

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-152

LABELING

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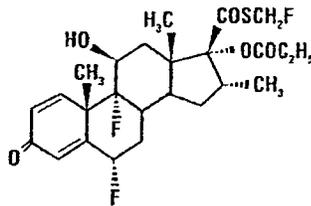
PRODUCT INFORMATION

7 **CUTIVATE®**
8 **(fluticasone propionate)**
9 **Lotion, 0.05%**
10 **Rx Only**

11 **FOR TOPICAL USE ONLY.**
12 **NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.**

13 **DESCRIPTION:** CUTIVATE (fluticasone propionate) Lotion, 0.05% contains fluticasone propionate
14 [S-(fluoromethyl) 6 α ,9-difluoro-11 β ,17-dihydroxy-16 α -methyl-3-oxoandrosta-1,4-diene-17 β -
15 carbothioate, 17-propionate], a synthetic fluorinated corticosteroid, for topical dermatologic use. The
16 topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and
antipruritic agents.

Chemically, fluticasone propionate is C₂₅H₃₁F₃O₅S. It has the following structural formula:



17 Fluticasone propionate is a white to off-white powder with a molecular weight of 500.6. It is
18 practically insoluble in water, freely soluble in dimethyl sulfoxide and dimethylformamide, and
19 slightly soluble in methanol and 95% ethanol.

20 Each gram of CUTIVATE Lotion contains 0.5mg fluticasone propionate in a base of cetostearyl
21 alcohol, isopropyl myristate, propylene glycol, cetomacrogol 1000, dimethicone 360, citric acid,
22 sodium citrate, and purified water, with imidurea, methylparaben, and propylparaben as preservatives.
23

24 **CLINICAL PHARMACOLOGY:** Like other topical corticosteroids, fluticasone propionate has anti-
25 inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory
26 activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the
27 induction of phospholipase A₂ inhibitory proteins, collectively called lipocortins. It is postulated that
28 these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and
29 leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is
30 released from membrane phospholipids by phospholipase A₂.

31 Although fluticasone propionate has a weak affinity for the progesterone receptor and virtually no
32 affinity for the mineralocorticoid, estrogen or androgen receptors, the clinical relevance as related to
33 safety is unknown. Fluticasone propionate is lipophilic and has strong affinity for the glucocorticoid

34 receptor. The therapeutic potency of glucocorticoids is related to the half-life of the glucocorticoid-
35 receptor complex. The half-life of the fluticasone propionate-glucocorticoid receptor complex is
36 approximately 10 hours.

37
38 **Pharmacokinetics: Absorption:** The extent of percutaneous absorption of topical corticosteroids is
39 determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusive
40 dressing enhances penetration. Topical corticosteroids can be absorbed from normal intact skin.
41 Inflammation and/or other disease processes in the skin increase percutaneous absorption.

42 **Distribution:** Following intravenous administration of 1 mg of fluticasone propionate in healthy
43 volunteers, the initial disposition phase for fluticasone propionate was rapid and consistent with its
44 high lipid solubility and tissue binding. The apparent volume of distribution averaged 4.2 L/kg (range,
45 2.3 to 16.7 L/kg). The percentage of fluticasone propionate bound to human plasma proteins averaged
46 91%. Fluticasone propionate is weakly and reversibly bound to erythrocytes. Fluticasone propionate is
47 not significantly bound to human transcortin.

48 **Metabolism:** No metabolites of fluticasone propionate were detected in an in vitro study of
49 radiolabeled fluticasone propionate incubated in a human skin homogenate. The total blood clearance
50 of systemically absorbed fluticasone propionate averages 1093 mL/min (range, 618 to 1702 mL/min)
51 after a 1-mg intravenous dose, with renal clearance accounting for less than 0.02% of the total.

52 Orally absorbed fluticasone propionate has demonstrated extensive first-pass metabolism with no
53 unchanged drug detected in the plasma up to 6 hours after dosing. Fluticasone propionate is
54 metabolized in the liver by cytochrome P450 3A4-mediated hydrolysis of the 5-fluoromethyl
55 carbothiolate grouping. This transformation occurs in 1 metabolic step to produce the inactive 17 β -
56 carboxylic acid metabolite, the only known metabolite detected in man. This metabolite has
57 approximately 2000 times less affinity than the parent drug for the glucocorticoid receptor of human
58 lung cytosol in vitro and negligible pharmacological activity in animal studies. Other metabolites
59 detected in vitro using cultured human hepatoma cells have not been detected in man.

