

PRODUCT MONOGRAPH

 **ELOCOM[®]**

Mometasone Furoate Cream, 0.1%
Mometasone Furoate Ointment, 0.1%
Mometasone Furoate Lotion, 0.1%

Corticosteroid

Merck Canada Inc.
16750 route Transcanadienne
Kirkland, Quebec H9H 4M7

Date of Preparation:
March 2, 2011

Date of Revision:
December 14, 2011

Control # 145174

[®]Registered trademark of Schering Canada Inc.

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION.....3
SUMMARY PRODUCT INFORMATION3
INDICATIONS AND CLINICAL USE.....3
CONTRAINDICATIONS3
WARNINGS AND PRECAUTIONS.....4
ADVERSE REACTIONS.....5
DRUG INTERACTIONS6
DOSAGE AND ADMINISTRATION.....7
OVERDOSAGE7
ACTION AND CLINICAL PHARMACOLOGY8
STORAGE AND STABILITY.....8
DOSAGE FORMS, COMPOSITION AND PACKAGING9

PART II: SCIENTIFIC INFORMATION10
PHARMACEUTICAL INFORMATION.....10
CLINICAL TRIALS.....11
DETAILED PHARMACOLOGY17
TOXICOLOGY18
REFERENCES20

PART III: CONSUMER INFORMATION.....27

ELOCOM[®]
Mometasone furoate

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Topical	Cream / 0.1%	For a complete listing see <i>Dosage Forms, Composition and Packaging</i> section.
	Ointment / 0.1%	
	Lotion / 0.1%	

INDICATIONS AND CLINICAL USE

ELOCOM (mometasone furoate) Cream, Ointment and Lotion 0.1%, are indicated for:

- the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses such as psoriasis and atopic dermatitis. The lotion formulation may be applied to scalp lesions.

CONTRAINDICATIONS

- ELOCOM (mometasone furoate) Cream, Ointment and Lotion 0.1% are contraindicated in patients who are sensitive to mometasone furoate, to other corticosteroids or to any component of these preparations. For a complete listing, see the Dosage Forms, Composition, and Packaging section of the product monograph.
- Topical steroids are contraindicated in untreated fungal, bacterial and viral (i.e. herpes simplex, chicken pox and vaccinia) infections involving the skin.

WARNINGS AND PRECAUTIONS

General

Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children. Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio. Use of topical corticosteroids in children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with growth and development of children.

Patients should be advised to inform subsequent physicians of the prior use of glucocorticoids.

Endocrine and Metabolism

Any of the side effects that have been reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

Although ELOCOM is poorly absorbed, nevertheless, application of corticosteroids over extensive lesions, or exceeding the dosage schedule may result in significant systemic absorption producing hypercorticism manifesting itself by adrenal suppression, moon facies, striae and suppression of growth.

Immune

During the use of topical corticosteroids, infections may occur. If an overt infection is present, appropriate antimicrobial treatment is indicated. If symptomatic response is not noted within a few days to a week, the local application of corticosteroids should be discontinued and the patient re-evaluated.

Ophthalmologic

ELOCOM is not formulated for ophthalmic use and should not be used in or near the eyes.

Skin

The lotion contains isopropyl alcohol and may cause stinging or burning upon application to abraded or sun-burned skin.

If irritation or sensitization develops with the use of ELOCOM products, treatment should be discontinued and appropriate therapy instituted.

Prolonged use of corticosteroid preparations may produce striae or atrophy of the skin or subcutaneous tissues. If this occurs, treatment should be discontinued.

Special Populations

Pregnant Women: Since safety of topical corticosteroid use in pregnant women has not been established, drugs of this class should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Nursing Women: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatrics: Evidence from clinical studies and experience suggests that use in the pediatric population is associated with differences in safety or effectiveness and a brief discussion can be found in the appropriate section. (See ***WARNINGS AND PRECAUTIONS, General, Endocrine and Metabolism CLINICAL TRIALS, Corticosteroid- Responsive Dermatoses in Pediatric Patients***)

Geriatrics: Suitable precautions should be taken in using topical glucocorticoids in patients with impaired circulation suffering from stasis dermatitis and other skin diseases.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Local adverse reactions reported very rarely with ELOCOM Cream 0.1% include paresthesia, pruritus and signs of skin atrophy. In <1% of patients, local adverse reactions reported with ELOCOM Cream 0.1% include abscess, burning, disease exacerbation, dry skin, erythema, furunculosis and pimples.

Local adverse reactions rarely reported with ELOCOM Ointment 0.1% include burning, pruritus, tingling/stinging and signs of skin atrophy. In <1% of patients, adverse reactions reported with ELOCOM Ointment 0.1% include aggravated allergy, dermatitis, erythema, furunculosis, increased lesion size, nausea (one patient) and vaginal discharge (one patient).

Local adverse reactions rarely reported with ELOCOM Lotion 0.1% include burning, folliculitis, acneiform reaction, pruritus and signs of skin atrophy. In <1% of patients, adverse reactions reported with ELOCOM Lotion 0.1% include, papule, pustule and stinging.

The following local adverse reactions have been reported infrequently with the use of other topical corticosteroids: irritation, hypertrichosis, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, striae and miliaria.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The following local adverse reactions have been reported with ELOCOM: **Cream**: During clinical studies in 319 patients: burning - 1, pruritus - 1, skin atrophy - 3. **Ointment**: During clinical studies in 812 patients: burning - 13, pruritus - 8, skin atrophy - 8, tingling/stinging - 7, and furunculosis - 3. **Lotion**: During clinical studies in 457 patients: burning - 9 (2%), pruritus - 4 (1%), skin atrophy - 6 (2%) (shininess, thinness, striae, telangiectasia), acneiform reactions - 3 (<1%).

The following local adverse reactions have been reported infrequently when other topical dermatologic corticosteroids have been used as recommended. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, miliaria.

Adrenal suppression has also been reported following topical corticosteroid therapy. Posterior subcapsular cataracts have been reported following systemic use of corticosteroids.

Cream: The overall incidence of side effects was 1.6%, i.e. 5 of 319 subjects and patients reported treatment-related adverse experiences. **Ointment**: The overall incidence of side effects was 4.9%, i.e. 40 of 812 subjects reported treatment-related adverse experiences. **Lotion**: The overall incidence of side effects was 5.1%, i.e. 31 of 613 subjects and patients reported treatment-related adverse experiences.

Side effects were mild to moderate and were those typically associated with topical corticosteroid formulations after seven days of treatment.

No systemic treatment-related adverse experiences were seen.

DRUG INTERACTIONS

Drug-Drug Interactions

Interactions with other drugs have not been established.

Drug-Food Interactions

Interaction with food has not been established.

Drug-Herb Interactions

Interaction with herbs has not been established.

