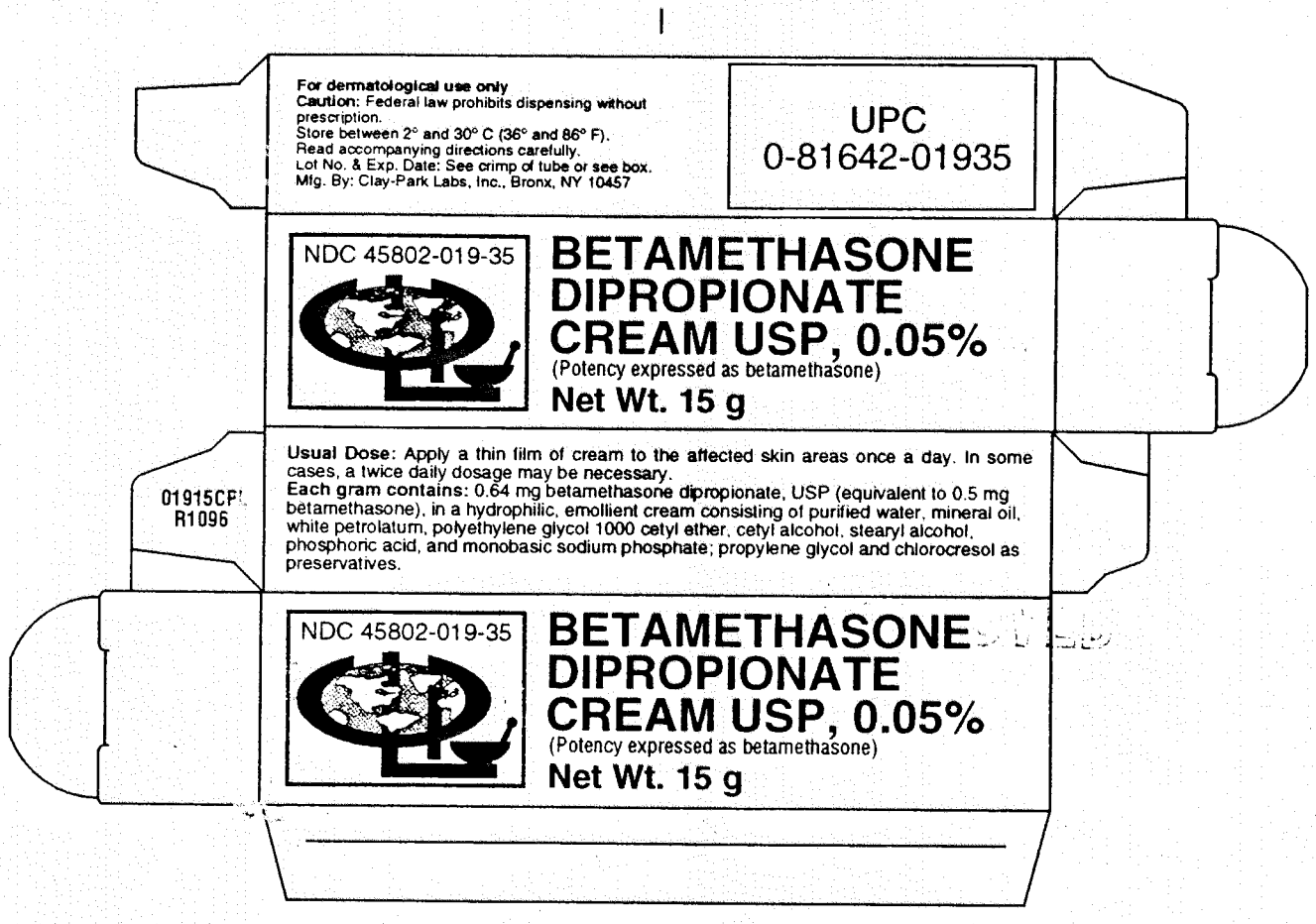
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 74-579

PRINTED LABELING



DIE # C8061 CODE # 108 PMS 320, BLACK

For dermatological use only
Caution: Federal law prohibits dispensing without prescription.
Store between 2° and 30° C (36° and 86° F).
Read accompanying directions carefully.
Lot No. & Exp. Date: See crimp of tube or see box.
Mfg. By: Clay Park Labs, Inc., Bronx, NY 10457

UPC
0-81642-01942

NDC 45802-019-42

BETAMETHASONE DIPROPIONATE CREAM USP, 0.05%

(Potency expressed as betamethasone)

Net Wt. 45 g

01945CPL
R1096

Usual Dose: Apply a thin film of cream to the affected skin areas once a day. In some cases, a twice daily dosage may be necessary.
Each gram contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg betamethasone), in a hydrophilic, emollient cream consisting of purified water, mineral oil, white petrolatum, polyethylene glycol 1000 cetyl ether, cetyl alcohol, stearyl alcohol, phosphoric acid, and monobasic sodium phosphate; propylene glycol and chlorocresol as preservatives.