60
61 **Excretion:** Following an intravenous dose of 1 mg in healthy volunteers, fluticasone propionate
62 showed polyexponential kinetics and had an average terminal half-life of 7.2 hours (range, 3.2 to 11.2
63 hours).

64 **Special Population (Pediatric):** Plasma fluticasone levels were measured in patients 2 years - 6
65 years of age in an HPA axis suppression study. A total of 13 (62%) of 21 patients tested had
66 measurable fluticasone at the end of 3 - 4 weeks of treatment. The mean \pm SD fluticasone plasma
67 values for patients aged under 3 years was 47.7 \pm 31.7 pg/mL and 175.5 \pm 243.6 pg/mL. Three patients
68 had fluticasone levels over 300 pg/mL, with one of these having a level of 819.81 pg/mL. No data was
69 obtained for patients < 2 years of age.

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CLINICAL STUDIES: CUTIVATE Lotion applied once daily was superior to vehicle in the treatment of atopic dermatitis in two studies. The two studies enrolled 438 patients with atopic dermatitis aged 3 months and older, of which 169 patients were selected as having clinically significant* signs of erythema, infiltration/papulation and erosion/oozing/crusting at baseline. Table 1 presents the percentage of patients who completely cleared of erythema, infiltration/papulation and erosion/oozing/crusting at Week 4 out of those patients with clinically significant baseline signs.

78 Table 1 - Complete Clearance Rate

	CUTIVATE Lotion	Vehicle
Study 1	9/45 (20%)	0/37 (0%)
Study 2	7/44 (16%)	1/43 (2%)

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*Clinically significant was defined as having moderate or severe involvement for at least two of the three signs (erythema, infiltration/papulation, or erosion/oozing/crusting) in at least 2 body regions. Patients who had moderate to severe disease in a single body region were excluded from the analysis.

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INDICATIONS AND USAGE: CUTIVATE (fluticasone propionate) Lotion is indicated for the relief of the inflammatory and pruritic manifestations of atopic dermatitis in patients 1 year of age or older. The safety and efficacy of drug use for longer than 4 weeks in this population have not been established. The safety and efficacy of CUTIVATE Lotion in pediatric patients below 1 year of age have not been established.

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CONTRAINDICATIONS: CUTIVATE Lotion is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

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PRECAUTIONS:

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General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

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Patients applying a potent topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using cosyntropin (ACTH₁₋₂₄) stimulation testing.

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103 Forty-two pediatric patients (4 months to < 6 years of age) with moderate to severe atopic eczema
104 who were treated with CUTIVATE Lotion for at least 3 -4 weeks were assessed for HPA axis
105 suppression and 40 of these subjects applied at least 90% of applications. None of the 40 evaluable
106 patients suppressed, where the sole criterion for HPA axis suppression is a plasma cortisol level of less
107 than or equal to 18 micrograms per deciliter after cosyntropin stimulation. Although HPA axis
108 suppression was observed in 0 of 40 pediatric patients (upper 95% confidence bound is 7.2%), the
109 occurrence of HPA axis suppression in any patient and especially with longer use cannot be ruled out.
110 In other studies with fluticasone propionate topical formulations, adrenal suppression has been
111 observed.

112 If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the
113 frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is
114 generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of
115 glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids. For
116 information on systemic supplementation, see prescribing information for those products.

117 Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their
118 larger skin surface to body mass ratios (see PRECAUTIONS: Pediatric Use).

119 Fluticasone propionate Lotion, 0.05% may cause local cutaneous adverse reactions (see
120 ADVERSE REACTIONS).

121 If irritation develops, CUTIVATE Lotion should be discontinued and appropriate therapy
122 instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to
123 heal rather than noting a clinical exacerbation as with most topical products not containing
124 corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

125 If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial
126 agent should be used. If a favorable response does not occur promptly, use of CUTIVATE Lotion
127 should be discontinued until the infection has been adequately controlled.