Drug-Laboratory Interactions

Interaction with laboratory testing has not been established.

Drug-Lifestyle Interactions

Interaction with lifestyle has not been established.

DOSAGE AND ADMINISTRATION

ELOCOM Cream/Ointment: Apply a thin film to the affected skin areas once daily.

ELOCOM Lotion: Apply a few drops of the lotion to the affected skin areas including scalp sites once daily; massage gently and thoroughly until medication disappears.

Do not use occlusive dressings.

OVERDOSAGE

No specific antidote is available and treatment should be symptomatic.

Symptoms: Excessive, prolonged use of topical corticosteroids can suppress pituitary-adrenal function resulting in secondary adrenal insufficiency, which may present with any combination of the following symptoms: fatigue, weakness, decreased appetite, constipation, nausea, vomiting, diarrhea, abdominal pain, skin colour darkening (especially on scars, elbows, knees, knuckles, toes, lips, and mucous membranes).

Percutaneous absorption of corticosteroids can occur when large amounts of corticosteroids are applied. Toxic effects may include ecchymosis of skin, peptic ulceration, hypertension, aggravation of infection, hirsutism, acne, edema and muscle weakness due to protein depletion.

Treatment: Appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are virtually reversible. Treat electrolyte imbalance, if necessary. In cases of chronic toxicity, slow withdrawal of corticosteroids is advised.

Treatment of a patient with systemic toxic manifestations consists of assuring and maintaining a patent airway and supporting ventilation using oxygen and assisted or controlled respiration as required. This will be sufficient in the management of most reactions. Should circulatory depression occur, vasopressors such as ephedrine or metaraminol and intravenous fluids may be used. Should a convulsion persist despite oxygen therapy, small increments of an ultra-short

acting barbiturate (pentobarbital or secobarbital) may be given intravenously. Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

ELOCOM (mometasone furoate) has anti-inflammatory, antipruritic and vasoconstrictive actions. The exact mechanism, however, of corticosteroids in each disease is uncertain. Mometasone furoate, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs.

Pharmacokinetics

Cream – The percutaneous absorption of mometasone furoate cream 0.1% was evaluated in subjects receiving a single application of radio-labeled ³H-mometasone furoate cream 0.1% which remained on intact skin for eight hours. Based on the amount of radioactivity excreted in the urine and feces during the five-day study period, approximately 0.4% of the applied dose was absorbed systemically. The radioactive content found in plasma and red blood cells remained a few counts above background levels (corresponding to ≤ 0.1 ng/ml) throughout the study.

Ointment - A percutaneous absorption study with radio-labeled ³H-mometasone furoate ointment was conducted in adult male volunteers with intact skin. Based on the amounts of radioactivity excreted after an eight-hour application of the active ointment and analysis of urine and feces, approximately 0.7% of the applied dose was absorbed systemically without occlusion.

Lotion - Due to the occlusive nature of the ointment base, the percutaneous absorption following application of a corticosteroid ointment is greater than that of a topical corticosteroid in a cream or lotion formulation. Consequently, absorption following application of mometasone furoate lotion 0.1% is expected to be no greater than that which may occur after application of the ointment formulation.

STORAGE AND STABILITY

Store between 15° and 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each gram of ELOCOM Cream 0.1% contains 1 mg mometasone furoate. Non medicinal ingredients include: aluminum starch octenylsuccinate, cetareth-20, hexylene glycol, propylene glycol monostearate, purified water stearyl alcohol and titanium dioxide, white petrolatum, white wax, and phosphoric acid to adjust the pH.

Each gram of ELOCOM Ointment 0.1% contains 1 mg mometasone furoate. Non medicinal ingredients include: hexylene glycol, propylene glycol monostearate, purified water, white petrolatum, white wax, and phosphoric acid to adjust the pH.

Each gram of ELOCOM Lotion 0.1% contains 1 mg mometasone furoate. Non medicinal ingredients include: hydroxypropylcellulose, isopropyl alcohol, phosphoric acid, propylene glycol, purified water and sodium phosphate monobasic.

ELOCOM Cream 0.1% is supplied in 15 g and 50 g tubes, boxes of one.

ELOCOM Ointment 0.1% is supplied in 15 g, and 50 g tubes, boxes of one.

ELOCOM Lotion 0.1% is supplied in 30 mL and 75 mL plastic bottles, boxes of one.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: mometasone furoate

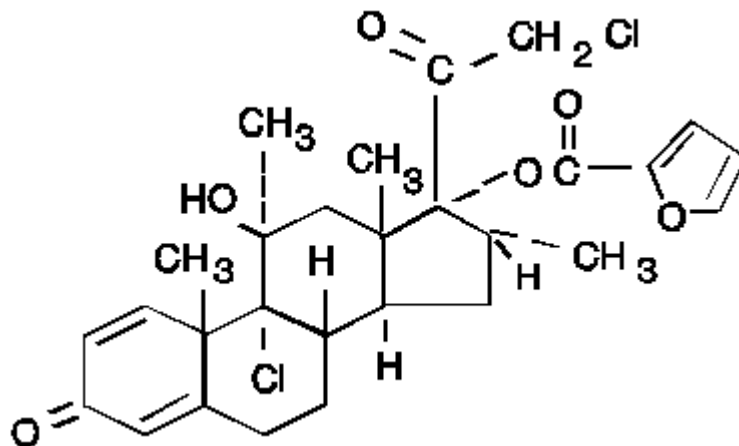
Chemical name:

9a,21-Dichloro-11b,17-dihydroxy-16a-methylpregna-1,4-diene-3,20-dione 17-(2-furoate)

Molecular formula and molecular mass:

$C_{27}H_{30}Cl_2O_6$ and a molecular weight of 521.4

Structural formula:



Physicochemical properties:

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

CLINICAL TRIALS

Efficacy Studies: Mometasone Furoate Cream 0.1%

Psoriasis -- A multicenter, double-blind, parallel-group study compared the efficacy of mometasone furoate cream 0.1% to that of its vehicle alone in patients with moderate to severe psoriasis. Mometasone furoate cream 0.1%, applied once a day (QD), was effective in ameliorating signs of psoriasis; it was significantly ($P<0.01$) more effective than the vehicle alone in reducing total disease sign score. After one week of treatment, improvement in the total disease sign scores averaged 25% for the mometasone-treated group and 15% for the vehicle-treated group, demonstrating a statistically significant ($P<0.01$) difference. After three weeks of treatment, a statistically significant ($P<0.01$) difference was again observed with the active cream. Improvement in total disease sign scores averaged 44% and 22% in the mometasone cream-and vehicle-treated patients, respectively. Results of the endpoint analysis also demonstrated that mometasone furoate was significantly ($P<0.01$) more effective than vehicle in reducing total disease sign scores. Furthermore, physician's global evaluation of overall change in disease status indicated significantly ($P<0.01$) greater improvement in the mometasone-treated patients compared to vehicle-treated patients at each evaluation over the entire three-week course of therapy.

