

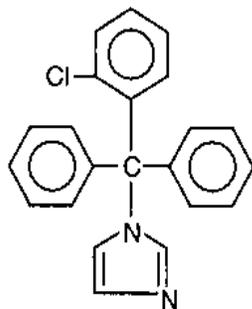
1 **LOTRISONE[®] Cream, USP**2 **LOTRISONE[®] Lotion**

3 (clotrimazole, USP and betamethasone dipropionate, USP)

4 **FOR TOPICAL USE ONLY, NOT FOR OPHTHALMIC, ORAL, OR**
 5 **INTRAVAGINAL USE, NOT RECOMMENDED FOR PATIENTS UNDER THE**
 6 **AGE OF 17 YEARS AND NOT RECOMMENDED FOR DIAPER DERMATITIS**

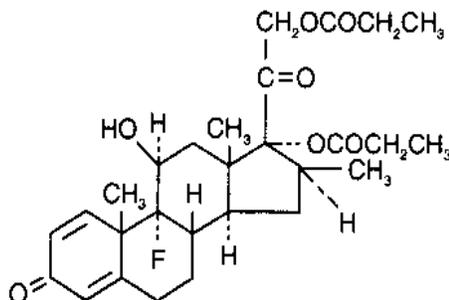
7 **DESCRIPTION** LOTRISONE Cream and Lotion contain combinations of
 8 clotrimazole, a synthetic antifungal agent, and betamethasone dipropionate, a
 9 synthetic corticosteroid, for dermatologic use.

10 Chemically, clotrimazole is 1-(*o*-chloro- α,α -diphenylbenzyl)imidazole, with the
 11 empirical formula $C_{22}H_{17}ClN_2$, a molecular weight of 344.84, and the following
 12 structural formula:



19 Clotrimazole is an odorless, white crystalline powder, insoluble in water and
 20 soluble in ethanol.

21 Betamethasone dipropionate has the chemical name 9-fluoro-11 β ,17,21-
 22 trihydroxy-16 β -methylpregna-1,4-diene-3,20-dione 17,21-dipropionate, with the
 23 empirical formula $C_{28}H_{37}FO_7$, a molecular weight of 504.59, and the following
 24 structural formula:



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

32 Each gram of **LOTRISONE Cream** contains 10 mg clotrimazole and 0.643 mg
33 betamethasone dipropionate (equivalent to 0.5 mg betamethasone), in a
34 hydrophilic cream consisting of purified water, mineral oil, white petrolatum, cetyl
35 alcohol plus stearyl alcohol, cetareth-30, propylene glycol, sodium phosphate
36 monobasic monohydrate, and phosphoric acid; benzyl alcohol, as preservative.

37 LORTISONE Cream is smooth, uniform, and white to off-white in color.

38 Each gram of **LOTRISONE Lotion** contains 10 mg clotrimazole and 0.643 mg
39 betamethasone dipropionate (equivalent to 0.5 mg betamethasone), in a
40 hydrophilic base of purified water, mineral oil, white petrolatum, cetyl alcohol plus
41 stearyl alcohol, cetareth-30, propylene glycol, sodium phosphate monobasic
42 monohydrate, and phosphoric acid, benzyl alcohol as a preservative.

43 LOTRISONE Lotion may contain sodium hydroxide. LOTRISONE Lotion is
44 opaque and white in color.

45 **CLINICAL PHARMACOLOGY**

46 **Clotrimazole and Betamethasone Dipropionate**

47 LORTISONE Cream has been shown to be least as effective as clotrimazole
48 alone in a different cream vehicle. No comparative studies have been conducted
49 with LOTRISONE Lotion and clotrimazole alone. Use of corticosteroids in the
50 treatment of fungal infection may lead to suppression of host inflammation
51 leading to worsening or decreased cure rate.

