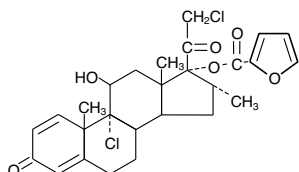


ELOCON® Ointment, 0.1% brand of (mometasone furoate ointment USP)

For Dermatologic Use Only Not for Ophthalmic Use

DESCRIPTION ELOCON® Ointment, 0.1% brand of (mometasone furoate ointment USP) 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:



Mometasone furoate is a white to off-white powder practically insoluble in water, slightly soluble in octanol, and moderately soluble in ethyl alcohol.

Each gram contains: 1 mg mometasone furoate USP in an ointment base of hexylene glycol; phosphoric acid; propylene glycol stearate (55% monoester); white wax; white petrolatum; and purified water.

CLINICAL PHARMACOLOGY Like other topical corticosteroids, mometasone furoate has anti-inflammatory, antipruritic, 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. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Studies performed with ELOCON Ointment, 0.1% 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 ointment on the hypothalamic-pituitary-adrenal (HPA) axis, 15 grams were applied twice daily for 7 days to six adult patients with psoriasis or atopic dermatitis. The ointment was applied without occlusion to at least 30% of the body surface. The results show that the drug caused a slight lowering of adrenal corticosteroid secretion.

In a pediatric trial, 24 atopic dermatitis patients, of which 19 patients were age 2 to 12 years, were treated with ELOCON Cream, 0.1% once daily. The majority of patients cleared within 3 weeks.

Sixty-three pediatric patients ages 6 to 23 months, with atopic dermatitis, were enrolled in an open-label, hypothalamic-pituitary-adrenal (HPA) axis safety study. ELOCON Ointment, 0.1% was applied once daily for approximately 3 weeks over a mean body surface area of 39% (range 15%-99%). In approximately 27% of patients who showed normal adrenal function by Cortrosyn test before starting treatment, adrenal suppression was observed at the end of treatment with ELOCON Ointment, 0.1%. 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 3 patients, using these same criteria.

INDICATIONS AND USAGE ELOCON® Ointment, 0.1% is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

ELOCON Ointment, 0.1% may be used in pediatric patients 2 years of age or older, although the safety and efficacy of drug use for longer than 3 weeks have not been established (see **PRECAUTIONS, Pediatric Use** section). Since safety and efficacy of ELOCON Ointment, 0.1% have not been adequately established in pediatric patients below 2 years of age, its use in this age group is not recommended.

CONTRAINDICATIONS ELOCON® Ointment, 0.1% 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 ointment on the hypothalamic-pituitary-adrenal (HPA) axis, 15 grams were applied twice daily for 7 days to six adult patients with psoriasis or atopic dermatitis. The ointment was applied without occlusion to at least 30% of the body surface. The results show that the drug caused a slight lowering of adrenal corticosteroid secretion.

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** section).

If irritation develops, ELOCON® Ointment, 0.1% 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 Ointment, 0.1% 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 Ointment, 0.1% in the treatment of diaper dermatitis. ELOCON Ointment, 0.1% 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 Ointment, 0.1% 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 Ointment, 0.1%. 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an mcg/m² basis.)

In rabbits, mometasone furoate caused multiple malformations (eg, 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an 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 Ointment, 0.1% on an 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 Ointment, 0.1% is administered to a nursing woman.

Pediatric Use ELOCON Ointment, 0.1% may be used with caution in pediatric patients 2 years of age or older, although the safety and efficacy of drug use for longer than 3 weeks have not been established. Use of ELOCON Ointment, 0.1% is supported by results from adequate and well-controlled studies in pediatric patients with corticosteroid-responsive dermatoses. Since safety and efficacy of ELOCON Ointment, 0.1% have not been adequately established in pediatric patients below 2 years of age, its use in this age group is not recommended.

ELOCON Ointment, 0.1% caused HPA axis suppression in approximately 27% 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 39% (range 15%-99%). 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 3 patients, using these same criteria. Long-term use of topical corticosteroids has not been studied in this population (see **CLINICAL PHARMACOLOGY, Pharmacokinetics** section).

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 children 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 Ointment, 0.1% should not be used in the treatment of diaper dermatitis.

Geriatric Use Clinical studies of ELOCON Ointment, 0.1% included 310 subjects who were 65 years of age and over and 57 subjects who were 75 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS In controlled clinical studies involving 812 patients, the incidence of adverse reactions associated with the use of ELOCON® Ointment, 0.1% was 4.8%. Reported reactions included burning, pruritus, skin atrophy, tingling/stinging, and furunculosis. Reports of rosacea associated with the use of ELOCON Ointment, 0.1% have been received. In controlled clinical studies (n=74) involving pediatric patients 2 to 12 years of age, the incidence of adverse experiences associated with the use of ELOCON Cream is approximately 7%. Reported reactions included stinging, pruritus, and furunculosis.

The following adverse reactions were reported to be possibly or probably related to treatment with ELOCON Ointment, 0.1% during a clinical study, in 5% of 63 pediatric patients 6 months to 2 years of age: decreased glucocorticoid levels, 1; an unspecified skin disorder, 1; and a bacterial skin infection, 1. The following signs of skin atrophy were also observed among 63 patients treated with ELOCON Ointment, 0.1% in a clinical study: shininess, 4; telangiectasia, 1; loss of elasticity, 4; loss of normal skin markings, 4; and thinness, 1. Striae 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, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae, and miliaria.

OVERDOSAGE Topically applied ELOCON® Ointment, 0.1% can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION Apply a thin film of ELOCON® Ointment, 0.1% to the affected skin areas once daily. ELOCON Ointment, 0.1% may be used in pediatric patients 2 years of age or older. Since safety and efficacy of ELOCON Ointment, 0.1% have not been adequately established in pediatric patients below 2 years of age, its use in this age group is not recommended (see **PRECAUTIONS, Pediatric Use** section).

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. Safety and efficacy of ELOCON Ointment, 0.1% in pediatric patients for more than 3 weeks have not been established.

ELOCON Ointment, 0.1% should not be used with occlusive dressings unless directed by a physician.

ELOCON Ointment, 0.1% should not be applied in the diaper area if the child still requires diapers or plastic pants, as these garments may constitute occlusive dressing.

HOW SUPPLIED ELOCON® Ointment, 0.1% is supplied in 15-g (NDC 0085-0370-01) and 45-g (NDC 0085-0370-02) tubes; boxes of one.

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

 Schering-Plough

Kenilworth, NJ 07033 USA

Rev. 9/08

Copyright © 1987, 2008, Schering Corporation. All rights reserved.

The trademarks depicted in this piece are owned by their respective companies.

18724243T