In another two parallel-group, multicentric studies the efficacy of mometasone furoate cream 0.1% applied QD was compared to that of fluocinolone acetonide cream 0.025% applied three times daily (TID) for three weeks and to that of triamcinolone acetonide cream 0.1% applied twice daily (BID) for three weeks.

Based on improvement in total disease sign scores and physician's global evaluation of overall change in disease status in both studies, mometasone furoate cream 0.1% was significantly ($P<0.01$) more effective than fluocinolone acetonide and comparable to triamcinolone acetonide cream. Improvement in total disease sign scores, which ranged from 22% to 26%, was observed as early as Day 4 in mometasone furoate treated patients. Comparable improvement (22%) was seen in the triamcinolone-treated group.

In contrast, the fluocinolone-treated patients had achieved 16% improvement by Day 4. By study end, percent improvement ranged from 44% to 55% with mometasone furoate cream compared to 51% and 33% with triamcinolone and fluocinolone, respectively.

Mean global scores for mometasone furoate-treated patients also indicated continuous improvement over the treatment course. At the end of each study period, moderate improvement was observed in the mometasone furoate and triamcinolone acetonide treatment groups. Yet, little improvement was observed in the fluocinolone acetonide treatment group over the same period. Mean global scores in this group were never indicative of greater than slight improvement at any time during the study.

In a bilateral-paired comparative study, mometasone furoate cream 0.1% and betamethasone valerate cream 0.1%^a were applied BID for two weeks to psoriatic patients. While both study agents were equally effective in many patients, some patients responded better to mometasone therapy.

^a VALISONE[®] Cream

Although at Day 4 lesions in more than one-half of patients had responded equally to either study preparation, most patients with differences in lesion response significantly favored treatment with mometasone furoate (P<0.03). By Day 15, total sign scores indicated that 56% of patients favored treatment with mometasone furoate as compared to 13% who favored treatment with betamethasone valerate and 31% of patients whose lesions responded equally to the two agents (P<0.01). Similarly, the physician's global evaluation scores at Day 15 indicated that lesions in 51% of patients responded more favorably to mometasone furoate cream as compared to lesions in 10% of patients who responded more favorably to betamethasone valerate cream (P<0.01). By treatment end, improvement in total disease sign scores averaged 59% in the mometasone-treated lesions and 49% in those treated with betamethasone valerate cream.

Atopic Dermatitis -- Another multicentric, double-blind, parallel-group study compared the efficacy of mometasone furoate cream 0.1% with that of its vehicle alone in patients with moderate to severe atopic dermatitis. Mometasone furoate cream applied QD was effective in ameliorating signs and symptoms of atopic dermatitis; it was significantly (P<0.01) more effective than vehicle alone. A rapid response to mometasone furoate was evident after seven treatment days when improvement in total disease sign/symptom scores averaged 50% and 28% in the mometasone cream and vehicle treatment groups, respectively, showing a statistically significant (P<0.01) difference. At Day 22, improvement in scores averaged 77% and 51% in the active cream- and vehicle treatment groups, respectively. Moreover, the endpoint analysis showed a 76% improvement in the mometasone cream-treated patients as compared to a 44% improvement in patients treated with the vehicle. Physician's global evaluation scores indicated that patients treated with the active cream had significantly (P<0.01) greater improvement in disease status than vehicle-treated patients at each evaluation over the entire course of therapy.

In two single-blind studies, mometasone furoate cream 0.1% applied QD was compared to hydrocortisone butyrate cream 0.05%[†] and to betamethasone valerate cream 0.1%,[‡] each applied BID for three weeks.

Results in the first study demonstrated that mometasone furoate was significantly (P<0.05) more effective than hydrocortisone butyrate at all times during the study. At Day 4, percent improvement averaged 35% in the mometasone furoate-treated patients as compared to 30% in the hydrocortisone butyrate patient group. By Day 22, the average percent improvement was 88% and 84% in the mometasone- and hydrocortisone-treated groups, respectively.

Mean global scores for the mometasone-treated patients were indicative of moderate improvement as early as Day 4, while only slight improvement was observed in the hydrocortisone group.

In the second study, the extent of improvement in mometasone furoate-treated patients was similar to that observed in other studies; comparable improvement was seen in the betamethasone-treated group. By Day 4, patients in both treatment groups showed approximately 40% improvement which

[†] LOCOID[®] Cream, Owen Laboratories, S.A. TX, USA

[‡] BETNOVATE[®] Cream, Glaxo Laboratories Limited, UK

progressed throughout the study. At the end of the study period, mean global scores in both treatment groups were indicative of marked improvement.

Corticosteroid-Responsive Dermatoses -- The efficacy of mometasone furoate cream 0.1% applied QD was compared to that of betamethasone valerate cream 0.1%^a applied BID in the treatment of various corticosteroid- responsive dermatoses. Mometasone furoate cream QD was as effective as betamethasone valerate applied BID as indicated by percent improvement in total disease sign/ symptoms scores and physician's global evaluation of overall change in disease status. Onset of action was rapid with both preparations, and progressive improvement occurred in both treatment groups throughout the three-week study period. By Day 22, percent improvement averaged 94% and 97% in the mometasone- and betamethasone-treated patients, respectively. Mean global scores for both treatment groups were indicative of moderate improvement as early as Day 4. At study end, mean global scores in the mometasone and betamethasone groups indicated complete clearing of lesions in most patients in each treatment group.

Corticosteroid-Responsive Dermatoses in Pediatric Patients -- Two randomized, parallel-group studies evaluated the efficacy of mometasone furoate cream 0.1% in the treatment of various corticosteroid-responsive dermatoses in pediatric patients.

In the first study, mometasone furoate cream 0.1% applied QD was compared to clobetasone butyrate cream 0.05%^b applied BID for three weeks. In the second study, mometasone furoate cream 0.1% applied QD was compared to betamethasone valerate cream 0.1% applied BID for three weeks.

Results of both studies demonstrated that daily single applications of mometasone furoate cream 0.1% were as effective as clobetasone 0.05% and betamethasone 0.1% each applied twice daily in ameliorating signs/symptoms of corticosteroid-responsive dermatoses. With mometasone furoate cream, symptomatic improvement was observed as early as Day 4 and ranged from 36% to 46%. Similarly, 28% improvement occurred with clobetasone butyrate cream and 52% with betamethasone valerate cream. At Day 22, percent improvement ranged from 94% to 99% with mometasone furoate cream and was 90% and 94% with clobetasone and betamethasone, respectively. Mean global scores in all treatment groups were indicative of rapid, progressive improvement in disease status throughout the study. At study end, mean global scores indicated complete clearing to marked improvement in most mometasone-treated patients, complete clearing in the betamethasone-treated patients, and marked improvement in the clobetasone group.

