
1 **LOTRISONE[®]**

2 **(clotrimazole and**
3 **betamethasone dipropionate)**
4 **CREAM and LOTION**

5

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

9

10 **DESCRIPTION** LOTRISONE Cream and Lotion contain combinations of
11 clotrimazole, a synthetic antifungal agent, and betamethasone dipropionate, a
12 synthetic corticosteroid, for dermatologic use.

13

14 Chemically, clotrimazole is 1-(*o*-chloro-*o*,-*o*-diphenylbenzyl)imidazole, with the
15 empirical formula C₂₂H₁₇ClN₂, a molecular weight of 344.84, and the following
16 structural formula:

17

18

19

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

22

23 Betamethasone dipropionate has the chemical name 9-fluoro-11 β ,17,21-
24 trihydroxy-16 β -methylpregna-1,4-diene-3,20-dione 17,21-dipropionate, with the
25 empirical formula C₂₈H₃₇FO₇, a molecular weight of 504.59, and the following
26 structural formula:

27

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

30

31 Each gram of **LOTRISONE Cream** contains 10 mg clotrimazole and 0.643 mg
32 betamethasone dipropionate (equivalent to 0.5 mg betamethasone), in a
33 hydrophilic cream consisting of purified water, mineral oil, white petrolatum,
34 cetearyl alcohol 70/30, cetareth-30, propylene glycol, monobasic sodium
35 phosphate, and phosphoric acid; benzyl alcohol, as preservative. **LORTISONE**
36 Cream is smooth, uniform, and white to off-white in color.

37

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, cetearyl alcohol
41 70/30, cetareth-30, propylene glycol, monobasic sodium phosphate, and
42 phosphoric acid, benzyl alcohol as a preservative. **LOTRISONE Lotion** may
43 contain sodium hydroxide. **LOTRISONE Lotion** is opaque and white in color.

44

45 **CLINICAL PHARMACOLOGY**

46

47 **Clotrimazole and Betamethasone Dipropionate**

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

53

54 **Clotrimazole**

55 Skin penetration and systemic absorption of clotrimazole following topical
56 application of **LOTRISONE Cream** or **Lotion** have not been studied. The following
57 information was obtained using 1% clotrimazole cream and solution formulations.
58 Six hours after the application of radioactive clotrimazole 1% cream and 1%
59 solution onto intact and acutely inflamed skin, the concentration of clotrimazole

60 varied from 100 mcg/cm³ in the stratum corneum, to 0.5 to 1 mcg/cm³ in the
61 reticular dermis, and 0.1 mcg/cm³ in the subcutis. No measurable amount of
62 radioactivity (<0.001 mcg/mL) was found in the serum within 48 hours after
63 application under occlusive dressing of 0.5 mL of the solution or 0.8 g of the
64 cream. Only 0.5% or less of the applied radioactivity was excreted in the urine.

65

66 **Microbiology**

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

73

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

78

79 Activity *In Vitro*: *In vitro*, clotrimazole has been shown to have activity against
80 many dermatophytes, **but the clinical significance of this information is**
81 **unknown.**

82

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

86

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

89

Betamethasone Dipropionate

90

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

94

95 **Pharmacokinetics:** The extent of percutaneous absorption of topical
96 corticosteroids is determined by many factors, including the vehicle, the integrity
97 of the epidermal barrier and the use of occlusive dressings. (See **DOSAGE AND**
98 **ADMINISTRATION** section). Topical corticosteroids can be absorbed from
99 normal intact skin. Inflammation and/or other disease processes in the skin may
100 increase percutaneous absorption of topical corticosteroids. Occlusive dressings
101 substantially increase the percutaneous absorption of topical corticosteroids (See
102 **DOSAGE AND ADMINISTRATION** section).

103

104 Once absorbed through the skin, the pharmacokinetics of topical corticosteroids
105 are similar to systemically administered corticosteroids. Corticosteroids are
106 bound to plasma proteins in varying degrees. Corticosteroids are metabolized
107 primarily in the liver and are then excreted by the kidneys. Some of the topical
108 corticosteroids and their metabolites are also excreted into the bile.

