

F-XXXXXXXX

ELOCON[®]

brand of mometasone furoate

Lotion 0.1%

For Dermatologic Use Only

Not for Ophthalmic Use

DESCRIPTION ELOCON (mometasone furoate topical solution) Lotion, 0.1%, contains mometasone furoate, USP for dermatologic use. Mometasone furoate is a synthetic corticosteroid with anti-inflammatory activity.

Chemically, mometasone furoate is 9 α ,21-dichloro-11 β ,17-dihydroxy-16 α -methylpregna-1,4-diene-3,20-dione 17-(2-furoate), with the empirical formula C₂₇H₃₀Cl₂O₆, a molecular weight of 521.4 and the following structural formula:

[Structure]

Mometasone furoate is a white to off-white powder insoluble in water, freely soluble in acetone and in methylene chloride and sparingly soluble in heptane.

Each gram of ELOCON Lotion, 0.1%, contains: 1 mg mometasone furoate, USP in a lotion base of isopropyl alcohol (40%), propylene glycol, hydroxypropylcellulose, sodium phosphate monobasic monohydrate and water. May also contain phosphoric acid used to adjust the pH to approximately 4.5.

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

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration; however, occlusion of hydrocortisone for 96 hours markedly enhances penetration. Studies in humans indicate that approximately 0.7% of the applied dose of ELOCON Ointment, 0.1%, enters the circulation after 8 hours of contact on normal skin without occlusion. A similar minimal degree of absorption of the corticosteroid from the lotion formulation would be anticipated. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Studies performed with ELOCON Lotion indicate that it is in the medium range of potency as compared with other topical corticosteroids.

In a study evaluating the effects of mometasone furoate lotion on the hypothalamic-pituitary-adrenal (HPA) axis, 15 mL were applied without occlusion twice daily (30 mL per day) for 7 days to 4 adult patients with scalp and body psoriasis. At the end of treatment, the plasma cortisol levels for each of the 4 patients remained within the normal range and changed little from baseline.

Sixty-five pediatric patients ages 6 to 23 months, with atopic dermatitis, were enrolled in an open-label, hypothalamic-pituitary-adrenal (HPA) axis safety study. ELOCON Lotion was applied once daily for approximately 3 weeks over a mean body surface area of 40% (range 16% to 90%). In approximately 29% of patients who showed normal adrenal function by Cortrosyn test before starting treatment, adrenal suppression was observed at the end of treatment with ELOCON Lotion. The criteria for suppression were: basal cortisol level of ≤ 5 mcg/dL, 30-minute post-stimulation level of ≤ 18 mcg/dL, or an increase of < 7 mcg/dL. Follow-up testing 2 to 4 weeks after stopping treatment, available for 8 of the patients, demonstrated suppressed HPA axis function in one patient, using these same criteria.

INDICATIONS AND USAGE ELOCON Lotion, 0.1%, is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Since safety and efficacy of ELOCON Lotion have not been established in pediatric patients below 12 years of age, its use in this age group is not recommended. (see **PRECAUTIONS - Pediatric Use**).

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

PRECAUTIONS

General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of 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.

Patients applying a topical steroid to a large surface area or areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests.

In a study evaluating the effects of mometasone furoate lotion on the hypothalamic-pituitary-adrenal (HPA) axis, 15 mL were applied without occlusion twice daily (30 mL per day) for 7 days to four adult patients with scalp and body psoriasis. At the end of treatment, the plasma cortisol levels for each of the four patients remained within the normal range and changed little from baseline.

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

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

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

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

Information for Patients: Patients using topical corticosteroids should receive the following information and instructions.

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped so as to be occlusive unless directed by the physician.
4. Patients should report to their physician any signs of local adverse reactions.
5. Parents of pediatric patients should be advised not to use ELOCON Lotion in the treatment of diaper dermatitis. ELOCON Lotion should not be applied in the diaper area, as diapers or plastic pants may constitute occlusive dressing (see **DOSAGE AND ADMINISTRATION**).
6. This medication should not be used on the face, underarms, or groin areas unless directed by the physician.
7. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.
8. Other corticosteroid-containing products should not be used with ELOCON Lotion without first consulting with the physician.

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

- ACTH stimulation test
- A.M. plasma cortisol test
- Urinary free cortisol test

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential of ELOCON (mometasone furoate lotion) Lotion. Long-term carcinogenicity studies of mometasone furoate were conducted by the inhalation route in rats and mice. In a 2-year carcinogenicity study in Sprague-Dawley rats, mometasone furoate demonstrated no statistically significant increase of tumors at inhalation doses up to 67 mcg/kg (approximately 0.04 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis). In a 19-month carcinogenicity study in Swiss CD-1 mice, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 160 mcg/kg (approximately 0.05 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

Mometasone furoate increased chromosomal aberrations in an *in vitro* Chinese hamster ovary cell assay, but did not increase chromosomal aberrations in an *in vitro* Chinese hamster lung cell assay. Mometasone furoate was not mutagenic in the Ames test or mouse lymphoma assay, and was not clastogenic in an *in vivo* mouse micronucleus assay, a rat bone marrow chromosomal aberration assay, or a mouse male germ-cell chromosomal aberration assay. Mometasone furoate also did not induce unscheduled DNA synthesis *in vivo* in rat hepatocytes.

In reproductive studies in rats, impairment of fertility was not produced in male or female rats by subcutaneous doses up to 15 mcg/kg (approximately 0.01 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

Pregnancy:

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

When administered to pregnant rats, rabbits, and mice, mometasone furoate increased fetal malformations. The doses that produced malformations also decreased fetal growth, as measured by lower fetal weights and/or delayed ossification. Mometasone furoate also caused dystocia and related complications when administered to rats during the end of pregnancy.