52 **Clotrimazole**

53 Skin penetration and systemic absorption of clotrimazole following topical
54 application of LOTRISONE Cream or Lotion have not been studied. The following
55 information was obtained using 1% clotrimazole cream and solution formulations.
56 Six hours after the application of radioactive clotrimazole 1% cream and 1%
57 solution onto intact and acutely inflamed skin, the concentration of clotrimazole
58 varied from 100 mcg/cm³ in the stratum corneum, to 0.5 to 1 mcg/cm³ in the
59 reticular dermis, and 0.1 mcg/cm³ in the subcutis. No measurable amount of
60 radioactivity (<0.001 mcg/mL) was found in the serum within 48 hours after

61 application under occlusive dressing of 0.5 mL of the solution or 0.8 g of the
62 cream. Only 0.5% or less of the applied radioactivity was excreted in the urine.

63 **Microbiology**

64 Mechanism of Action: Clotrimazole is an imidazole antifungal agent. Imidazoles
65 inhibit 14- α -demethylation of lanosterol in fungi by binding to one of the
66 cytochrome P-450 enzymes. This leads to the accumulation of 14- α -
67 methylsterols and reduced concentrations of ergosterol, a sterol essential for a
68 normal fungal cytoplasmic membrane. The methylsterols may affect the electron
69 transport system, thereby inhibiting growth of fungi.

70 Activity *In Vivo*: Clotrimazole has been shown to be active against most strains of
71 the following dermatophytes, both *in vitro* and in clinical infections as described in
72 the **INDICATIONS AND USAGE** section: *Epidermophyton floccosum*,
73 *Trichophyton mentagrophytes*, and *Trichophyton rubrum*.

74 Activity *In Vitro*: *In vitro*, clotrimazole has been shown to have activity against
75 most dermatophytes, **but the clinical significance of this information is**
76 **unknown.**

77 Drug Resistance: Strains of dermatophytes having a natural resistance to
78 clotrimazole have not been reported. Resistance to azoles including clotrimazole
79 has been reported in some *Candida* species.

80 No single-step or multiple-step resistance to clotrimazole has developed during
81 successive passages of *Trichophyton mentagrophytes*.

82 **Betamethasone Dipropionate**

83 Betamethasone dipropionate, a corticosteroid, has been shown to have topical
84 (dermatologic) and systemic pharmacologic and metabolic effects characteristic
85 of this class of drugs.

86 **Pharmacokinetics:** The extent of percutaneous absorption of topical
87 corticosteroids is determined by many factors, including the vehicle, the integrity
88 of the epidermal barrier and the use of occlusive dressings. (See **DOSAGE AND**
89 **ADMINISTRATION** section). Topical corticosteroids can be absorbed from
90 normal intact skin. Inflammation and/or other disease processes in the skin may
91 increase percutaneous absorption of topical corticosteroids. Occlusive dressings

92 substantially increase the percutaneous absorption of topical corticosteroids (See
93 **DOSAGE AND ADMINISTRATION** section).

94 Once absorbed through the skin, the pharmacokinetics of topical corticosteroids
95 are similar to systemically administered corticosteroids. Corticosteroids are
96 bound to plasma proteins in varying degrees. Corticosteroids are metabolized
97 primarily in the liver and are then excreted by the kidneys. Some of the topical
98 corticosteroids and their metabolites are also excreted into the bile.

99 Studies performed with LOTRISONE Cream and Lotion indicate that these
100 topical combination anti-fungal/corticosteroids may have vasoconstrictor
101 potencies in a range that is comparable to high potency topical corticosteroids.
102 Therefore use is not recommended in patients less than 17 years of age, in
103 diaper dermatitis, and under occlusion.

104 **CLINICAL STUDIES (LOTRISONE Cream)**

105 In clinical studies of tinea corporis, tinea cruris, and tinea pedis, patients treated
106 with LOTRISONE Cream showed a better clinical response at the first return visit
107 than patients treated with clotrimazole cream. In tinea corporis and tinea cruris,
108 the patient returned 3 to 5 days after starting treatment, and in tinea pedis, after 1
109 week. Mycological cure rates observed in patients treated with LOTRISONE
110 Cream were as good as or better than in those patients treated with clotrimazole
111 cream. In these same clinical studies, patients treated with LORTISONE Cream
112 showed better clinical responses and mycological cure rates when compared
113 with patients treated with betamethasone dipropionate cream.