Efficacy Studies: Mometasone Furoate Ointment 0.1%

Psoriasis -- In two bilateral-paired comparison trials, the efficacy of BID applications of mometasone furoate ointment in concentrations of 0.1% and 0.05% was compared to that of betamethasone valerate ointment also applied BID for 14 days. Results showed that the 0.1% formulation of mometasone furoate ointment was significantly ($P<0.05$) more effective than

^a VALISONE[®] Cream

^b EUMOVATE[®] Cream

betamethasone valerate ointment^c. As demonstrated by the physician's global evaluation of change in disease status, 60% of patients responded more favorably to mometasone furoate ointment 0.1%, while 13% experienced a comparable response in the betamethasone valerate-treated group. Improvement from baseline in total disease sign score was 51% and 40% for mometasone furoate ointment 0.1% and betamethasone valerate ointment, respectively. Furthermore, these results also demonstrated that mometasone furoate ointment 0.05% was superior to betamethasone valerate ointment but not as effective as the 0.1% mometasone furoate ointment formulation.

In a third bilateral-paired comparative study of mometasone furoate ointment 0.1% and betamethasone dipropionate ointment^d applied BID for 14 days, percent improvement in total disease scores was similar between the two preparations, 63% and 58% for mometasone furoate ointment 0.1% and betamethasone dipropionate ointment, respectively. However, 38% of patients responded more favorably to mometasone furoate ointment 0.1% while 3% responded better to betamethasone dipropionate ointment.

Furthermore, three randomized, multicentric, parallel group studies were conducted in patients with psoriasis to compare the efficacy of mometasone furoate ointment 0.1% applied QD to that of triamcinolone acetonide^e applied BID, fluocinolone acetonide^f applied TID or to that of the vehicle alone applied QD for 21 days. Mometasone furoate ointment 0.1% was significantly ($P<0.01$) better than triamcinolone acetonide, fluocinolone acetonide and the vehicle as demonstrated by the percent improvement in total disease sign scores. The superior efficacy of mometasone furoate ointment applied QD was observed despite the more frequent administrations of the two comparative agents. Physician's global evaluation of disease status at endpoint analysis also confirmed that mometasone furoate ointment 0.1% was significantly ($P<0.01$) more effective than triamcinolone acetonide, fluocinolone acetonide or the vehicle alone in the treatment of patients with psoriasis.

Two additional studies in psoriatic patients compared QD applications of mometasone furoate ointment 0.1% with QD applications of betamethasone dipropionate 0.05% and BID applications of betamethasone valerate 0.1%^g respectively for three weeks. Mometasone furoate ointment 0.1% QD was significantly ($P<0.01$) more effective than betamethasone valerate BID and comparable to betamethasone dipropionate QD as demonstrated by percent improvement in total disease sign scores at endpoint analysis. Physician's overall evaluation of disease status also indicated that mometasone furoate ointment was significantly ($P<0.01$) more effective than betamethasone valerate in the treatment of psoriasis. At the end of the three-week study period, mean scores were indicative of marked to moderate improvement in most patients treated with mometasone furoate ointment. Comparable improvement was effected with betamethasone dipropionate and moderate to slight improvement was observed in the betamethasone valerate-treated group.

^c VALISONE[®] Ointment

^d DIPROSONE[®] Ointment

^e KENALOG[®] ER Squibb & Sons, Inc., Princeton, NJ USA

^f SYNALAR[®] Syntax Laboratories, Palo Alto, CA USA

^g BETNOVATE[®] Ointment, Glaxo Laboratories, UK

Atopic Dermatitis -- Patients with atopic dermatitis participated in a bilateral-paired comparative study, which evaluated the efficacy of mometasone furoate ointment 0.1% against that of betamethasone valerate ointment. Results demonstrated that mometasone furoate ointment 0.1% was equivalent in activity to betamethasone valerate ointment when both agents were applied BID. Another three randomized, multicentric parallel-group studies compared the efficacy of mometasone furoate ointment 0.1% QD with that of betamethasone valerate ointment BID, the ointment vehicle alone applied QD, or hydrocortisone butyrate ointment 0.1%^h applied BID for three weeks. In these studies, mometasone furoate was equivalent to the known standard agents, betamethasone valerate and hydrocortisone butyrate, even though mometasone furoate was applied less frequently than each of these comparatives. Percent improvement in total disease sign score at end-point analysis in the three studies were 82%, 83% and 60%, respectively, for mometasone furoate ointment 0.1% as compared to 79%, 24% and 46% for betamethasone valerate ointment, the vehicle and hydrocortisone butyrate, respectively (P<0.01). Furthermore, global scores at endpoint reflected marked improvement in the mometasone furoate and betamethasone valerate-treatment groups, moderate improvement in the hydrocortisone-treated group and slight improvement in the vehicle-treated group.

Corticosteroid-Responsive Dermatoses -- In three parallel-group studies, the efficacy of mometasone furoate ointment 0.1% was compared to that of betamethasone valerate 0.05% and clobetasone butyrate 0.025%ⁱ in the treatment of various corticosteroid-responsive dermatoses. Mometasone furoate ointment was applied QD while the comparative agents were each applied BID for three weeks. After one treatment week, improvement in disease signs ranged from 58% to 90% with QD mometasone furoate administration, 52% to 77% with BID application of betamethasone valerate and 69% with BID administration of clobetasone butyrate. By treatment end, percent improvement averaged 93% for mometasone furoate, 89% and 93% for betamethasone valerate and 90% for clobetasone butyrate. At endpoint evaluation, global scores indicated disease clearance in the majority of mometasone-treated patients; marked improvement was observed in most patients treated with betamethasone valerate or clobetasone butyrate.

Efficacy Studies: Mometasone Furoate Lotion 0.1%

Scalp Psoriasis -- The efficacy of mometasone furoate lotion 0.1% in the treatment of patients with scalp psoriasis was evaluated in three randomized, parallel-group studies.

The first study compared QD application of mometasone furoate lotion 0.1% to that of the lotion vehicle alone. A second study compared mometasone furoate lotion 0.1% to betamethasone dipropionate lotion 0.05%^j both applied QD. In the third study, mometasone lotion 0.1% applied QD was compared to betamethasone valerate lotion 0.1%^k applied BID.

