 38245-679-70 6

NDC 38245-679-70

HYDROCORTISONE VALERATE CREAM USP, 0.2%

15 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

NDC 38245-679-70
HYDROCORTISONE VALERATE
CREAM USP, 0.2%
15 g

CAR603900

AUG 12 1998

WARNING!
DO NOT MODIFY DIE LINE
PRINT SIDE SHOWN

For topical use only.
Not for use in eyes.
USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully
Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

NDC 38245-679-70

HYDROCORTISONE VALERATE CREAM USP, 0.2%

15 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

APPROVED
AUG 12 1998

CAR603900

For topical use only.
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Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

3 38245-679-70 6

NDC 38245-679-70

HYDROCORTISONE VALERATE CREAM USP, 0.2%

15 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

NDC 38245-679-70
HYDROCORTISONE VALERATE CREAM USP, 0.2%
15 g

CAR603900

0577E1A1
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RT CTN

WARNING!
DO NOT MODIFY DIE LINE

PRINT SIDE SHOWN

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

NDC 38245-679-72

HYDROCORTISONE VALERATE CREAM USP, 0.2%

45 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

CAR604000

AUG 12 1998

APPROVED

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

3 38245-679-72 0

NDC 38245-679-72

HYDROCORTISONE VALERATE CREAM USP, 0.2%

45 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

NDC 38245-679-72
HYDROCORTISONE VALERATE CREAM USP, 0.2%
45 g

CAR604000

0577E3A1
PRINTED SIDE SHOWN

WARNING!
DO NOT MODIFY DIE LINE

PRINT SIDE SHOWN

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

NDC 38245-679-73

HYDROCORTISONE VALERATE CREAM USP, 0.2%

60 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

AUG 1 2

CAR604100

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

APPROVED

3 38245-679-73 7

NDC 38245-679-73

HYDROCORTISONE VALERATE CREAM USP, 0.2%

60 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

CAR604100

NDC 38245-679-73
HYDROCORTISONE VALERATE
CREAM USP, 0.2% 60 g

0577E3A1

PRINTED SIDE SHOWN

WARNING!
DO NOT MODIFY DIE LINE

PRINT SIDE SHOWN

APPROVED
AUG 12 1998

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

NDC 38245-679-75

HYDROCORTISONE VALERATE CREAM USP, 0.2%

120 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

For topical use only.

Not for use in eyes.

USUAL DOSAGE: Apply a small amount to affected areas 2 or 3 times daily. Read accompanying information carefully.

Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and purified water.

3 38245-679-75 1

NDC 38245-679-75

HYDROCORTISONE VALERATE CREAM USP, 0.2%

120 g

CAUTION: Federal law prohibits dispensing without prescription.

Store below 26°C (78°F).

Copley Pharmaceutical, Inc.
Canton, MA 02021

NDC 38245-679-75
HYDROCORTISONE VALERATE CREAM USP, 0.2%
120 g

CAR603800

HYDROCORTISONE VALERATE CREAM USP, 0.2%

For topical use only. Not for use in eyes.

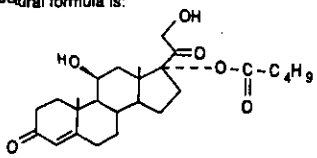
LEA504800
Revised: July 1996

LEA504800

LEA504800

DESCRIPTION

Hydrocortisone Valerate Cream is a topical formulation containing hydrocortisone valerate, a non-fluorinated steroid. It has the chemical name Pregn-4-ene-3,20-dione, 11(21-dihydroxy-17-[(1-oxopentyl) oxy]-,(11β)-; the empirical formula is $C_{26}H_{38}O_6$; the molecular weight is 446.58, and the CAS registry number is: 57524-89-7. The structural formula is:



AUG 12 1998

APPROVED

Each gram of Hydrocortisone Valerate Cream USP, 0.2% contains 2 mg hydrocortisone valerate in a hydrophilic base composed of white petrolatum, stearyl alcohol, propylene glycol, amphoteric-9, carbomer 940, dibasic sodium phosphate anhydrous, sodium lauryl sulfate, sorbic acid and water.

CLINICAL PHARMACOLOGY

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

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear.[1] Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids.[2] There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.[3]

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.[4,5,6]

Topical corticosteroids can be absorbed from normal intact skin.[5,6,7] Inflammation and/or other disease processes in the skin increase percutaneous absorption.[8] Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids.[4,7] 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

Hydrocortisone valerate cream is indicated for the relief of the inflammatory and pruritic manifestations of the 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.[9]

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.[10]

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.[10] Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.[11,12]

Pediatric patients may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity[13,14] (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 dressing.

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.[15,16]

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 corticosteriods. 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.[17,18] 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

Hydrocortisone valerate cream should be applied to the affected area as a thin film two or three 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.

HOW SUPPLIED

Hydrocortisone Valerate Cream USP, 0.2% is supplied in the following tube sizes:

15 g NDC 38245-679-70
45 g NDC 38245-679-72
60 g NDC 38245-679-73
120 g NDC 38245-679-75

Store below 26°C (78°F).

Caution: Federal law prohibits dispensing without prescription.

REFERENCES -

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Copley Pharmaceutical, Inc.
Canton, MA 02021

Revised: July 1996
LEA504800
MG #12193