114 **CLINICAL STUDIES (LOTRISONE Lotion)**

115 In the treatment of tinea pedis twice daily for four weeks, LOTRISONE Lotion
116 was shown to be superior to vehicle in relieving symptoms of erythema, scaling,
117 pruritus, and maceration at week 2. LOTRISONE Lotion was also shown to have
118 a superior mycological cure rate compared to vehicle two weeks after
119 discontinuation of treatment. It is unclear if the relief of symptoms at 2 weeks in
120 this clinical study with LOTRISONE Lotion was due to the contribution of
121 betamethasone dipropionate, clotrimazole, or both.

122 In the treatment of tinea cruris twice daily for two weeks, LOTRISONE Lotion was
123 shown to be superior to vehicle in the relief of symptoms of erythema, scaling,
124 and pruritus after 3 days. It is unclear if the relief of symptoms after 3 days in this
125 clinical study with LOTRISONE Lotion was due to the contribution of
126 betamethasone dipropionate, clotrimazole, or both.

127 The comparative efficacy and safety of LOTRISONE Lotion versus clotrimazole
128 alone in a lotion vehicle have not been studied in the treatment of tinea pedis,
129 tinea cruris, and tinea corporis. The comparative efficacy and safety of
130 LOTRISONE Lotion and LOTRISONE Cream have also not been studied.

131 **INDICATIONS AND USAGE**

132 LOTRISONE Cream and Lotion are indicated in patients 17 years and older for
133 the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris and
134 tinea corporis due to *Epidermophyton floccosum*, *Trichophyton mentagrophytes*,
135 and *Trichophyton rubrum*. Effective treatment without the risks associated with
136 topical corticosteroid use may be obtained using a topical antifungal agent that
137 does not contain a corticosteroid, especially for noninflammatory tinea infections.
138 The efficacy of LOTRISONE Cream or Lotion for the treatment of infections
139 caused by zoophilic dermatophytes (e.g., *Microsporum canis*) has not been
140 established. Several cases of treatment failure of Lotrisone Cream in the
141 treatment of infections caused by *Microsporum canis* have been reported.

142 **CONTRAINDICATIONS**

143 LOTRISONE Cream or Lotion is contraindicated in patients who are sensitive to
144 clotrimazole, betamethasone dipropionate, other corticosteroids or imidazoles, or
145 to any ingredient in these preparations.

146 **PRECAUTIONS**

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

153 Conditions which augment systemic absorption include use over large surface
154 areas, prolonged use, and use under occlusive dressings. Use of more than one
155 corticosteroid-containing product at the same time may increase total systemic
156 glucocorticoid exposure. Patients applying LOTRISONE Cream or Lotion to a
157 large surface area or to areas under occlusion should be evaluated periodically
158 for evidence of HPA-axis suppression. This may be done by using the ACTH
159 stimulation, morning plasma cortisol, and urinary free cortisol tests.

160 If HPA-axis suppression is noted, an attempt should be made to withdraw the
161 drug, to reduce the frequency of application, or to substitute a less potent
162 corticosteroid. Recovery of HPA axis function is generally prompt upon
163 discontinuation of topical corticosteroids. Infrequently, signs and symptoms of
164 glucocorticosteroid insufficiency may occur, requiring supplemental systemic
165 corticosteroids.