128 CUTIVATE Lotion should not be used in the presence of preexisting skin atrophy and should not
129 be used where infection is present at the treatment site. CUTIVATE Lotion should not be used in the
130 treatment of rosacea and perioral dermatitis.

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132 **Information for Patients:** Patients using CUTIVATE Lotion should receive the following
133 information and instructions:

- 134 1. CUTIVATE Lotion is to be used as directed by the physician. It is for external use only. Avoid
135 contact with the eyes.
- 136 2. CUTIVATE Lotion should not be used for any disorder other than that for which it was prescribed.
- 137 3. The treated skin area should not be bandaged or otherwise covered or wrapped so as to be occlusive
138 unless directed by the physician.
- 139 4. Patients should report to their physician any signs of local adverse reactions.
- 140 5. Parents of pediatric patients should be advised not to use this medication in the treatment of diaper
141 dermatitis unless directed by the physician. CUTIVATE Lotion should not be applied in the diaper
142 areas as diapers or plastic pants may constitute occlusive dressing (see DOSAGE AND
143 ADMINISTRATION).
- 144 6. CUTIVATE Lotion should not be used on the face, underarms, or groin areas unless directed by a
145 physician.
- 146 7. CUTIVATE Lotion therapy should be discontinued if control is achieved before 4 weeks. If no
147 improvement is seen within 2 weeks, contact a physician. The safety of the use of CUTIVATE Lotion
148 for longer than 4 weeks has not been established.

149

50 **Laboratory Tests:** The cosyntropin (ACTH₁₋₂₄) stimulation test may be helpful in evaluating patients
151 for HPA axis suppression.

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153 **Carcinogenesis, Mutagenesis, and Impairment of Fertility:** No studies were conducted to determine
154 the photoco-carcinogenic potential of CUTIVATE Lotion.

155

156 In an oral (gavage) mouse carcinogenicity study, doses of 0.1, 0.3 and 1 mg/kg/day fluticasone
157 propionate were administered to mice for 18 months. Fluticasone propionate demonstrated no
158 tumorigenic potential at oral doses up to 1 mg/kg/day (less than the MRHD in adults based on body
159 surface area comparisons) in this study.

160

161 In a dermal mouse carcinogenicity study, 0.05% fluticasone propionate ointment (40 µl) was topically
162 administered for 1, 3 or 7 days/week for 80 weeks. Fluticasone propionate demonstrated no
163 tumorigenic potential at dermal doses up to 6.7 µg/kg/day (less than the MRHD in adults based on
164 body surface area comparisons) in this study.

165

166 Fluticasone propionate revealed no evidence of mutagenic or clastogenic potential based on the results
167 of five in vitro genotoxicity tests (Ames assay, *E. coli* fluctuation test, *S. cerevisiae* gene conversion
168 test, Chinese hamster ovary cell chromosome aberration assay and human lymphocyte chromosome
169 aberration assay) and one in vivo genotoxicity test (mouse micronucleus assay).

170 No evidence of impairment of fertility or effect on mating performance was observed in a fertility and
171 general reproductive performance study conducted in male and female rats at subcutaneous doses up to
172 50 µg/kg/day (less than the MRHD in adults based on body surface area comparisons).
173

174 **Pregnancy: Teratogenic Effects:** Pregnancy Category C. Corticosteroids have been shown to be
175 teratogenic in laboratory animals when administered systemically at relatively low dosage levels.
176 Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.
177

178 Systemic embryofetal development studies were conducted in mice, rats and rabbits. Subcutaneous
179 doses of 15, 45 and 150 µg/kg/day of fluticasone propionate were administered to pregnant female
180 mice from gestation days 6 – 15. A teratogenic effect characteristic of corticosteroids (cleft palate)
181 was noted after administration of 45 and 150 µg/kg/day (less than the MRHD in adults based on body
182 surface area comparisons) in this study. No treatment related effects on embryofetal toxicity or
183 teratogenicity were noted at 15 µg/kg/day (less than the MRHD in adults based on body surface area
184 comparisons).
185