NDC 45802-019-42

BETAMETHASONE DIPROPIONATE CREAM USP, 0.05%

(Potency expressed as betamethasone)

Net Wt. 45 g

DIE # C7062G CODE # 108 PMS 320, BLACK

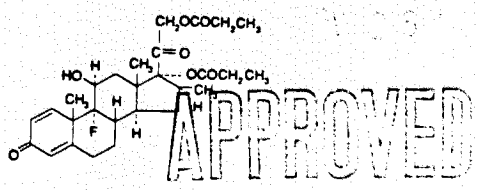
BETAMETHASONE DIPROPIONATE

Cream, USP 0.05%
Lotion, USP 0.05% w/w
(Potency Expressed as Betamethasone)
For Dermatologic Use Only - Not for Ophthalmic Use

DESCRIPTION

Betamethasone Dipropionate products contain betamethasone dipropionate, USP, a synthetic adrenocorticosteroid, for dermatologic use. Betamethasone, an analog of prednisolone, has high corticosteroid activity and slight mineralocorticoid activity. Betamethasone dipropionate is the 17, 21-dipropionate ester of betamethasone.

Chemically, betamethasone dipropionate is 9-Fluoro-11, 17, 21-trihydroxy-16-methyl-pregna-1,4-diene-3, 20-dione 17, 21-dipropionate, with the molecular formula $C_{28}H_{37}FO_7$, a molecular weight of 504.6, and the following structural formula:



APPROVED

Betamethasone dipropionate is a white to creamy white, odorless crystalline powder, insoluble in water.

Each gram of Betamethasone Dipropionate Cream 0.05% contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg betamethasone), in a hydrophilic emollient cream consisting of purified water, mineral oil, white petrolatum, polyethylene glycol 1000 cetyl ether, cetyl alcohol, stearyl alcohol, phosphoric acid, and monobasic sodium phosphate, propylene glycol and chlorocresol as preservatives.

Each gram of Betamethasone Dipropionate Lotion 0.05% w/w contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg betamethasone), in a lotion base of isopropyl alcohol (46.8%) and purified water slightly thickened with carbopol 934-P; the pH is adjusted to approximately 4.7 with sodium hydroxide.

CLINICAL PHARMACOLOGY

The corticosteroids are a class of compounds comprising steroid hormones secreted by the adrenal cortex and their synthetic analogs. In pharmacologic doses corticosteroids are used primarily for their anti-inflammatory and/or immunosuppressive effects.

Topical corticosteroids, such as betamethasone dipropionate, are effective in the treatment of corticosteroid-responsive dermatoses primarily because of their anti-inflammatory, antipruritic, and vasoconstrictive actions. However, while the physiologic, pharmacologic, and clinical effects of the corticosteroids are well-known, the exact mechanisms of their actions in each disease are uncertain. Betamethasone dipropionate, a corticosteroid, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs.

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. (See **DOSAGE AND ADMINISTRATION** section.)

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. (See DOSAGE AND ADMINISTRATION section.)

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

Betamethasone Dipropionate products are indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Betamethasone Dipropionate products are contraindicated in patients who are hypersensitive to betamethasone dipropionate, to other corticosteroids, or to any ingredient in these preparations.

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. (See **DOSAGE AND ADMINISTRATION** section.)

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area 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 Patients

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. (See **DOSAGE AND ADMINISTRATION** section.)
4. Patients should report any signs of local adverse reactions.
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. (See **DOSAGE AND ADMINISTRATION** section.)

Laboratory Tests

The following tests may be helpful in evaluating 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 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 prescribed for 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 greater skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children 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 children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently when Betamethasone Dipropionate products are used as recommended in the **DOSAGE AND ADMINISTRATION** section. 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.

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.

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

Betamethasone Dipropionate cream: Apply a thin film of Betamethasone Dipropionate Cream 0.05% to the affected skin areas once daily. In some cases, a twice daily dosage may be necessary.

Betamethasone Dipropionate lotion: Apply a few drops Betamethasone Dipropionate lotion 0.05% to the affected area; massage lightly until it disappears. Apply twice daily, in the morning and at night. For the most effective and economical use, apply nozzle very close to affected area and gently squeeze bottle.