166 In a small study, LOTRISONE Cream was applied using large dosages, 7 g daily
167 for 14 days (BID) to the crural area of normal adult subjects. Three of the eight
168 normal subjects on whom LOTRISONE Cream was applied exhibited low
169 morning plasma cortisol levels during treatment. One of these subjects had an
170 abnormal Cortrosyn test. The effect on morning plasma cortisol was transient
171 and subjects recovered one week after discontinuing dosing. In addition, two
172 separate studies in pediatric patients demonstrated adrenal suppression as
173 determined by cosyntropin testing (See **PRECAUTIONS – Pediatric Use**
174 section).

175 Pediatric patients may be more susceptible to systemic toxicity from equivalent
176 doses due to their larger skin surface to body mass ratios. (See **PRECAUTIONS**
177 **- Pediatric Use** section)

178 If irritation develops, LOTRISONE Cream or Lotion should be discontinued and
179 appropriate therapy instituted.

180 **THE SAFETY OF LOTRISONE CREAM OR LOTION HAS NOT BEEN**
181 **DEMONSTRATED IN THE TREATMENT OF DIAPER DERMATITIS. ADVERSE**
182 **EVENTS CONSISTENT WITH CORTICOSTEROID USE HAVE BEEN**
183 **OBSERVED IN PATIENTS TREATED WITH LOTRISONE CREAM FOR**

184 **DIAPER DERMATITIS. THE USE OF LOTRISONE CREAM OR LOTION IN**
185 **THE TREATMENT OF DIAPER DERMATITIS IS NOT RECOMMENDED.**

186 **Information for Patients:** Patients using LOTRISONE Cream or Lotion should
187 receive the following information and instructions:

- 188 1. The medication is to be used as directed by the physician and is not
189 recommended for use longer than the prescribed time period. It is for
190 external use only. Avoid contact with the eyes, mouth, or intravaginally.
- 191 2. This medication is to be used for the full prescribed treatment time, even
192 though the symptoms may have improved. Notify the physician if there is no
193 improvement after 1 week of treatment for tinea cruris or tinea corporis, or
194 after 2 weeks for tinea pedis.
- 195 3. This medication should only be used for the disorder for which it was
196 prescribed.
- 197 4. Other corticosteroid-containing products should not be used with
198 LOTRISONE without first talking with your physician.
- 199 5. The treated skin area should not be bandaged, covered, or wrapped so as to
200 be occluded. (See **DOSAGE AND ADMINISTRATION** section.)
- 201 6. Any signs of local adverse reactions should be reported to your physician.
- 202 7. Patients should avoid sources of infection or reinfection.
- 203 8. When using LOTRISONE Cream or Lotion in the groin area, patients should
204 use the medication for two weeks only, and apply the cream or lotion
205 sparingly. Patients should wear loose-fitting clothing. Notify the physician if
206 the condition persists after 2 weeks.
- 207 9. The safety of LORTISONE Cream or Lotion has not been demonstrated in the
208 treatment of diaper dermatitis. Adverse events consistent with corticosteroid
209 use have been observed in patients treated with LOTRISONE Cream for
210 diaper dermatitis. The use of LOTRISONE Cream or Lotion in the treatment
211 of diaper dermatitis is not recommended.

212 **Laboratory Tests:** If there is a lack of response to LOTRISONE Cream or
213 Lotion, appropriate confirmation of the diagnosis, including possible mycological
214 studies, is indicated before instituting another course of therapy.

215 The following tests may be helpful in evaluating HPA-axis suppression due to the
216 corticosteroid components:

217 Urinary free cortisol test

218 Morning plasma cortisol test

219 ACTH (cosyntropin) stimulation test

220 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** There are no adequate
221 laboratory animal studies with either the combination of clotrimazole and
222 betamethasone dipropionate or with either component individually to evaluate
223 carcinogenesis.

224 Betamethasone was negative in the bacterial mutagenicity assay (*Salmonella*
225 *typhimurium* and *Escherichia coli*), and in the mammalian cell mutagenicity assay
226 (CHO/HGPRT). It was positive in the *in vitro* human lymphocyte chromosome
227 aberration assay, and equivocal in the *in vivo* mouse bone marrow micronucleus
228 assay. This pattern of response is similar to that of dexamethasone and
229 hydrocortisone.

