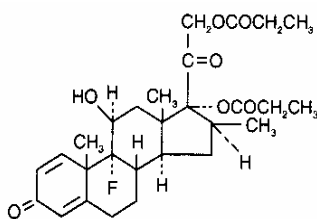


1 DIPROLENE®
2 **Brand of augmented betamethasone dipropionate lotion***
3 **Lotion 0.05% (potency expressed as betamethasone)**
4 * Vehicle augments the penetration of the steroid.
5 **For Dermatologic Use Only**
6 **Not for Ophthalmic Use**
7

8 **DESCRIPTION** DIPROLENE® (augmented betamethasone dipropionate lotion) Lotion
9 contains betamethasone dipropionate, USP, a synthetic adrenocorticosteroid, for
10 dermatologic use. Betamethasone, an analog of prednisolone, has a high degree of
11 corticosteroid activity and a slight degree of mineralocorticoid activity. Betamethasone
12 dipropionate is the 17, 21-dipropionate ester of betamethasone.
13 Chemically, betamethasone dipropionate is 9-fluoro-11β,
14 17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate, with the
15 empirical formula C₂₈H₃₇FO₇, a molecular weight of 504.6 and the following structural
16 formula:



17 It is a white to creamy-white, odorless powder insoluble in water; freely soluble in
18 acetone and in chloroform; sparingly soluble in alcohol.
19 Each gram of DIPROLENE Lotion 0.05% contains 0.643 mg betamethasone
20 dipropionate, USP (equivalent to 0.5 mg betamethasone), in an augmented lotion base
21 of purified water; isopropyl alcohol (30%); hydroxypropylcellulose; propylene glycol;
22 sodium phosphate; phosphoric acid and sodium hydroxide used to adjust the pH.

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

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

34 **Pharmacokinetics:** The extent of percutaneous absorption of topical corticosteroids is
35 determined by many factors including the vehicle, the integrity of the epidermal barrier,
36 and the use of occlusive dressings. (See **DOSAGE AND ADMINISTRATION** section).

37 Topical corticosteroids can be absorbed through normal intact skin. Inflammation and/or
38 other disease processes in the skin may increase percutaneous absorption. Occlusive
39 dressings substantially increase the percutaneous absorption of topical corticosteroids.
40 (See **DOSAGE AND ADMINISTRATION** section.)

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

46 Studies performed with DIPROLENE Lotion indicate that it is in the super-high range of
47 potency as compared with other topical corticosteroids.

48 **INDICATIONS AND USAGE** DIPROLENE Lotion is a super-high potency corticosteroid
49 indicated for the relief of the inflammatory and pruritic manifestations of
50 corticosteroid-responsive dermatoses in patients 13 years and older. The total dose
51 should not exceed 50 mL per week because of the potential for the drug to suppress the
52 hypothalamic-pituitary-adrenal (HPA) axis.

53 **CONTRAINDICATIONS** DIPROLENE Lotion is contraindicated in patients who are
54 hypersensitive to betamethasone dipropionate, to other corticosteroids, or to any
55 ingredient in this preparation.

56 **PRECAUTIONS** Systemic absorption of topical corticosteroids has produced reversible
57 HPA axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and
58 glucosuria in some patients.

59 Conditions which augment systemic absorption include the application of the more
60 potent corticosteroids, use over large surface areas, prolonged use, and the addition of
61 occlusive dressings. Use of more than one corticosteroid-containing product at the

62 same time may increase total systemic glucocorticoid exposure. (See **DOSAGE AND**
63 **ADMINISTRATION** section.)

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

69 Recovery of HPA axis function is generally prompt and complete upon discontinuation
70 of the drug. Patients should not be treated with amounts of DIPROLENE Lotion greater
71 than 50 mL per week because of the potential for the drug to suppress HPA axis.
72 Patients receiving super-potent corticosteroids should not be treated for more than 2
73 weeks at a time and only small areas should be treated at any one time due to the
74 increased risk of HPA axis suppression.

75 DIPROLENE Lotion was applied once daily at 7 mL per day for 21 days to diseased
76 scalp and body skin in patients with scalp psoriasis to study its effects on the HPA axis.
77 In 2 out of 11 patients, the drug lowered plasma cortisol levels below normal limits. HPA
78 axis suppression in these patients was transient and returned to normal within a week.
79 In one of these patients, plasma cortisol levels returned to normal while treatment
80 continued.

81 Infrequently, signs and symptoms of steroid withdrawal may occur, requiring
82 supplemental systemic corticosteroids.

83 Pediatric patients may absorb proportionally larger amounts of topical corticosteroids
84 and thus be more susceptible to systemic toxicity. (See **PRECAUTIONS-Pediatric**
85 **Use.**)

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

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

92 DIPROLENE Lotion should not be used in the treatment of rosacea or perioral
93 dermatitis, and it should not be used on the face, groin or in the axillae.

94 **Information for Patients:** Patients using topical corticosteroids should receive the
95 following information and instructions. This information is intended to aid in the safe and
96 effective use of this medication. It is not a disclosure of all possible adverse or intended
97 effects.

- 98 1. This medication is to be used as directed by the physician and should not be used
99 longer than the prescribed time period. It is for external use only. Avoid contact
100 with the eyes.