186 Subcutaneous doses of 10, 30 and 100 µg/kg/day of fluticasone propionate were administered to
187 pregnant female rats in two embryofetal development studies (one study administered fluticasone
188 propionate from gestation days 6 – 15 and the other study from gestation days 7 – 17). In the presence
189 of maternal toxicity, fetal effects noted at 100 µg/kg/day (less than the MRHD in adults based on body
190 surface area comparisons) included decreased fetal weights, omphalocele, cleft palate, and retarded
191 skeletal ossification. No treatment related effects on embryofetal toxicity or teratogenicity were noted
192 at 10 µg/kg/day (less than the MRHD in adults based on body surface area comparisons).
193

194 Subcutaneous doses of 0.08, 0.57 and 4 µg/kg/day of fluticasone propionate were administered to
195 pregnant female rabbits from gestation days 6 – 18. Fetal effects noted at 4 µg/kg/day (less than the
196 MRHD in adults based on body surface area comparisons) included decreased fetal weights, cleft
197 palate and retarded skeletal ossification. No treatment related effects on embryofetal toxicity or
198 teratogenicity were noted at 0.57 µg/kg/day (less than the MRHD in adults based on body surface area
199 comparisons).
200

201 Oral doses of 3, 30 and 300 µg/kg/day fluticasone propionate were administered to pregnant female
202 rabbits from gestation days 8 – 20. No fetal or teratogenic effects were noted at oral doses up to 300
203 µg/kg/day (less than the MRHD in adults based on body surface area comparisons) in this study.
204 However, no fluticasone propionate was detected in the plasma in this study, consistent with the
205 established low bioavailability following oral administration (see CLINICAL PHARMACOLOGY).
206

207 Fluticasone propionate crossed the placenta following administration of a subcutaneous or an oral dose
208 of 100 µg/kg tritiated fluticasone propionate to pregnant rats.

.09 There are no adequate and well-controlled studies in pregnant women. During clinical trials of
210 CUTIVATE Lotion, women of childbearing potential were required to use contraception to avoid
211 pregnancy. Therefore, CUTIVATE Lotion should be used during pregnancy only if the potential
212 benefit justifies the potential risk to the fetus.

213

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

220

221 **Pediatric Use:** CUTIVATE Lotion may be used in pediatric patients as young as 1 year of age. The
222 safety and efficacy of CUTIVATE Lotion in pediatric patients below 1 year of age have not been
223 established.

224 Forty-two pediatric patients (4 months to < 6 years of age) with moderate to severe atopic eczema
225 who were treated with CUTIVATE Lotion for at least 3 -4 weeks were assessed for HPA axis
226 suppression and 40 of these subjects applied at least 90% of applications. None of the 40 evaluable
227 patients suppressed, where the sole criterion for HPA axis suppression is a plasma cortisol level of less
228 than or equal to 18 micrograms per deciliter after cosyntropin stimulation. Although HPA axis
229 suppression was observed in 0 of 40 pediatric patients (upper 95% confidence bound is 7.2%), the
230 occurrence of HPA axis suppression in any patient and especially with longer use cannot be ruled out.

231 In other studies with fluticasone propionate topical formulations, adrenal suppression has been
232 observed. CUTIVATE (fluticasone propionate) Cream, 0.05% caused HPA axis suppression in 2 of 43
233 pediatric patients, aged 2 and 5 years old, who were treated for 4 weeks covering at least 35% of the
234 body surface area. Follow-up testing 12 days after treatment discontinuation, available for 1 of the 2
235 patients, demonstrated a normally responsive HPA axis.

236 HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and
237 intracranial hypertension have been reported in pediatric patients receiving topical corticosteroids.
238 Manifestations of adrenal suppression in pediatric patients include low plasma cortisol levels to an
239 absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging
240 fontanelles, headaches, and bilateral papilledema.

241 In addition, local adverse events including cutaneous atrophy, striae, telangiectasia, and
242 pigmentation change have been reported with topical use of corticosteroids in pediatric patients

243 **Geriatric Use:** A limited number of patients above 65 years of age have been treated with CUTIVATE
 244 Lotion in US and non-US clinical trials. Specifically only 8 patients above 65 years of age were
 245 treated with CUTIVATE Lotion in controlled clinical trials. The number of patients is too small to
 246 permit separate analyses of efficacy and safety.