230 Reproductive studies with betamethasone dipropionate carried out in rabbits at
231 doses of 1.0 mg/kg by the intramuscular route and in mice up to 33 mg/kg by the
232 intramuscular route indicated no impairment of fertility except for dose-related
233 increases in fetal resorption rates in both species. These doses are
234 approximately 5- and 38- fold the maximum human dose based on body surface
235 areas, respectively.

236 In a combined study of the effects of clotrimazole on fertility, teratogenicity, and
237 postnatal development, male and female rats were dosed orally (diet admixture)
238 with levels of 5, 10, 25, or 50 mg/kg/day (approximately 1-8 times the maximum
239 dose in a 60 kg adult based on body surface area) from 10 weeks prior to mating
240 until 4 weeks postpartum. No adverse effects on the duration of estrous cycle,
241 fertility, or duration of pregnancy were noted.

242 **Pregnancy: Teratogenic Effects: Pregnancy Category C:** There have been no
243 teratogenic studies performed in animals or humans with the combination of
244 clotrimazole and betamethasone dipropionate. Corticosteroids are generally

245 teratogenic in laboratory animals when administered at relatively low dosage
246 levels.

247 Studies in pregnant rats with intravaginal doses up to 100 mg/kg (15 times the
248 maximum human dose) revealed no evidence of fetotoxicity due to clotrimazole
249 exposure.

250

251 No increase in fetal malformations was noted in pregnant rats receiving oral
252 (gastric tube) clotrimazole doses up to 100 mg/kg/day during gestation days 6-
253 15. However, clotrimazole dosed at 100 mg/kg/day was embryotoxic (increased
254 resorptions), fetotoxic (reduced fetal weights) and maternally toxic (reduced body
255 weight gain) to rats. Clotrimazole dosed at 200 mg/kg/day (30 times the
256 maximum human dose) was maternally lethal, and therefore fetuses were not
257 evaluated in this group. Also in this study, doses up to 50 mg/kg/day (8 times the
258 maximum human dose) had no adverse effects on dams or fetuses. However, in
259 the combined fertility, teratogenicity, and postnatal development study described
260 above, 50 mg/kg clotrimazole, was associated with reduced maternal weight gain
261 and reduced numbers of offspring reared to 4 weeks.

262

263 Oral clotrimazole doses of 25, 50, 100, and 200 mg/kg/day (2-15 times the
264 maximum human dose) were not teratogenic in mice. No evidence of maternal
265 toxicity or embryotoxicity was seen in pregnant rabbits dosed orally with 60, 120,
266 or 180 mg/kg/day (18-55 times the maximum human dose).

267

268 Betamethasone dipropionate has been shown to be teratogenic in rabbits when
269 given by the intramuscular route at doses of 0.05 mg/kg. This dose is
270 approximately one-fifth the maximum human dose. The abnormalities observed
271 included umbilical hernias, cephalocele and cleft palates.

272

273 Betamethasone dipropionate has not been tested for teratogenic potential by the
274 dermal route of administration. Some corticosteroids have been shown to be
275 teratogenic after dermal application to laboratory animals.

276

277 There are no adequate and well-controlled studies in pregnant women of the
278 teratogenic effects of topically applied corticosteroids. Therefore, Lotrisone
279 Cream or Lotion should be used during pregnancy only if the potential benefit
280 justifies the potential risk to the fetus.

281 **Nursing Mothers:** Systemically administered corticosteroids appear in human
282 milk and could suppress growth, interfere with endogenous corticosteroids
283 production, or cause other untoward effects. It is not known whether topical
284 administration of corticosteroids could result in sufficient systemic absorption to
285 product detectable quantities in human milk. Because many drugs are excreted
286 in human milk, caution should be exercised when LOTRISONE Cream or Lotion
287 is administered to a nursing woman.