109

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

115

CLINICAL STUDIES (LOTRISONE Cream)

117 In clinical studies of tinea corporis, tinea cruris, and tinea pedis, patients treated
118 with LOTRISONE Cream showed a better clinical response at the first return visit
119 than patients treated with clotrimazole cream. In tinea corporis and tinea cruris,

120 the patient returned 3 to 5 days after starting treatment, and in tinea pedis, after 1
121 week. Mycological cure rates observed in patients treated with LOTRISONE
122 Cream were as good as or better than in those patients treated with clotrimazole
123 cream. In these same clinical studies, patients treated with LORTISONE Cream
124 showed better clinical responses and mycological cure rates when compared
125 with patients treated with betamethasone dipropionate cream.

126

127 **CLINICAL STUDIES (LOTRISONE Lotion)**

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

135

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

141

142 The comparative efficacy and safety of LOTRISONE Lotion versus clotrimazole
143 alone in a lotion vehicle have not been studied in the treatment of tinea pedis,
144 tinea cruris, and tinea corporis. The comparative efficacy and safety of
145 LOTRISONE Lotion and LOTRISONE Cream have also not been studied.

146

147 **INDICATIONS AND USAGE**

148 LOTRISONE Cream and Lotion are indicated in patients 17 years and older for
149 the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris and

150 tinea corporis due to *Epidermophyton floccosum*, *Trichophyton mentagrophytes*,
151 and *Trichophyton rubrum*. Effective treatment without the risks associated with
152 topical corticosteroid use may be obtained using a topical antifungal agent that
153 does not contain a corticosteroid, especially for noninflammatory tinea infections.
154 The efficacy of LOTRISONE Cream or Lotion for the treatment of infections
155 caused by zoophilic dermatophytes (e.g., *Microsporum canis*) has not been
156 established. Several cases of treatment failure of LOTRISONE Cream in the
157 treatment of infections caused by *Microsporum canis* have been reported.

158

159 **CONTRAINDICATIONS**

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

163

164 **PRECAUTIONS**

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

171

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

179

180 If HPA-axis suppression is noted, an attempt should be made to withdraw the
181 drug, to reduce the frequency of application, or to substitute a less potent
182 corticosteroid. Recovery of HPA axis function is generally prompt upon
183 discontinuation of topical corticosteroids. Infrequently, signs and symptoms of
184 glucocorticosteroid insufficiency may occur, requiring supplemental systemic
185 corticosteroids.

186

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

196

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

200

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

203

204 **THE SAFETY OF LOTRISONE CREAM OR LOTION HAS NOT BEEN**
205 **DEMONSTRATED IN THE TREATMENT OF DIAPER DERMATITIS. ADVERSE**
206 **EVENTS CONSISTENT WITH CORTICOSTEROID USE HAVE BEEN**
207 **OBSERVED IN PATIENTS TREATED WITH LOTRISONE CREAM FOR**
208 **DIAPER DERMATITIS. THE USE OF LOTRISONE CREAM OR LOTION IN**
209 **THE TREATMENT OF DIAPER DERMATITIS IS NOT RECOMMENDED.**

210

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

213

214 1. The medication is to be used as directed by the physician and is not
215 recommended for use longer than the prescribed time period. It is for
216 external use only. Avoid contact with the eyes, mouth, or intravaginally.

217

218 2. This medication is to be used for the full prescribed treatment time, even
219 though the symptoms may have improved. Notify the physician if there is no
220 improvement after 1 week of treatment for tinea cruris or tinea corporis, or
221 after 2 weeks for tinea pedis.

222

223 3. This medication should only be used for the disorder for which it was
224 prescribed.

225

226 4. Other corticosteroid-containing products should not be used with
227 LOTRISONE without first talking with your physician.

228

229 5. The treated skin area should not be bandaged, covered, or wrapped so as to
230 be occluded. (See **DOSAGE AND ADMINISTRATION** section.)

231

232 6. Any signs of local adverse reactions should be reported to your physician.

233

234 7. Patients should avoid sources of infection or reinfection.

235

236 8. When using LOTRISONE Cream or Lotion in the groin area, patients should
237 use the medication for two weeks only, and apply the cream or lotion
238 sparingly. Patients should wear loose-fitting clothing. Notify the physician if
239 the condition persists after 2 weeks.