Results of these studies demonstrated that mometasone furoate lotion 0.1% was significantly (P<0.001) more effective than the vehicle and slightly superior in efficacy to betamethasone dipropionate and to betamethasone valerate applied QD and BID, respectively. Endpoint percent

^h LOCOID[®] Ointment, Owen Laboratories, SA TX USA

^j DIPROSONE[®] Lotion

^k BETNOVATE[®] Lotion, Glaxo Laboratories Limited, UK

improvement in total sign/symptom scores ranged from 76% to 96% in the mometasone-treated groups and from 24% to 88% in the comparative groups. Endpoint analysis of physician's global evaluation also confirmed that mometasone-treated patients had significantly ($P \leq 0.02$) greater improvement in overall disease status than patients treated with betamethasone dipropionate or vehicle alone.

Seborrheic Dermatitis -- Two parallel-group studies in patients with seborrheic dermatitis compared the efficacy of QD application of mometasone furoate lotion 0.1% to that of the lotion vehicle alone and to that of betamethasone valerate lotion 0.1% applied BID. In these studies, mometasone furoate was significantly ($P < 0.001$) more effective than the vehicle and comparable in efficacy to betamethasone valerate lotion. Endpoint percent improvement in total sign/symptom scores was 86% and 89% in the mometasone-treated groups compared to 53% and 87%, in the vehicle and comparative groups, respectively. Similarly, endpoint mean global scores reflected marked improvement in the mometasone and betamethasone valerate-treated patients and slight improvement in the vehicle.

Onset of Action: Cream -- Onset of action was investigated in several clinical trials with both pediatric and adult patients with various dermatologic conditions. A rapid onset of action with mometasone cream 0.1% was demonstrated after one week of treatment by percent improvement from baseline in total disease sign/symptom score (ranging from 25% to 81%). In these studies, percent improvement for the comparative agents were: betamethasone valerate (ranged from 43% to 81%); clobetasone butyrate (59%); hydrocortisone butyrate (54%); fluocinolone acetonide (24%); triamcinolone acetonide (36%); and for the vehicle alone (15% and 28%). Furthermore, in two of these studies, mometasone furoate cream 0.1% was significantly more effective than fluocinolone acetonide ($P < 0.001$) and hydrocortisone butyrate ($P \leq 0.05$) at Day 4 evaluation.

Onset of Action: Ointment -- Mometasone furoate ointment 0.1% QD also had a rapid onset of action in psoriatic patients as evidenced by percent improvement from baseline in total disease sign/symptom scores after one treatment week (ranging from 38% to 59%). Percent improvements for comparative agents were triamcinolone acetonide (28%), fluocinolone acetonide (33%), betamethasone dipropionate (23%), betamethasone valerate (56%) and vehicle alone (43%). In two of these studies mometasone furoate was significantly more effective than triamcinolone acetonide or fluocinolone acetonide at Day 4 evaluation ($P < 0.01$).

The effects of mometasone furoate ointment 0.1% in the treatment of patients with atopic dermatitis also were rapid in onset as demonstrated by mean percent improvement and mean global evaluation scores at Day 4 and Week 1. Mometasone furoate-treated patients showed an improvement in total sign/symptom score that ranged from 27% to 47% at Day 4 and 51% to 64% at Week 1. In comparison, hydrocortisone butyrate and betamethasone valerate demonstrated 17% and 43% improvement, respectively, at Day 4 and 24% and 65%, respectively, at Week 1. Global scores at one-week indicated moderate improvement in patients treated with mometasone furoate or betamethasone valerate and slight improvement in those treated with hydrocortisone butyrate.

Onset of Action: Lotion -- Mometasone furoate lotion 0.1% showed rapid onset of action after one treatment week in patients with scalp psoriasis. As demonstrated by results at Day 8 in one study,

improvement in total sign/symptom scores was significantly ($P<0.01$) greater in mometasone-treated patients than in those treated with betamethasone valerate 0.1%.

Safety Studies -- No evidence of HPA axis suppression occurred in a study in which 15 g of mometasone furoate cream were applied BID for seven days to patients with psoriasis or atopic dermatitis. The cream was applied without occlusion to at least 30% of body surface. Plasma cortisol levels were within the lower limit of the normal range in these patients following application of the cream formulation.

In a study of the effects of mometasone furoate ointment on the HPA axis, 15 g were applied BID for seven days to patients with psoriasis or atopic dermatitis. The ointment was applied without occlusion to at least 30% of body surface. The results suggest that the drug caused a slight reduction of urinary-free cortisol. However, this change was not considered clinically important since it was not accompanied by subnormal levels of plasma cortisol or 17-OHC.

The results of other local and systemic safety studies also showed that mometasone furoate cream and ointment 0.1% have minimal percutaneous absorption and do not cause adrenal suppression. In other investigations, mometasone furoate cream and ointment 0.1% demonstrated minimal potential for irritation, sensitization, photocontact allergenicity and phototoxic reactions when used as recommended. Furthermore, when compared to hydrocortisone ointment 0.1% mometasone furoate ointment 0.1% has a low atrophogenic potential. No clinical meaningful changes in laboratory test values were observed with either mometasone furoate cream or ointment.

A special safety study to determine contact irritation and sensitization potential demonstrated that mometasone furoate lotion 0.1% has minimal potential to cause skin irritation and/or sensitization reactions. Doses of approximately 0.2 g of mometasone furoate lotion, mometasone lotion vehicle, betamethasone dipropionate lotion 0.05% betamethasone lotion vehicle, or USP white petrolatum were applied under occlusion for 48 to 72 hours, three times a week for three weeks (induction phase) to normal volunteers. Following a rest period, subjects were administered a challenge dose of two successive 48-hour applications to a previously untreated site. During the induction phase, irritation reactions to mometasone and one or more of the test preparations were observed in some subjects at isolated times. However, irritation reactions to mometasone were not uniform; they occurred at various times during the study but did not follow a specific pattern. Furthermore, no sensitization reactions occurred following the two successive challenge applications.

Other safety data indicated that adverse reactions related to treatment with mometasone furoate lotion 0.1% were local in nature and similar to those commonly associated with topical corticosteroid therapy. Evaluation of laboratory findings showed no indication of organ or organ system toxicity.

DETAILED PHARMACOLOGY

Pre-Clinical Data

Pharmacodynamics -- The pharmacologic profile of mometasone furoate was determined by standard laboratory methods. Relative to betamethasone valerate, the anti-inflammatory activity and anti-psoriatic activity of mometasone furoate were evaluated in mice and guinea pigs, respectively. Hypothalamic-pituitary-adrenal (HPA) axis suppression, thymolysis and skin atrophy were evaluated in mice.

In the croton oil assay in mice, mometasone furoate ($ED_{50} = 0.02 \mu\text{g}/\text{ear}$) was equipotent to betamethasone valerate after single application, and was approximately eight times as potent as betamethasone valerate after five daily applications (ED_{50} values = $0.002 \mu\text{g}/\text{ear}/\text{day}$ vs $0.014 \mu\text{g}/\text{ear}/\text{day}$). In guinea pigs, mometasone furoate was approximately twice as potent as betamethasone valerate in reducing M. Ovalis-induced epidermal acanthosis after 14 daily applications.