HOW SUPPLIED

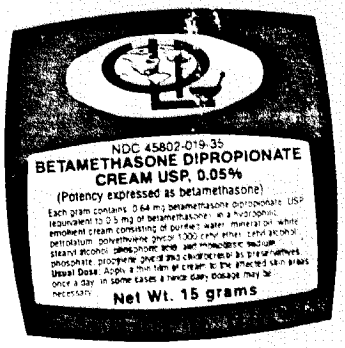
Betamethasone Dipropionate Cream 0.05% is supplied in 15 gram (NDC 45802-019-35) and 45 gram (NDC 45802-019-35) tubes; boxes of one.

Betamethasone Dipropionate Lotion 0.05% w/w is available in 20 mL (NDC 45802-021-97) and 60 mL (NDC 45802-021-46) plastic squeeze bottles; boxes of one. **Protect from light. Store in carton until contents are used.**

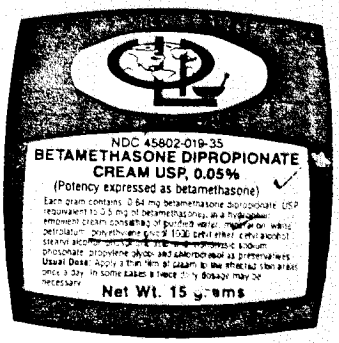
Store all BETAMETHASONE DIPROPIONATE preparations between 2° and 30° C (36° and 86° F).

Clay-Park Labs, Inc.
Bronx, NY 10457

Mfg. by Clay-Park Labs, Inc., Bronx, NY 10457
Rev. 11/95



For dermatological use only
Caution: Federal law prohibits dispensing without prescription.
Read accompanying directions carefully.
Store between 2° and 30° C (36° and 86° F).
Lot No. & Exp. Date: See crimp of tube or see box. R1
Mfg. By: Clay-Park Labs, Inc. Bronx, NY 10457



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Lot No. & Exp. Date: See crimp of tube or see ...x. R1
Mfg. By: Clay-Park Labs, Inc. Bronx, NY 1045...

BLF. GREEN

Date:

01915CPL

BDN

Each gram contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg of betamethasone) a hydrophilic, emollient cream consisting of purified water, mineral oil, white petrolatum, polyethylene glycol 1000 cetyl ether, cetyl alcohol, stearyl alcohol, phosphoric acid, and monobasic sodium phosphate; propylene glycol and chlorocresol as preservatives.
Usual Dose: Apply a thin film of cream to the affected skin areas once a day. In some cases a twice daily dosage may be necessary.

NDC 45802-019-35

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 15 g

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Mfg. By: Clay-Park Labs, Inc. Bronx, NY 10457

R0795

0 81642 01935 3

NDC 45802-019-35

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 15 g

R0795

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01945CPL

NDC 45802-019-42

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 45 g

For dermatological use only
Caution: Federal law prohibits dispensing without prescription.
Read accompanying directions carefully.
Store between 2° and 30° C (36° and 86° F).
Lot No. & Exp. Date: See crimp of tube or see box. R1
Mfg. By: Clay-Park Labs, Inc. Bronx, NY 10457

0 81642 01942 1

NDC 45802-019-42

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 45 g

NDC 45802-019-42

BETAMETHASONE DIPROPIONATE CREAM USP, 0.05%

(Potency expressed as betamethasone)

Each gram contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg of betamethasone) in a hydrophilic emollient cream consisting of purified water, mineral oil, white petrolatum, polyethylene glycol 1000 cetyl ether, cetyl alcohol, stearyl alcohol, phosphoric acid, and monobasic sodium phosphate, propylene glycol and chlorocresol as preservatives.

Usual Dose: Apply a thin film of cream to the affected skin areas once a day. In some cases a twice daily dosage may be necessary.

Net Wt. 45 grams

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Store between 2° and 30° C (36° and 86° F).
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Net Wt. 45 grams

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Lot No. & Exp. Date: See crimp of tube or see box. R1
Mfg. By: Clay-Park Labs, Inc. Bronx, NY 10457

BLA GREEN

Date:

01915CPL

Each gram contains: 0.64 mg betamethasone dipropionate, USP (equivalent to 0.5 mg of betamethasone) a hydrophilic, emollient cream consisting of purified water, mineral oil, white petrolatum, polyethylene glycol 1000 cetyl ether, cetyl alcohol, stearyl alcohol, phosphoric acid, and monobasic sodium phosphate; propylene glycol and chlorocresol as preservatives.
Usual Dose: Apply a thin film of cream to the affected skin areas once a day. In some cases a twice daily dosage may be necessary.

BDN

NDC 45802-019-35

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 15 g

For dermatological use only
Caution: Federal law prohibits dispensing without prescription.
Read accompanying directions carefully.
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R0795

0 81642 01935 3

NDC 45802-019-35

BETAMETHASONE DIPROPIONATE CREAM USP, 0.5%

(Potency expressed as betamethasone)

NET WT. 15 g

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01945CPL

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(Potency expressed as betamethasone)

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