240

241 9. The safety of LORTISONE Cream or Lotion has not been demonstrated in the
242 treatment of diaper dermatitis. Adverse events consistent with corticosteroid
243 use have been observed in patients treated with LOTRISONE Cream for
244 diaper dermatitis. The use of LOTRISONE Cream or Lotion in the treatment
245 of diaper dermatitis is not recommended.

246

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

250

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

253

254 Urinary free cortisol test

255 Morning plasma cortisol test

256 ACTH (cosyntropin) stimulation test

257

258 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** There are no
259 laboratory animal studies with either the combination of clotrimazole and
260 betamethasone dipropionate or with either component individually to evaluate
261 carcinogenesis.

262

263 Betamethasone was negative in the bacterial mutagenicity assay (*Salmonella*
264 *typhimurium* and *Escherichia coli*), and in the mammalian cell mutagenicity assay
265 (CHO/HGPRT). It was positive in the *in vitro* human lymphocyte chromosome
266 aberration assay, and equivocal in the *in vivo* mouse bone marrow micronucleus
267 assay. This pattern of response is similar to that of dexamethasone and
268 hydrocortisone.

269

270 In genotoxicity testing of clotrimazole, chromosomes of the spermatophores of
271 Chinese hamsters, which had been exposed to five daily oral clotrimazole doses
272 of 100 mg/kg body weight, were examined for structural changes during the
273 metaphase. The results of this study showed that clotrimazole had no mutagenic
274 effect.

275

276 Reproductive studies with betamethasone dipropionate carried out in rabbits at
277 doses of 1.0 mg/kg by the intramuscular route and in mice up to 33 mg/kg by the
278 intramuscular route indicated no impairment of fertility except for dose-related
279 increases in fetal resorption rates in both species. These doses are
280 approximately 5- and 38- fold the human dose based on a mg/m² comparison,
281 respectively.

282

283 Oral doses of clotrimazole in mice resulted in decreased litter size at doses of
284 120 mg/kg and higher. This dose is approximately 10- fold the human dose
285 based on a mg/m² comparison.

286

287 A Segment I (fertility and general reproduction) study of clotrimazole was
288 conducted in rats. Males and females were dosed orally (diet admixture) at
289 doses of 5, 10, 25 or 50 mg/kg/day for 10 weeks prior to mating. At 50 mg/kg
290 (approximately 8 times the human dose based on a mg/m² comparison), there
291 was an adverse effect on maternal body weight gain and rearing of the offspring.
292 Doses of 25 mg/kg (approximately 4 times the human dose based on a mg/m²
293 comparison) and lower were well tolerated and produced no adverse effects on
294 fertility or reproduction.

295

296 **Pregnancy Category C:** There have been no teratogenic studies performed in
297 animals or humans with the combination of clotrimazole and betamethasone
298 dipropionate. Corticosteroids are generally teratogenic in laboratory animals
299 when administered at relatively low dosage levels.

300

301 A Segment II (teratology) study in pregnant rats with intravaginal doses up to 100
302 mg/kg clotrimazole have revealed no evidence of harm to the fetus. This dose is
303 approximately 17- fold the human dose based on a mg/m^2 comparison.

304

305 Segment II (teratology) studies of clotrimazole were conducted by the oral
306 (gavage) route in rats, mice, and rabbits. In rats administered 25, 50, 100, or 200
307 mg/kg/day, no increase in malformations was seen at doses up to 200 mg/kg.
308 Doses of 100 and 200 mg/kg were embryotoxic (increased resorptions) as well
309 as maternally toxic, while doses of 25 and 50 mg/kg were well tolerated by both
310 the dams and the fetuses. These doses were approximately 4-, 8-, 17- and 34-
311 fold the human dose based on a mg/m^2 comparison, respectively.

312

313 In pregnant mice, clotrimazole at oral doses of 25, 50, 100, or 200 mg/kg/day
314 was not teratogenic and was well tolerated by both the dams and the fetuses.
315 These doses were approximately 2-, 4-, 8- and 17-fold the human dose based on
316 a mg/m^2 comparison, respectively.

317

318 No evidence of maternal toxicity or embryotoxicity was seen in pregnant rabbits
319 dosed orally with 60, 120, or 180 mg/kg/day. These doses were approximately
320 20-, 40- and 61-fold the human dose based on a mg/m^2 comparison,
321 respectively.