288 **Pediatric Use:** Adverse events consistent with corticosteroid use have been
289 observed in patients under 12 years of age treated with LOTRISONE Cream. In
290 open-label studies, 17 of 43 (39.5%) evaluable pediatric patients (aged 12 to 16
291 years old) using LOTRISONE Cream for treatment of tinea pedis demonstrated
292 adrenal suppression as determined by cosyntropin testing. In another open-label
293 study, 8 of 17 (47.1%) evaluable pediatric patients (aged 12 to 16 years old)
294 using LOTRISONE Cream for treatment of tinea cruris demonstrated adrenal
295 suppression as determined by cosyntropin testing. **THE USE OF LOTRISONE**
296 **CREAM OR LOTION IN THE TREATMENT OF PATIENTS UNDER 17 YEARS**
297 **OF AGE OR PATIENTS WITH DIAPER DERMATITIS IS NOT**
298 **RECOMMENDED.**

299 Because of higher ratio of skin surface area to body mass, pediatric patients
300 under the age of 12 years are at a higher risk with LOTRISONE Cream or Lotion.
301 The studies described above suggest that pediatric patients under the age of 17
302 years may also have this risk. They are at increased risk of developing Cushing's
303 syndrome while on treatment and adrenal insufficiency after withdrawal of
304 treatment. Adverse effects, including striae and growth retardation, have been
305 reported with inappropriate use of LOTRISONE Cream in infants and children
306 (see **PRECAUTIONS** and **ADVERSE REACTIONS** sections).

307 Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome,
308 linear growth retardation, delayed weight gain and intracranial hypertension have
309 been reported in children receiving topical corticosteroids. Manifestations of
310 adrenal suppression in children include low plasma cortisol levels and absence of
311 response to ACTH stimulation. Manifestations of intracranial hypertension
312 include bulging fontanelles, headaches, and bilateral papilledema.

313 **Geriatric Use:** Clinical studies of LOTRISONE Cream or Lotion did not include
314 sufficient numbers of subjects aged 65 and over to determine whether they
315 respond differently from younger subjects. Post-market adverse events reporting
316 for LOTRISONE Cream in patients aged 65 and above includes reports of skin
317 atrophy and rare reports of skin ulceration. Caution should be exercised with the
318 use of these corticosteroid containing topical products on thinning skin. **THE USE**
319 **OF LOTRISONE CREAM OR LOTION UNDER OCCLUSION, SUCH AS IN**
320 **DIAPER DERMATITIS, IS NOT RECOMMENDED.**

321 **ADVERSE REACTIONS**

322 Adverse reactions reported for LOTRISONE Cream in clinical trials were
323 paresthesia in 1.9% of patients, and rash, edema, and secondary infection, each
324 in 1% of patients.

325 Adverse reactions reported for LOTRISONE Lotion in clinical trials were burning
326 and dry skin in 1.6% of patients and stinging in less than 1% of patients.

327 The following local adverse reactions have been reported with topical
328 corticosteroids and may occur more frequently with the use of occlusive
329 dressings. These reactions are listed in an approximate decreasing order of
330 occurrence: itching, irritation, dryness, folliculitis, hypertrichosis, acneiform
331 eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis,
332 maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. In
333 the pediatric population, reported adverse events for LOTRISONE Cream include
334 growth retardation, benign intracranial hypertension, Cushing's syndrome (HPA
335 axis suppression), and local cutaneous reactions, including skin atrophy.

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

339 Adverse reactions reported with the use of clotrimazole are as follows: erythema,
340 stinging, blistering, peeling, edema, pruritus, urticaria and general irritation of the
341 skin.

342 **OVERDOSAGE**

343 Amounts greater than 45 g/week of LOTRISONE Cream or 45 mL/week of
344 LOTRISONE Lotion should not be used. Acute overdosage with topical
345 application of LOTRISONE Cream or Lotion is unlikely and would not be
346 expected to lead to life-threatening situation. LOTRISONE Cream or Lotion
347 should not be used for longer than the prescribed time period.