247
 248 **ADVERSE REACTIONS:** In 2 multicenter vehicle-controlled clinical trials of once-daily application
 249 of CUTIVATE Lotion by 196 adult and 242 pediatric patients, the total incidence of adverse reactions
 250 considered drug related by investigators was approximately 4%. Events were local cutaneous events,
 251 usually mild and self-limiting, and consisted primarily of burning/stinging (2%). All other drug-
 252 related events occurred with an incidence of less than 1%, and inclusively were contact dermatitis,
 253 exacerbation of atopic dermatitis, folliculitis of legs, pruritus, pustules on arm, rash, and skin
 254 infection.

255 The incidence of drug-related events on drug compared to vehicle (4% and 5%, respectively) was
 256 similar. The incidence of drug-related events between study populations of 242 pediatric patients (age
 257 3 months to < 17 years) and 196 adult patients (17 years or older) (4% and 5%, respectively) was also
 258 similar.

259 In an open-label study of 44 pediatric patients applying CUTIVATE Lotion to at least 35% of body
 260 surface area twice daily for 3 or 4 weeks, the overall incidence of drug-related adverse events was
 261 14%. Events were local, cutaneous, and inclusively were dry skin (7%), stinging at application site
 262 (5%), and excoriation (2%).

63

264 **Table 2: Drug Related Adverse Events from Controlled Clinical Trials (n=438)**

Adverse Events	CUTIVATE Lotion N=221	Vehicle N=217
Burning/Stinging skin	4 (2%)	3 (1%)
Contact Dermatitis	0	1 (<1%)
Exacerbation of Atopic dermatitis	0	1 (<1%)
Folliculitis of legs	2 (<1%)	0
Irritant Contact Dermatitis	0	1 (<1%)
Pruritus	1 (<1%)	1 (<1%)
Pustules on Arms	1 (<1%)	0
Rash	1 (<1%)	2 (<1%)
Skin Infection	0	3 (1%)

265

.66

267

Table 3: Drug Related Adverse Events From Pediatric Open Label Trial (n=44)

Adverse Events	CUTIVATE Lotion Twice Daily
Dry skin at multiple sites	3 (7%)
Stinging at Application Sites	2 (5%)
Excoriation	1 (2%)

268

269

The table below summarizes all adverse events by body system that occurred in at least 1% of patients in either the drug or vehicle group in controlled clinical trials.

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271

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Table 4: Adverse Events Occurring in ≥ 1% of Patients from Either Arm from Controlled Clinical Trials (n=438)

273

Body System	CUTIVATE Lotion N = 221	Vehicle Lotion N = 217
Any Adverse Event	77 (35%)	82 (38%)
Skin		
Burning and Stinging	4 (2%)	3 (1%)
Pruritus	3 (1%)	5 (2%)
Rash	2 (<1%)	3 (1%)
Skin Infection	0	3 (1%)
Ear, Nose, Throat		
Common Cold	9 (4%)	5 (2%)
Ear Infection	3 (1%)	3 (1%)
Nasal Sinus Infection	2 (<1%)	4 (2%)
Rhinitis	1 (<1%)	3 (1%)
Upper Respiratory Tract Infection	6 (3%)	7 (3%)
Gastrointestinal		
Normal Tooth Eruption	2 (< 1%)	3 (1%)
Diarrhea	3 (1%)	0
Vomiting	3 (1%)	2 (<1%)
Lower Respiratory		
Cough	7 (3%)	6 (3%)
Influenza	5 (2%)	0
Wheeze	0	3 (1%)
Neurology		
Headache	4 (2%)	5 (2%)
Non-Site Specific		
Fever	8 (4%)	8 (4%)
Seasonal Allergy	2 (<1%)	3 (1%)