With respect to pharmacologic activities commonly associated with corticosteroids, mometasone furoate ($ED_{50} = 5.3 \mu\text{g}/\text{ear}/\text{day}$) was less potent than betamethasone valerate ($ED_{50} = 3.1 \mu\text{g}/\text{ear}/\text{day}$) in suppressing the HPA axis in mice after five daily applications. In the thymolysis assay, mometasone furoate ($ED_{50} = 26.6 \mu\text{g}/\text{ear}/\text{day}$) was approximately two times as potent as betmethasone valerate ($ED_{50} = 51.6 \mu\text{g}/\text{ear}/\text{day}$) when applied topically, and following subcutaneous administration for five days, mometasone furoate ($ED_{50} = 11.2 \mu\text{g}/\text{mouse}$) was approximately six times as potent as betamethasone valerate ($ED_{50} = 59.8 \mu\text{g}/\text{mouse}$). At doses five to 5000 times the effective anti-inflammatory doses, mometasone furoate was three to eight times more potent than betamethasone valerate with respect to skin thinning in mice. Based on the ratio of systemic potency (HPA suppression or thymolysis) to topical anti-inflammatory potency, the therapeutic indexes for mometasone furoate were approximately three to ten times greater than those for the comparative, betamethasone valerate. Therefore, mometasone furoate would be expected to have a superior safety margin to that of betamethasone valerate.

Pharmacokinetics -The percutaneous absorption and excretion of ^3H mometasone furoate cream and/or ointment was evaluated in rats, rabbits and dogs with doses ranging from 5.2 to $22 \mu\text{g}/\text{cm}^2$. Additionally, the tissue distribution of absorbed radioactivity was determined in rabbits.

Systemic absorption of ^3H -mometasone furoate was minimal in all species studied, ranging from approximately 2% in dogs to 6% in rabbits over a 5 to 7-day period. The cream and ointment formulations were comparable with respect to systemic absorption. Plasma levels were low ranging from <0.1 to $<1 \text{ ng}/\text{ml}$. Less than 1.3% of the applied dose was excreted in urine of all species and from 1.5 to 4.2% was excreted in feces. Characterization of urinary metabolites was not possible due to the low levels of drug in urine. However, it is well known that corticosteroids are metabolized to inactive water-soluble substances such as sulfate esters or glucuronides and are excreted as such. In rabbits, there was no unusual accumulation of radioactivity in any tissue.

TOXICOLOGY

Toxicology -- A program consisting of evaluation of local and systemic toxicity, reproductive toxicity, genetic toxicity, dermal irritation and sensitization potential and ocular irritation was conducted to determine the safety of mometasone furoate cream and ointment. Acute toxicity was evaluated in mice, rats and dogs including young (21-day old) mice and rats. Repeated dose toxicity was evaluated in rats, rabbits and dogs by subcutaneous and/or topical routes. Reproduction studies were conducted in rats and rabbits and included evaluation of teratology, peri and post-natal development and general reproductive performance. Sensitization potential was determined in guinea pigs and dermal and ocular irritation were evaluated in rabbits. *In vitro* and *in vivo* genetic toxicology studies were conducted to evaluate potential mutagenicity and clastogenicity (capacity to induce chromosomal changes).

The acute subcutaneous LD₅₀ values of mometasone furoate were determined to be between 200 and 2000 mg/kg in mice, 2000 mg/kg or greater in rats and >200 mg/kg in dogs. Following oral administration the LD₅₀ values were >2000 mg/kg in mice and rats. As expected, the LD₅₀ values for young (21-day old) mice and rats were 2 to 20 times lower than those for adult animals.

Following repeated administration of mometasone furoate in rats, rabbits and dogs at doses up to 670 times the anticipated maximum human dose for up to 6 months, findings were typical of corticosteroid administration in all species. These included (1) slight reduction in body weight gain, (2) skeletal muscle wasting, (3) abdominal distention, (4) decrease in lymphocytes and eosinophils and increase in neutrophils, (5) increase in serum transaminases (SGPT and SGOT), cholesterol and triglycerides, (6) lipemia, and (7) organ changes (atrophy of spleen and thymus, local skin thinning, increased liver and kidney weights and reduced osteogenesis). These changes were generally observed more frequently or more severe in animals receiving the comparative agent, betamethasone valerate. No unusual systemic effects were observed with either drug. Dermal responses to repeated application of mometasone furoate or betamethasone valerate cream were limited to transient episodes of slight to moderate erythema, skin wrinkling, desquamation and the presence of papules and/or pustules.

In reproduction studies, mometasone furoate produced effects which are known to be associated with corticosteroids and/or progestational agents such as reduced maternal body weight gain, suppression of fetal growth, delayed ossification, umbilical hernias, prolonged gestation, difficult and prolonged labor and inability to deliver.

In genetic toxicity studies, mometasone furoate was not mutagenic in bacteria (Ames test) or mammalian (mouse lymphoma) cells and was not clastogenic in the mouse micronucleus test.

Following repeated topical application in rabbits for ten days, the dermal response to mometasone furoate cream was minimal and characterized by very slight erythema, the occasional appearance of papules, atonia, desquamation and wrinkling. Mometasone furoate was not a sensitizer in guinea pigs and was not significantly irritating to the eyes of rabbits.

