BETAMETHASONE DIPROPIONATE- betamethasone dipropionate ointment
Warrick Pharmaceuticals Corporation

Augmented Betamethasone Dipropionate*
Ointment 0.05%
(potency expressed as betamethasone)

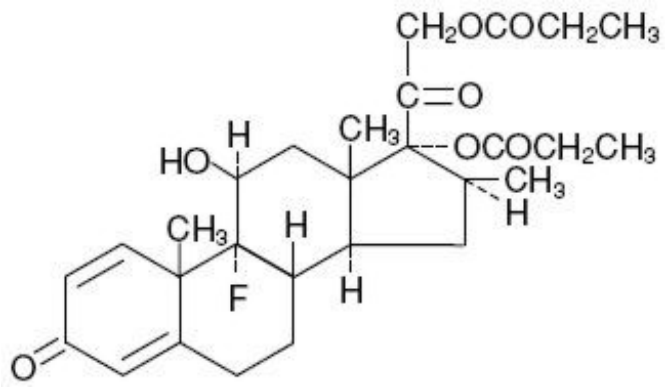
For Dermatologic Use Only– Not for Ophthalmic Use

PRODUCT INFORMATION

DESCRIPTION

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

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



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

Each gram of Augmented Betamethasone Dipropionate Ointment 0.05% contains: 0.643 mg betamethasone dipropionate, USP (equivalent to 0.5 mg betamethasone), in ACTIBASE®, an optimized vehicle of propylene glycol; propylene glycol stearate (55% monoester); white wax; and white petrolatum.

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 may 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 enter 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.

At 14 g per day, Augmented Betamethasone Dipropionate Ointment was shown to depress the plasma levels of adrenal cortical hormones following repeated application to diseased skin in patients with psoriasis. Adrenal depression in these patients was transient, and rapidly returned to normal upon cessation of treatment. At 7 g per day (3.5 g b.i.d.), Augmented Betamethasone Dipropionate Ointment was shown to cause minimal inhibition of the hypothalamic-pituitary-adrenal (HPA) axis when applied two times daily for 2 to 3 weeks, in normal patients and in patients with psoriasis and eczematous disorders.

With 6 g to 7 g of Augmented Betamethasone Dipropionate Ointment applied once daily for 3 weeks, no significant inhibition of the HPA axis was observed in patients with psoriasis and atopic dermatitis, as measured by plasma cortisol and 24-hour urinary 17-hydroxy-corticosteroid levels.

INDICATIONS AND USAGE

Augmented Betamethasone Dipropionate Ointment is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Augmented Betamethasone Dipropionate Ointment is contraindicated in patients who are hypersensitive to betamethasone dipropionate, to other corticosteroids, or to any ingredient in this preparation.

PRECAUTIONS

General

Systemic absorption of topical corticosteroids has produced reversible 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 corticosteroids, 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, reduce the frequency of application, or 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 and should not be used longer than the prescribed time period. 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 that 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.

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 topically applied corticosteroids.

Studies to determine mutagenicity with prednisolone have revealed negative results.

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 of the teratogenic effects of topically applied corticosteroids in pregnant women. 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

Data regarding use of Augmented Betamethasone Dipropionate Ointment in pediatric patients are not available, so use of this product in patients under the age of 12 is not recommended.

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 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 local adverse reactions reported with Augmented Betamethasone Dipropionate Ointment applied either once or twice a day during clinical studies are as follows: erythema, 3 per 767 patients; folliculitis, 2 per 767 patients; pruritus, 2 per 767 patients; vesiculation, 1 per 767 patients.

The following local adverse reactions are reported infrequently when topical corticosteroids are used as recommended. 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 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

Apply a thin film of Augmented Betamethasone Dipropionate Ointment to the affected skin areas once or twice daily. Treatment with Augmented Betamethasone Dipropionate Ointment should be limited to 45 g per week.

Augmented Betamethasone Dipropionate Ointment is not to be used with occlusive dressings.

HOW SUPPLIED

Augmented Betamethasone Dipropionate Ointment 0.05% is supplied in 15-g (NDC 59930-1575-1) and 50-g (NDC 59930-1575-3) tubes; boxes of one.

Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature]

Warrick Pharmaceuticals Corporation
Reno, NV 89506 USA

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BETAMETHASONE DIPROPIONATE

betamethasone dipropionate ointment

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:59930-1575
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
betamethasone dipropionate (UNII: 826Y60901U) (betamethasone - UNII:9842X06Q6M)		0.5 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
propylene glycol (UNII: 6DC9Q167V3)	
propylene glycol stearate ()	
white wax ()	
white petrolatum ()	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:59930-1575-1	1 in 1 BOX		
1		15 g in 1 TUBE		
2	NDC:59930-1575-3	1 in 1 BOX		
2		50 g in 1 TUBE		

Labeler - Warrick Pharmaceuticals Corporation

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