348

349 Topically applied corticosteroids, such as the one contained in LOTRISONE
350 Cream or Lotion can be absorbed in sufficient amounts to produce systemic
351 effects (see **PRECAUTIONS** section).

352 **DOSAGE AND ADMINISTRATION**

353 Gently massage sufficient LOTRISONE Cream or Lotion into the affected skin
354 areas twice a day, in the morning and evening.

355 **LOTRISONE Cream or Lotion should not be used longer than 2 weeks in**
356 **the treatment of tinea corporis or tinea cruris, and amounts greater than 45**
357 **g per week of LOTRISONE Cream or amounts greater than 45 mL per week**
358 **of LOTRISONE Lotion should not be used.** If a patient with tinea corporis or
359 tinea cruris shows no clinical improvement after one week of treatment with
360 LOTRISONE Cream or Lotion, the diagnosis should be reviewed.

361 **LOTRISONE Cream or Lotion should not be used longer than 4 weeks in**
362 **the treatment of tinea pedis and amounts greater than 45 g per week of**
363 **LOTRISONE Cream or amounts greater than 45 mL per week of**
364 **LOTRISONE Lotion should not be used.** If a patient with tinea pedis shows no
365 clinical improvement after 2 weeks of treatment with LOTRISONE Cream or
366 Lotion, the diagnosis should be reviewed.

367 LOTRISONE Cream or Lotion should not be used with occlusive dressings.

368 **HOW SUPPLIED**

369 LOTRISONE Cream is supplied in 15-gram (NDC 0085-0924-01) and 45-gram
370 tubes (NDC 0085-0924-02); boxes of one. **Store between 2°C and 30°C (36°F**
371 **and 86°F).**

372 LOTRISONE Lotion is supplied in 30-mL bottles (NDC 0085-0809-01), box of
373 one. **Store at 25°C (77°F) in the upright position only; excursions permitted**
374 **between 15°C and 30°C (59°F and 86°F).**

375 **SHAKE WELL BEFORE EACH USE.**

376 **Rx only**

377 **Manufactured by:** Schering/KEY

378 Schering Corporation/KEY Pharmaceuticals, Inc.

379 Kenilworth, NJ 07033 USA

380 3/10/03

381 Copyright© 2000 Schering Corporation. All Rights reserved.

382 **TEAR AT PERFORATION**

383 **GIVE TO PATIENT**

384 **Patient's Instructions for Use**

385 **SHAKE WELL BEFORE EACH USE**

386 **LOTRISONE[®] Cream, USP**

387 **LOTRISONE[®] Lotion**

388 **(clotrimazole, USP and betamethasone dipropionate, USP)**

389 **Patient Information Leaflet**

390 **What is LOTRISONE Cream or Lotion?**

391 LOTRISONE Cream and Lotion are medications used on the skin to treat fungal
392 infections of the feet, groin and body, as diagnosed by your doctor. LOTRISONE
393 Cream or Lotion should be used for fungal infections that are inflamed and have
394 symptoms of redness and/or itching. Talk to your doctor if your fungal infection
395 does not have these symptoms. LOTRISONE Cream and Lotion contain a
396 corticosteroid. Notify your doctor if you notice side effects with the use of
397 LOTRISONE Cream or Lotion (see "**What are the possible side effects of**
398 **LOTRISONE Cream and Lotion?**" below). LOTRISONE Cream or Lotion is not
399 to be used in the eyes, in the mouth, or in the vagina.

400 **How do LOTRISONE Cream and Lotion Work?**

401 LOTRISONE Cream and Lotion are combinations of an antifungal agent
402 (clotrimazole) and a corticosteroid (betamethasone dipropionate). Clotrimazole
403 works against fungus. Betamethasone dipropionate, a corticosteroid, is used to
404 help relieve redness, swelling, itching, and other discomforts of fungal infections.