322

323 Betamethasone dipropionate has been shown to be teratogenic in rabbits when
324 given by the intramuscular route at doses of 0.05 mg/kg. This dose is
325 approximately one-fifth the human dose based on a mg/m^2 comparison. The
326 abnormalities observed included umbilical hernias, cephalocele and cleft palates.

327

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

331

332 **Nursing Mothers:** Systemically administered corticosteroids appear in human
333 milk and could suppress growth, interfere with endogenous corticosteroid
334 production, or cause other untoward effects. It is not known whether topical
335 administration of corticosteroids could result in sufficient systemic absorption to
336 produce detectable quantities in human milk. Because many drugs are excreted
337 in human milk, caution should be exercised when LOTRISONE Cream or Lotion
338 is administered to a nursing woman.

339

340 **Pediatric Use:** Adverse events consistent with corticosteroid use have been
341 observed in patients under 12 years of age treated with LOTRISONE cream. In
342 open-label studies, 17 of 43 (39.5%) evaluable pediatric patients (aged 12 to 16
343 years old) using LOTRISONE Cream for treatment of tinea pedis demonstrated
344 adrenal suppression as determined by cosyntropin testing. In another open-label
345 study, 8 of 17 (47.1%) evaluable pediatric patients (aged 12 to 16 years old)
346 using LOTRISONE Cream for treatment of tinea cruris demonstrated adrenal
347 suppression as determined by cosyntropin testing. **THE USE OF LOTRISONE**
348 **CREAM OR LOTION IN THE TREATMENT OF PATIENTS UNDER 17 YEARS**
349 **OF AGE OR PATIENTS WITH DIAPER DERMATITIS IS NOT**
350 **RECOMMENDED.**

351

352 Because of higher ratio of skin surface area to body mass, pediatric patients
353 under the age of 12 years are at a higher risk with LOTRISONE Cream or Lotion.
354 The studies described above suggest that pediatric patients under the age of 17
355 years may also have this risk. They are at increased risk of developing Cushing's
356 syndrome while on treatment and adrenal insufficiency after withdrawal of
357 treatment. Adverse effects, including striae and growth retardation, have been

358 reported with inappropriate use of LOTRISONE Cream in infants and children
359 (see **PRECAUTIONS** and **ADVERSE REACTIONS** sections).

360

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

367

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

376

377 **ADVERSE REACTIONS**

378 Adverse reactions reported for LOTRISONE Cream in clinical trials were
379 paresthesia in 1.9% of patients, and rash, edema, and secondary infection, each
380 in less than 1% of patients.

381

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

384

385 The following local adverse reactions have been reported with topical
386 corticosteroids and may occur more frequently with the use of occlusive
387 dressings. These reactions are listed in an approximate decreasing order of

388 occurrence: itching, irritation, dryness, folliculitis, hypertrichosis, acneiform
389 eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis,
390 maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. In
391 the pediatric population, reported adverse events for LOTRISONE Cream include
392 growth retardation, benign intracranial hypertension, Cushing's syndrome (HPA
393 axis suppression), and local cutaneous reactions, including skin atrophy.

394

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

398

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

402

403 **OVERDOSAGE**

404 Amounts greater than 45 g/week of LOTRISONE Cream or 45 mL/week of
405 LOTRISONE Lotion should not be used. Acute overdosage with topical
406 application of LOTRISONE Cream or Lotion is unlikely and would not be
407 expected to lead to life-threatening situation. LOTRISONE Cream or Lotion
408 should not be used for longer than the prescribed time period. Topically applied
409 corticosteroids, such as the one contained in LOTRISONE Cream or Lotion can
410 be absorbed in sufficient amounts to produce systemic effects (see
411 **PRECAUTIONS** section).

412

413 **DOSAGE AND ADMINISTRATION**

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

416

417 **LOTRISONE Cream or Lotion should not be used longer than 2 weeks in**
418 **the treatment of tinea corporis or tinea cruris, and amounts greater than 45**
419 **g per week of LOTRISONE Cream or amounts greater than 45 mL per week**
420 **of LOTRISONE Lotion should not be used.** If a patient with tinea corporis or
421 tinea cruris shows no clinical improvement after one week of treatment with
422 LOTRISONE Cream or Lotion, the diagnosis should be reviewed.