REFERENCES

1. Schering International. SCH 32088 a High Potency Topical Anti-inflammatory Corticosteroid, (P-4809), Mometasone Furoate Cream 0.1%. Health Registration Dossier; 1987.
2. Schering Corporation, Kenilworth, N.J. Percutaneous Absorption of ³H-SCH 32088 (Ointment) in the Rabbit, (P-5039); 1984.
3. Schering Corporation, Kenilworth, N.J. Percutaneous Absorption and Tissue Distribution of ³H-SCH 32088 (Ointment) in the Rabbit, (P-5027); 1984.
4. Schering Corporation, Kenilworth, N.J. Percutaneous Absorption of ³H-SCH 32088 in the Rabbit, (P-5133); 1986.
5. Schering Corporation, Kenilworth, N.J. Percutaneous Absorption of ³H-SCH 32088 in the Dog, (P-5045); 1985.
6. Schering Corporation, Kenilworth, N.J. Acute Oral and Subcutaneous Toxicity Studies of SCH 32088 in Rats and Mice, (P-4865); 1982.
7. Schering Corporation, Kenilworth, N.J. Acute Subcutaneous Toxicity Study of SCH 32088 in Young (21-Day Old) Mice, (P-5165); 1986.
8. Schering Corporation, Kenilworth, N.J. Acute Subcutaneous Toxicity Study of SCH 32088 in Young (21-Day Old) Rats, (P-5168); 1986.
9. Schering Corporation, Kenilworth, N.J. Acute Subcutaneous Toxicity Study of SCH 32088 in Dogs, (P-4868); 1982.
10. Schering Corporation, Kenilworth, N.J. Two-Week Subcutaneous Toxicity Study of SCH 32088 in Rats, (P-4895); 1983.
11. Schering Corporation, Kenilworth, N.J. Three-Week Dermal Toxicity Study of SCH 32088 Ointment in Rabbits with Intact or Abraded Skin, (P-4919); 1983,.
12. Schering Corporation, Kenilworth, N.J. Three-Week Dermal Toxicity Study of SCH 32088 Cream (0.1%) in Rabbits with Intact or Abraded Skin, (P-4960); 1984.
13. Schering Corporation, Kenilworth, N.J. Three-Month Dermal Toxicity Study of SCH 32088 Ointment (0.1%) in Rabbits with Intact Skin, (P-5010); 1985.
14. Schering Corporation, Kenilworth, N.J. Two-Week Subcutaneous Toxicity Study of SCH 32088 in Beagle Dogs, (P-4883); 1983.

15. Schering Corporation, Kenilworth, N.J. Six-Month Dermal Toxicity Study of SCH 32088 Ointment (0.1%) in Dogs with Intact Skin, (P-5013); 1985.
16. Schering Corporation, Kenilworth, N.J. Dermal Teratology (Segment II) Study of SCH 32088 Ointment (0.1%) in Rats, (P-5054); 1985.
17. Schering Corporation, Kenilworth, N.J. Dermal Teratology (Segment II) Study of SCH 32088 Ointment (0.1%) in Rats, (P-5066); 1985.
18. Schering Corporation, Kenilworth, N.J. Perinatal and Postnatal Reproduction (Segment III) Study of SCH 32088 in Rats, (P-5164); 1986.
19. Schering Corporation, Kenilworth, N.J. Fertility and General Reproduction Study (Segment I) of SCH 32088 in Rats, (P-5174); 1987.
20. Schering Corporation, Kenilworth, N.J. Dermal Sensitization Study of SCH 32088 in Guinea Pigs, (P-4879); 1983.
21. Schering Corporation, Kenilworth, N.J. Ten-Day Dermal Irritation Study of Two SCH 32088 Creams (0.1%) in Rabbits with Intact Skin, (P-5056); 1985.
22. Schering Corporation, Kenilworth, N.J. Acute Ocular Irritation Study of SCH 32088 Ointment in Rabbits, (P-4933); 1983.
23. Schering Corporation, Kenilworth, N.J. Acute Ocular Irritation Study of SCH 32088 Cream in Rabbits, (P-4950); 1984.
24. Schering Corporation, Kenilworth, N.J. Salmonella/ Mammalian Microsome Bioassay of SCH 32088. (P-4988); 1984.
25. Schering Corporation, Kenilworth, N.J. L5178 TK +/-, TK -/- Mouse Lymphoma Cell Mutagenicity Assay of SCH 32088. (P-5011); 1984.
26. Schering Corporation, Kenilworth, N.J. Mouse Bone Marrow Erythrocyte Micronucleus Assay of SCH 32088. (P-5050); 1985.
27. Cohn, A., Percutaneous Absorption of ^3H -Mometasone Furoate (^3H -SCH 32088) In Male Volunteers Following Topical Application of a 0.1% Cream Formulation (C87-065-01), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International, 1988.
28. Nagabhushan, N. et al, Percutaneous Absorption of ^3H -SCH 32088 in Male Volunteers, (C84-103), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.

29. Katz, H.I., et al, Double-blind, Parallel-group, Cooperative Efficacy and Safety Study in Psoriasis Comparing Once Daily Applications of SCH 32088 Cream 0.1% and Its Vehicle, (C84-075), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
30. Medansky, R.S., et al, Mometasone Furoate Ointment and Cream 0.1% in Treatment of Psoriasis: Comparison with Ointment and Cream Formulations of Fluocinolone Acetonide 0.25% and Triamcinolone Acetonide 0.1%, Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1988.
31. Cornell, R.C., et al, Bilateral Comparison Study of SCH 32088 Cream 0.1% and VALISONE Cream 0.1% in Psoriasis, (C85-008), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
32. McCormick, G.E., et al, Double-blind Parallel-group, Cooperative Efficacy and Safety Study in Atopic Dermatitis Comparing Once Daily Applications of SCH 32088 Cream 0.1% and Its Vehicle, (C84-076), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
33. Gip, L., et al, Single-blind Efficacy and Safety Study in Atopic and Seborrheic Dermatitis Patients Comparing Once Daily Applications of Mometasone Furoate Cream 0.1% and Twice Daily Applications of LOCOID® Cream 0.1% (I86-313), Mometasone Furoate Cream 0.1%, Health Registration Dossier, Schering International; 1988.
34. Dvorkin D., et al, Single-blind Efficacy and Safety Study in Atopic Dermatitis Comparing Once Daily Applications of Mometasone (SCH 32088) Cream 0.1% and Twice Daily Applications of Betamethasone Valerate Cream 0.1% (C84-084), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1988.
35. Viglioglia, P., Single-blind Efficacy and Safety Study in Steroid Responsive Dermatitis Comparing Once Daily Applications of Mometasone Furoate Cream 0.1% and Twice Daily Applications of BETNOVATE® Cream 0.05% (I86-116), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1988.
36. Dominguez, L., Single-blind Efficacy and Safety Study in Steroid-responsive Dermatoses Patients 6 to 12 Years of Age Comparing Once Daily Applications of Mometasone Furoate Cream 0.1% and Twice Daily Applications of EUMOVATE® Cream 0.05%, (I86-112), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1988.
37. Falabella, R., Single-blind Efficacy and Safety Study in Steroid-responsive Dermatoses Patients 6 to 12 Years of Age Comparing Once Daily Applications of Mometasone Furoate Cream 0.1% and Twice Daily Applications of BETNOVATE® Cream 0.1% (I86-