- 101 2. This medication should not be used for any disorder other than that for which it was
102 prescribed.
- 103 3. The treated skin area should not be bandaged, or otherwise covered or wrapped,
104 so as to be occlusive (See DOSAGE AND ADMINISTRATION section). .
- 105 4. Patients should report to their physician any signs of local adverse reactions.
- 106 5. Patients should be advised not to use DIPROLENE Lotion in the treatment of diaper
107 dermatitis. DIPROLENE Lotion should not be applied in the diaper areas as diapers
108 or plastic pants may constitute occlusive dressing (See **DOSAGE AND**
109 **ADMINISTRATION**).
- 110 6. This medication should not be used on the face, underarms, or groin areas unless
111 directed by the physician.
- 112 7. As with other corticosteroids, therapy should be discontinued when control is
113 achieved. If no improvement is seen within 2 weeks, contact the physician.
- 114 8. Other corticosteroid-containing products should not be used with Diprolene Lotion.

115 **Laboratory Tests:** The following tests may be helpful in evaluating patients for HPA
116 axis suppression:

- 117 ACTH stimulation test
118 Urinary free cortisol test

119 **Carcinogenesis, mutagenesis, and impairment of fertility:** Long-term animal studies
120 have not been performed to evaluate the carcinogenic potential of betamethasone
121 dipropionate. Betamethasone was negative in the bacterial mutagenicity assay
122 (*Salmonella typhimurium* and *Escherichia coli*), and in the mammalian cell mutagenicity
123 assay (CHO/HGPRT). It was positive in the *in-vitro*, human lymphocyte chromosome
124 aberration assay, and equivocal in the *in-vivo* mouse bone marrow micronucleus assay.
125 This pattern of response is similar to that of dexamethasone and hydrocortisone.
126 Studies in rabbits, mice and rats using intramuscular doses up to 1, 33 and, 2, mg/kg,
127 respectively, resulted in dose related increases in fetal resorptions in rabbits and mice.

128 **Pregnancy: Teratogenic effects: Pregnancy category C.** Corticosteroids have been
129 shown to be teratogenic in laboratory animals when administered systemically at
130 relatively low dosage levels. Some corticosteroids have been shown to be teratogenic
131 after dermal application in laboratory animals. Betamethasone dipropionate has been
132 shown to be teratogenic in rabbits when given by the intramuscular route at doses of
133 0.05 mg/kg. This dose is approximately 0.2 times the human topical dose of
134 DIPROLENE Lotion in mg/m² of body surface area, assuming 100% absorption and the
135 use in a 60 kg person of 7 g per day. The abnormalities observed included umbilical
136 hernias, cephalocele and cleft palate. There are no adequate and well-controlled
137 studies in pregnant women on teratogenic effects from topically applied corticosteroids.
138 DIPROLENE Lotion should be used during pregnancy only if the potential benefit
139 justifies the potential risk to the fetus.

140 **Nursing Mothers:** Systemically administered corticosteroids appear in human milk and
141 could suppress growth, interfere with endogenous corticosteroid production, or cause
142 other untoward effects. It is not known whether topical administration of corticosteroids
143 could result in sufficient systemic absorption to produce detectable quantities in human
144 milk. Because many drugs are excreted in human milk, caution should be exercised
145 when DIPROLENE Lotion is administered to a nursing woman.

146 **Pediatric Use:** Use of DIPROLENE Lotion, 0.05%, in pediatric patients 12 years of age
147 and younger is not recommended. (See **CLINICAL PHARMACOLOGY** and **ADVERSE**
148 **REACTIONS** sections.)

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

152 Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and
153 intracranial hypertension have been reported in children receiving topical
154 corticosteroids. Manifestations of adrenal suppression in children include linear growth
155 retardation, delayed weight gain, low plasma cortisol levels and absence of response to
156 ACTH stimulation. Manifestations of intracranial hypertension include bulging
157 fontanelles, headaches, and bilateral papilledema. Chronic corticosteroid therapy may
158 interfere with the growth and development of children.

159 **ADVERSE REACTIONS** The local adverse reactions which were reported with
160 DIPROLENE Lotion during controlled clinical trials were as follows: erythema, folliculitis,
161 pruritus and vesiculation each occurring in less than 1 % of patients.

162 The following additional local adverse reactions have been reported with topical
163 corticosteroids, and they may occur more frequently with the use of occlusive dressings
164 and higher potency corticosteroids. These reactions are listed in an approximately
165 decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis,
166 hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic
167 contact dermatitis, secondary infection, skin atrophy, striae and miliaria.

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

171 **OVERDOSAGE** Topically applied DIPROLENE Lotion can be absorbed in sufficient
172 amounts to produce systemic effects (See **PRECAUTIONS**).

173 **DOSAGE AND ADMINISTRATION** Apply a few drops of DIPROLENE Lotion to the
174 affected skin once or twice daily and massage lightly until the lotion disappears.

175 DIPROLENE Lotion is a super-high potency topical corticosteroid. **Treatment with**
176 **DIPROLENE Lotion should be limited to two weeks, and amounts greater than 50**
177 **mL per week should not be used.**

178 As with other highly active corticosteroids, therapy should be discontinued when control
179 is achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may
180 be necessary.

181 **DIPROLENE Lotion should not be used with occlusive dressings.** DIPROLENE
182 Lotion should not be applied to the diaper area if the patient requires diapers or plastic
183 pants as these garments may constitute occlusive dressing.

184 **HOW SUPPLIED** DIPROLENE Lotion 0.05% is supplied in 30 mL (29g) (NDC
185 0085-0962-01), and 60 mL (58g) (NDC 0085-0962-02), plastic squeeze bottles; boxes
186 of one.

187 **Store between 2° and 25°C (36°and 77°F).**

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189 Kenilworth, NJ 07033 USA

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