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277 During the clinical trials, eczema herpeticum occurred in a 33-year-old male patient treated with
278 CUTIVATE Lotion. Additionally, a 4-month-old patient treated with CUTIVATE Lotion in the open-
279 label trial had marked elevations of the hepatic enzymes AST and ALT. Reported systemic post-
280 marketing systemic adverse events with CUTIVATE Cream and CUTIVATE Ointment have included:
281 immunosuppression/Pneumocystis carinii pneumonia/leukopenia/thrombocytopenia;
282 hyperglycemia/glycosuria; Cushing syndrome; generalized body edema/blurred vision; and acute
283 urticarial reaction (edema, urticaria, pruritus, and throat swelling). A causal role of CUTIVATE in
284 most cases could not be determined because of the concomitant use of topical corticosteroids,
285 confounding medical conditions, and insufficient clinical information.

286

287 The following local adverse reactions have been reported infrequently with topical
288 corticosteroids, and they may occur more frequently with the use of occlusive dressings and higher
289 potency corticosteroids. These reactions are listed in an approximately decreasing order of occurrence:
290 irritation, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact
291 dermatitis, secondary infection, skin atrophy, striae, and miliaria. Also, there are reports of the
292 development of pustular psoriasis from chronic plaque psoriasis following reduction or discontinuation
293 of potent topical corticosteroid products.

294

295 **OVERDOSAGE:** Topically applied CUTIVATE Lotion can be absorbed in sufficient amounts to
296 produce systemic effects (see PRECAUTIONS).

297

298 **DOSAGE AND ADMINISTRATION:** CUTIVATE Lotion may be used in adult and pediatric
299 patients 1 year of age or older. The safety and efficacy of CUTIVATE Lotion in pediatric patients
300 below 1 year of age have not been established (see PRECAUTIONS: Pediatric Use).

301 **Atopic Dermatitis:** Apply a thin film of CUTIVATE Lotion to the affected skin areas once daily. Rub
302 in gently.

303

304 As with other corticosteroids, therapy should be discontinued when control is achieved. If no
305 improvement is seen within 2 weeks, reassessment of diagnosis may be necessary. The safety and
306 efficacy of drug use for longer than 4 weeks have not been established.

306

307 CUTIVATE Lotion should not be used with occlusive dressings or applied in the diaper area unless
directed by a physician.

308

309 **HOW SUPPLIED:** CUTIVATE Lotion is supplied in 60 mL bottle (NDC 0173-0708-00).

310 Store between 15° and 30°C (59° and 86°F). Do not refrigerate. Keep container tightly

311 sealed.

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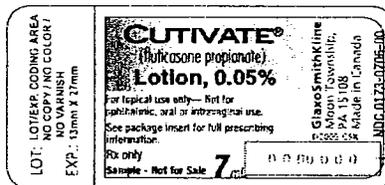
315 GLAXOSMITHKLINE CONSUMER HEALTHCARE, L.P.

316 Moon Township, PA 15108

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318 March 2005

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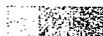
PART NUMBER
SEE NOTE 1

FOR YOUR PROTECTION ONLY
PLEASE EXAMINE CAREFULLY

GlaxoSmithKline		PACKAGING SPECIFICATION		Date: Art for Pegasus (03.23.05)
S A M 1000 GSK Drive, Moon Township, PA 15108				
PACE NO.:		UPC/SKU NO.:		
BRAND: Cultivate Lotion		E.V. NO. & FORMAT: N/A		
DESCRIPTION: fluticasone propionate 0.05%		DIMENSIONS: 57.15mm x 27mm		
COMPONENT: Label		DIE NO.: CUT0003LB		
VOLUME CONTENTS/SIZE: 7mL		PACKAGING SITE: Mississauga		
FORM NO.:		PRINTER: Jones Packaging		
COUNTRY: U.S.A.		PREPRESS: Schawk		
Computer Software: Adobe Illustrator 10		REPLACES FORM NO.: New		
Artist: Christina Pochiba		REVISION 1:		
KEYWORDS:		REVISION 2:		
S C H A W K Kalamazoo 2325 N. Burdick St. • Kalamazoo, MI 49007 • (269) 381-3820				
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PRINTER PLEASE NOTE YOUR RESPONSIBILITIES:		SALES SERVICE:		
* Inspect all incoming materials upon receipt.		BAR:		
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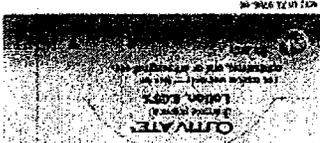


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Scale

NO COPY AREA



LOT/EXP CODE AREA
NO COPY/COLOR
8mm X 14mm

Caution: For external use only. Do not use if you are pregnant or breastfeeding. Do not use if you are allergic to any of the ingredients. Do not use if the product has expired. Do not use if the product is damaged. Do not use if the product is contaminated. Do not use if the product is expired.