423

424 **LOTRISONE Cream or Lotion should not be used longer than 4 weeks in**
425 **the treatment of tinea pedis and amounts greater than 45 g per week of**
426 **LOTRISONE Cream or amounts greater than 45 mL per week of**
427 **LOTRISONE Lotion should not be used.** If a patient with tinea pedis shows no
428 clinical improvement after 2 weeks of treatment with LOTRISONE Cream or
429 Lotion, the diagnosis should be reviewed.

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

431

432 **HOW SUPPLIED**

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

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

439 **SHAKE WELL BEFORE EACH USE.**

440 **Rx only**

441 **Manufactured by:** Schering/KEY

442 Schering Corporation/KEY Pharmaceuticals, Inc.

443 Kenilworth, NJ 07033 USA

444 11/08/02

445

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447 **TEAR AT PERFORATION**

448 **GIVE TO PATIENT**

449 **Patient's Instructions for Use**

450 **SHAKE WELL BEFORE EACH USE**

451

452 **LOTRISONE Cream**

453 **LOTRISONE Lotion**

454

455 **Patient Information Leaflet**

456

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

458 LOTRISONE Cream and Lotion are medications used on the skin to treat fungal
459 infections of the feet, groin and body, as diagnosed by your doctor. LOTRISONE
460 Cream or Lotion should be used for fungal infections that are inflamed and have
461 symptoms of redness and/or itching. Talk to your doctor if your fungal infection
462 does not have these symptoms. LOTRISONE Cream and Lotion contain a
463 corticosteroid. Notify your doctor if you notice side effects with the use of
464 LOTRISONE Cream or Lotion (see **“What are the possible side effects of**
465 **LOTRISONE Cream and Lotion?”** below). LOTRISONE Cream or Lotion is not
466 to be used in the eyes, in the mouth, or in the vagina.

467

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

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

473

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

475 LOTRISONE Cream and Lotion are not recommended for use in patients under
476 the age of 17 years. LOTRISONE Cream or Lotion is not recommended for use
477 in diaper rash.

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

481

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

483 Gently massage sufficient LOTRISONE Cream or Lotion into the affected and
484 surrounding skin areas twice a day, in the morning and evening. Treatment for 2
485 weeks on the groin or on the body, and for 4 weeks on the feet is recommended.
486 The use of LOTRISONE Cream or Lotion for longer than 4 weeks is not
487 recommended for any condition. Prolonged use of LOTRISONE Cream or Lotion
488 may lead to unwanted side effects.

489

490 **What other important information should I know about LOTRISONE Cream**
491 **and Lotion?**

- 492 1. This medication is to be used for the full prescribed treatment time, even
493 though the symptoms may have improved. Notify your doctor if there is no
494 improvement after 1 week of treatment on the groin or body or after 2 weeks
495 on the feet.
- 496 2. This medication should only be used for the disorder for which it was
497 prescribed.
- 498 3. The treated skin area should not be bandaged or otherwise covered or
499 wrapped.
- 500 4. Other corticosteroid-containing products should not be used with
501 LOTRISONE without first talking with your physician.
- 502 5. Any signs of side effects where LOTRISONE Cream or Lotion is applied
503 should be reported to your doctor.

504 6. When using LOTRISONE Cream or Lotion in the groin area, it is especially
505 important to use the medication for two weeks only, and to apply the cream or
506 lotion sparingly. You should tell your doctor if your problem persists after 2
507 weeks. You should also wear loose-fitting clothing so as to avoid tightly
508 covering the area where LOTRISONE Cream is applied.

509 7. This medication is not recommended for use in diaper rash.

510

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

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

520

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

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

525

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

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

528 **LOTRISONE Lotion should only be stored in an upright position between**
529 **15°C and 30°C (59°F and 86°F). Shake well before using LOTRISONE Lotion.**

530

531 **General advice about prescription medicines**

532 This medicine was prescribed for your particular condition. Only use
533 LOTRISONE Cream or Lotion to treat the condition for which your doctor has

534 prescribed. Do not give LOTRISONE Cream or Lotion to other people. It may
535 harm them.

536

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

541

542 Rx only

543 Schering/Key

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545 Schering Corporation/Key Pharmaceuticals

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