In mice, mometasone furoate caused cleft palate at subcutaneous doses of 60 mcg/kg and above. Fetal survival was reduced at 180 mcg/kg. No toxicity was observed at 20 mcg/kg. (Doses of 20, 60 and 180 mcg/kg in the mouse are approximately 0.01, 0.02 and 0.05 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

In rats, mometasone furoate produced umbilical hernias at topical doses of 600 mcg/kg and above. A dose of 300 mcg/kg produced delays in ossification, but no malformations. (Doses of 300 and 600 mcg/kg in the rat are approximately 0.2 and 0.4 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

In rabbits, mometasone furoate caused multiple malformations (e.g., flexed front paws, gallbladder agenesis, umbilical hernia, hydrocephaly) at topical doses of 150 mcg/kg and above (approximately 0.2 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis). In an oral study, mometasone furoate increased resorptions and caused cleft palate and/or head malformations (hydrocephaly and domed head) at 700 mcg/kg. At 2800 mcg/kg most litters were aborted or resorbed. No toxicity was observed at 140 mcg/kg. (Doses of 140, 700 and 2800 mcg/kg in the rabbit are approximately 0.2, 0.9 and 3.6 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

When rats received subcutaneous doses of mometasone furoate throughout pregnancy or during the later stages of pregnancy, 15 mcg/kg caused prolonged and difficult labor and reduced the number of live births, birth weight and early pup survival. Similar effects were not observed at 7.5 mcg/kg. (Doses of 7.5 and 15 mcg/kg in the rat are approximately 0.005 and 0.01 times the estimated maximum clinical topical dose from ELOCON Lotion on a mcg/m² basis).

There are no adequate and well-controlled studies of teratogenic effects from topically applied corticosteroids in pregnant women. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in

sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when ELOCON Lotion is administered to a nursing woman.

Pediatric Use: Since safety and efficacy of ELOCON Lotion have not been established in pediatric patients below 12 years of age, its use in this age group is not recommended.

ELOCON Lotion caused HPA axis suppression in approximately 29% of pediatric patients ages 6 to 23 months who showed normal adrenal function by Cortrosyn test before starting treatment, and were treated for approximately 3 weeks over a mean body surface area of 40% (range 16% to 90%). The criteria for suppression were: basal cortisol level of ≤ 5 mcg/dL, 30-minute post-stimulation level of ≤ 18 mcg/dL, or an increase of < 7 mcg/dL. Follow-up testing 2 to 4 weeks after stopping treatment, available for 8 of the patients, demonstrated suppressed HPA axis function in one patient, using these same criteria. Long-term use of topical corticosteroids has not been studied in this population. (see **CLINICAL PHARMACOLOGY - Pharmacokinetics**).

Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are, therefore, also at greater risk of glucocorticosteroid insufficiency during and/or after withdrawal of treatment. Pediatric patients may be more susceptible than adults to skin atrophy, including striae, when they are treated with topical corticosteroids. Pediatric patients applying topical corticosteroids to greater than 20% of body surface are at higher risk of HPA axis suppression.

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

ELOCON (mometasone furoate lotion) Lotion should not be used in the treatment of diaper dermatitis.

Geriatric Use: Clinical studies of ELOCON Lotion did not include sufficient number of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious.

ADVERSE REACTIONS In clinical studies involving 209 patients, the incidence of adverse reactions associated with the use of ELOCON Lotion was 3%. Reported reactions included acneiform reaction, 2; burning, 4; and itching, 1. In an irritation/sensitization study involving 156 normal subjects, the incidence of folliculitis was 3% (4 subjects).

The following adverse reactions were reported to be possibly or probably related to treatment with ELOCON Lotion during a clinical study, in 14% of 65 pediatric patients 6 months to 2 years of age: decreased glucocorticoid levels, 4; paresthesia, 2; dry mouth, 1; an unspecified endocrine disorder, 1; pruritus, 1; and an unspecified skin disorder, 1. The following signs of skin atrophy were also observed among 65 patients treated with ELOCON Lotion in a clinical study: shininess 4, telangiectasia 2, loss of elasticity 2, and loss of normal skin markings 3. Striae, thinness and bruising were not observed in this study.

The following additional local adverse reactions have been reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence: irritation, dryness, hypertrichosis, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

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

DOSAGE AND ADMINISTRATION Apply a few drops of ELOCON Lotion to the affected skin areas once daily and massage lightly until it disappears. For the most effective and economical use, hold the nozzle of the bottle very close to the affected areas and gently squeeze. Since safety and efficacy of ELOCON Lotion have not been established in pediatric patients below 12 years of age, its use in this age group is not recommended. (see **PRECAUTIONS - Pediatric Use**).

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

ELOCON Lotion should not be used with occlusive dressings unless directed by a physician. ELOCON Lotion should not be applied in the diaper area if the patient requires diapers or plastic pants as these garments may constitute occlusive dressing.

HOW SUPPLIED ELOCON Lotion, 0.1%, is supplied in 30-mL (27.5 g) (NDC-0085-0854-01) and 60-mL (55 g) (NDC-0085-0854-02) bottles; boxes of one.

Store ELOCON Lotion between 2° C and 30° C (36° F and 86° F).

SP Schering Corporation
Kenilworth, NJ 07033 USA

Rev. 7/17/02 17980912

B-XXXXXXXXX

Copyright 1989, 1991, 1994, 1999, 2001, Schering Corporation. All rights reserved.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Jonathan Wilkin
7/17/02 06:26:04 PM