Usual Dosage: Apply a thin layer of cream to the affected area twice daily. Do not use for more than 14 days. Do not use for more than 14 days. Do not use for more than 14 days. Do not use for more than 14 days.

GlaxoSmithKline Consumer Healthcare, Inc.
Mason Township, PA 15705, USA & Canada
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Once Daily Dosing

Tamper Evident Feature:
Do not use if the seal is broken or if the seal is missing or if the seal is damaged.

REC 0173 0106-30



For topical use only - Not for oral use. Do not use if you are pregnant or breastfeeding. Do not use if you are allergic to any of the ingredients. Do not use if the product has expired. Do not use if the product is damaged. Do not use if the product is contaminated. Do not use if the product is expired.

6mm x 7mm



Once Daily Dosing

GLUE FLAP
NO COPY/HORNISH

PART NO.
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PART NO.

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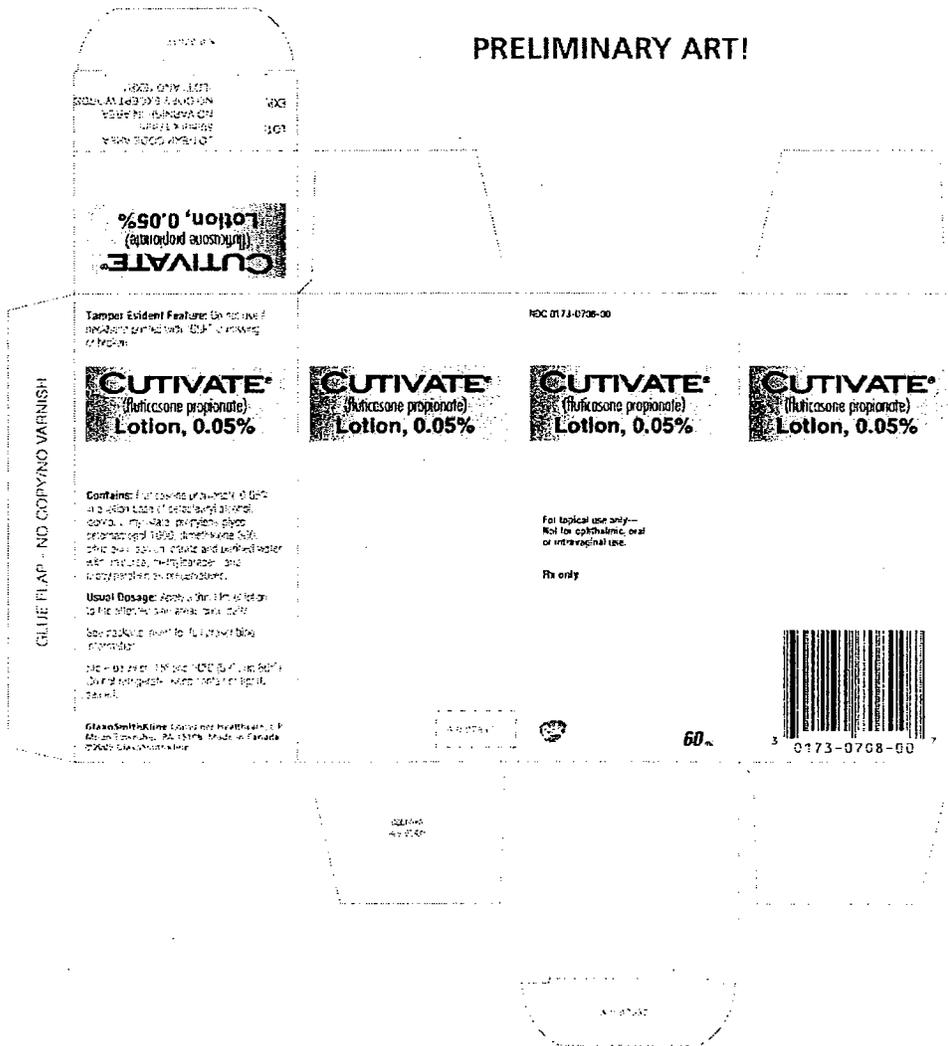


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PRELIMINARY ART!