405 **Who should NOT use LOTRISONE Cream or Lotion?**

406 LOTRISONE Cream and Lotion are not recommended for use in patients under
407 the age of 17 years. LOTRISONE Cream or Lotion is not recommended for use
408 in diaper rash.

409 Patients who are sensitive to clotrimazole and betamethasone dipropionate,
410 other corticosteroids or imidazoles or any ingredients in the preparation should
411 not use LOTRISONE Cream and Lotion.

412 **How should I use LOTRISONE Cream or Lotion?**

413 Gently message sufficient LOTRISONE Cream or Lotion into the affected and
414 surrounding skin areas twice a day, in the morning and evening. Treatment for 2
415 weeks on the groin or on the body, and for 4 weeks on the feet is recommended.
416 The use of LOTRISONE Cream or Lotion for longer than 4 weeks is not
417 recommended for any condition. Prolonged use of LOTRISONE Cream or Lotion
418 may lead to unwanted side effects.

419 **What other important information should I know about LOTRISONE Cream**
420 **and Lotion?**

- 421 1. This medication is to be used for the full prescribed treatment time, even
422 though the symptoms may have improved. Notify your doctor if there is no
423 improvement after 1 week of treatment on the groin or body or after 2 weeks
424 on the feet.
- 425 2. This medication should only be used for the disorder for which it was
426 prescribed.
- 427 3. The treated skin area should not be bandaged or otherwise covered or
428 wrapped.
- 429 4. Other corticosteroid-containing products should not be used with
430 LOTRISONE without first talking with your physician.
- 431 5. Any signs of side effects where LOTRISONE Cream or Lotion is applied
432 should be reported to your doctor.
- 433 6. When using LOTRISONE Cream or Lotion in the groin area, it is especially
434 important to use the medication for two weeks only, and to apply the cream or
435 lotion sparingly. You should tell your doctor if your problem persists after 2
436 weeks. You should also wear loose-fitting clothing so as to avoid tightly
437 covering the area where LOTRISONE Cream is applied.
- 438 7. This medication is not recommended for use in diaper rash.

439 **What are the possible side effects of LOTRISONE Cream and Lotion?**

440 The following side effects have been reported with topical corticosteroid
441 medications: itching, irritation, dryness, infection of the hair follicles, increased
442 hair, acne, change in skin color, allergic skin reaction, skin thinning, and stretch
443 marks. In children, reported adverse events for LOTRISONE Cream include
444 slower growth, Cushing's syndrome (a type of hormone imbalance that can be
445 very serious), and local skin reactions, including thinning skin and stretch marks.
446 Hormone imbalance (adrenal suppression) was demonstrated in clinical studies
447 in children.

448 **Can LOTRISONE Cream or Lotion be used if I am pregnant or plan to**
449 **become pregnant or if I am nursing?**

450 Before using LOTRISONE Cream or Lotion, tell your doctor if you are pregnant
451 or plan to become pregnant. Also, tell your doctor if you are nursing.

452 **How should LOTRISONE Cream or Lotion be stored?**

453 LOTRISONE Cream should be stored between 2° and 30°C (36° and 86°F).

454 LOTRISONE Lotion should only be stored in an upright position between 15°C
455 and 30°C (59°F and 86°F). Shake well before using LOTRISONE Lotion.

456 **General advice about prescription medicines**

457 This medicine was prescribed for your particular condition. Only use
458 LOTRISONE Cream or Lotion to treat the condition for which your doctor has
459 prescribed. Do not give LOTRISONE Cream or Lotion to other people. It may
460 harm them.

461 This leaflet summarizes the most important information about LOTRISONE
462 Cream and Lotion. If you would like more information, talk with your doctor. You
463 can ask your pharmacist or doctor for information about LOTRISONE Cream and
464 Lotion that is written for health professionals.

465 Rx only

466 Schering/Key

467 Schering Corporation/Key Pharmaceuticals

468 Kenilworth, NJ 07033

469 Copyright® 2000, Schering Corp. All rights reserved.

470 3/10/03