LAYOUT PURPOSES ONLY
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GlaxoSmithKline		PACKAGING SPECIFICATION		Date: Art for Pegasus (US 23 05)
S A M 1400 GEN Drive, Merck Research, PA 19380				
PAGE NO.	1	UPD 54U NO:	5-0173-0708-00-7	
BRAND	Cutivate Lotion	REV. NO. & FORMAT	NEW	
DESCRIPTION	Miconazole propionate 0.05%	DIMENSIONS	50mm x 50 mm x 105mm	
COMPONENT	Clonaz	DIE NO. CUTJECT		
VOLUME CONTENTS/SIZE	30ml	PACKAGING SITE	Marietta, GA	
FORM NO.		PRINTER	John Packaging	
COUNTRY	U.S.A.	PREPRESS	Senwak	
Computer Software	Amiga (320x200) 10	REPLACES FORM NO.	New	
ATAI	Chlorine Routine	REVISION	1	
KEYWORDS		REVISION 2		
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JOB NUMBER		DATE		
		OPERATOR		
		SALES SERVICE		
		BAR		
		DISTORTION	100% x 100%	
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PRELIMINARY ART!

NDC 0173-0708-00



CUTIVATE®
(fluticasone propionate)
Lotion, 0.05%

For topical use only—
Not for ophthalmic, oral
or intravaginal use.

Rx only

Contains: Fluticasone propionate 0.05% in a lotion base of cetostearyl alcohol, isopropyl myristate, propylene glycol, cetomacrogol 1000, dimethicone 360, citric acid, sodium citrate and purified water with imidurea, methylparaben, and propylparaben as preservatives.

Usual Dosage: Apply a thin film of lotion to the affected skin areas once daily.

See package insert for full prescribing information.

Store between 15° and 30°C (59° and 86°F). Do not refrigerate. Keep container tightly sealed.

Tamper Evident Feature: Do not use if neckband printed with "GSK" is missing or broken.

GlaxoSmithKline
Consumer Healthcare, L.P.
Moon Township, PA 15108 00000XA
Made in Canada Rev. 00/00



0173-0708-00 7

LOT: 15mm X 30mm
NO VARNISH
NO COPY EXCEPT WORDS
LOT AND EXP.

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60 mL A U 07636

SHOWN HERE @ 150% FOR PROOFING ONLY!

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0173-0708-00 7

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60 mL A U 07636

ACTUAL SIZE

GlaxoSmithKline		PACKAGING SPECIFICATION	Date: Art for Pegasus (3.23.05)
S A M 1000 GSK Drive Moon Township, PA 15108			
PACE NO.:	UPC/SKU NO.: 3-0173-0708-00-7 (Retail)		
BRAND: Cutivate Lotion	E.V. NO. & FORMAT: N/A		
DESCRIPTION: fluticasone propionate 0.05%	DIMENSIONS: 100mm x 46mm		
COMPONENT: Label	DIE NO.: CUT0002LB		
VOLUME CONTENTS/SIZE: 60mL	PACKAGING SITE: Mississauga		
FORM NO.:	PRINTER: Jones Packaging		
COUNTRY: U.S.A.	PREPRESS: Schawk		
Computer Software: Adobe Illustrator 10	REPLACES FORM NO.: New		
Artist: Christina Pochiba	REVISION 1:		
KEYWORDS:	REVISION 2:		
S C H A W K Kalamazoo 2325 N. Burdick St. • Kalamazoo, MI 49007 • (269) 381-3820			
JOB NUMBER:	DATE:	OPERATOR:	
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	BAR:		
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/s/

Jonathan Wilkin
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