- 117), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1988.
38. Medansky, R., Bilateral Paired Comparison Study of SCH 32088 Ointment 0.1% and VALISONE Ointment 0.1% in Psoriasis, (C83066), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 39. Medansky, R., Bilateral Paired Comparison Study of SCH 32088 Ointment 0.05% and VALISONE Ointment 0.1% in Psoriasis, (C83-067), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 40. Medansky, R., Bilateral Paired Comparison Study of SCH 32088 Ointment 0.1% and DIPROSONE Ointment 0.05% in Psoriasis, (C84-03), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 41. Liebsohn, E., et al, Single-blind Cooperative Efficacy and Safety Study of SCH 32088 Ointment 0.1% QD and KENALOG Ointment 0.1% BID in Psoriasis, (C84-043), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 42. Lasser, A., et al, Single-blind Cooperative Efficacy and Safety Study of SCH 32088 Ointment 0.1% QD and SYNALAR Ointment 0.025% TID in Psoriasis, (C84-047), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 43. Kanof, N., et al, Double-blind Cooperative Efficacy and Safety Study of SCH 32088 Ointment 0.1% QD and Its Vehicle QD in Psoriasis, (C84-055), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 44. Daniel, J. and Thivolet, J., Single-blind Efficacy and Safety Study in Psoriasis Patients Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1 and DIPROSONE Ointment 0.05%, (I86-211-01, 02), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 45. Rosenthal, D. and Duke, E., Single-blind Efficacy and Safety Study in Psoriasis Patients Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1% and Twice Daily Applications of BETNOVATE® Ointment 0.1%, (I86-308-01, 02), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 46. Hanifin, J., Bilateral Paired Comparison Study of SCH 32088 Ointment 0.1% and VALISONE Ointment 0.1% in Atopic Dermatitis, (C84-020), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 47. Roth, H., et al, Single-blind Cooperative Efficacy and Safety Study of SCH 32088 Ointment 0.1% QD and VALISONE Ointment 0.1% BID in Atopic Dermatitis, (C84-

- 048), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
48. Rex, I., et al, Double-blind Cooperative Efficacy and Safety Study of SCH 32088 Ointment in Psoriasis Comparing 0.1% and Its Vehicle QD in Atopic Dermatitis, (C84-065), Mometasone Furoate Ointment 0.1%, Health Registration Dossier, Schering International; 1987.
 49. Cerio, R. and MacDonald, D.M., Single-blind Efficacy and Safety Study in Atopic Dermatitis Patients Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1% and Twice Daily Applications of LOCOID® Ointment 0.1%, (I86-309-01,02), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 50. Jaimovich, L., Single-blind Efficacy and Safety Study in Patients with Steroid-responsive Dermatoses Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1% and Twice Daily Applications of BETNOVATE® Ointment 0.1%, (I86-118), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 51. Moncada, B., Single-blind Efficacy and Safety Study in Patients with Steroid-responsive Dermatoses Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1% and Twice Daily Applications of EUMOVATE® Ointment 0.05%, (I86-119), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 52. Meinicke, K. et al, Single-blind Efficacy and Safety Study in Patients with Steroid-responsive Dermatoses Comparing Once Daily Applications of Mometasone Furoate Ointment 0.1% and Twice Daily Applications of Betnovate® Ointment 0.1%, (I87-211-01, 02, 03, 04), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
 53. Menter, M.A. et al, Double-blind Efficacy and Safety Study in Scalp Psoriasis Comparing Once Daily Applications of Mometasone Furoate Lotion 0.1% and Its Vehicle, (C86-018-01, 02, 03, 04, 05), Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
 54. Chevrant-Breton, J. and Sayag-Hadida, J., Double-blind Efficacy and Safety Study in Scalp Psoriasis Patients Comparing Once Daily Applications of Mometasone Furoate Lotion 0.1% and DIPROSONE Lotion 0.05%, (I86-217-01, 02), Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
 55. Wong, E. et al, Single-blind Efficacy and Safety Study in Scalp Psoriasis Patients Comparing Once Daily Applications of Mometasone Furoate Lotion 0.1% and Twice Daily Applications of BETNOVATE Lotion 0.1%, (I86-312-01, 02, I87-200-01,02),

- Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
56. Katz, H.I. et al, Double-blind Efficacy and Safety Study in Seborrheic Dermatitis Comparing Once Daily Applications of Mometasone Furoate Lotion 0.1% and Its Vehicle, (C86-011-01, 02, 03, 04, 05), Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
 57. Cabrera, H.N. et al, Single-blind Efficacy and Safety Study in Seborrheic Dermatitis Patients Comparing Once Daily Applications of Mometasone Furoate Lotion 0.1% and Twice Daily Applications of BETNOVATE Lotion 0.1%, Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
 58. Cornell, R.C., Systemic Tolerance to Topical Applications of SCH 32088 Cream 0.1% in Patients with Psoriasis or Atopic Dermatitis, (C85-057), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
 59. Katz, H., Systemic Tolerance to Topical Applications of SCH 32088 Ointment 0.1% in In-patients with Psoriasis or Atopic Dermatitis, (C84-052), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 60. Kaidbey, K., Evaluation of the Contact and Sensitization Potentials of SCH 32088 and Its Vehicle Using a Sodium Lauryl Sulfate Maximization Procedure, (C85-041), Mometasone Furoate Cream 0.1%, Health Registration Dossier, Schering International; 1987.
 61. Kaidbey, K., A Cumulative Irritancy Assay to Determine the Relative Irritation Potential of SCH 32088 Cream, (C84-050), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
 62. Kaidbey, K., Evaluation of the Photocontact Allergenicity Potential of SCH 32088 Cream 0.1% and Its Vehicle, (C85-036), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
 63. Kaidbey, K., Evaluation of the Phototoxicity Potential of SCH 32088 Cream 0.1% and Its Vehicle, (C85-037), Mometasone Furoate Cream 0.1% Health Registration Dossier, Schering International; 1987.
 64. Kaidbey, K., Evaluation of Photocontact Allergenicity Potential of SCH 32088 Ointment 0.1% and Its Vehicle, (C84-039), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
 65. Kaidbey, K., Evaluation of Phototoxicity Potential of SCH 32088 Ointment 0.1% and its Vehicle, (C84-040), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.

66. Jordan, W., A Cumulative Irritancy Assay To Determine the Relative Irritation Potential of SCH 32088 Ointment, (C83-091) Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
67. Jordan, W., Evaluation of the Irritation and Sensitization Potentials of SCH 32088 Ointment and Its Vehicle, (C83-092), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1987.
68. Bressinck, R., et al, Effect of Mometasone Furoate Ointment 0.1% and Hydrocortisone Ointment 1% on Adrenocortical Function in Psoriasis Patients, (C85-077), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
69. Katz, H., Bilateral-paired Comparison Study of the Atrophogenic Potential of Mometasone (SCH 32088) Ointment, 0.1% and Hydrocortisone Ointment, 1.0% (HYTONE® in Psoriasis, (C86-064-01), Mometasone Furoate Ointment 0.1% Health Registration Dossier, Schering International; 1988.
70. Willis, I., Evaluation of the Contact Irritation and Sensitization Potential of DIPROLENE Lotion 0.05%, SCH 32088 Lotion 0.1% and Their Vehicles: A Repeat Insult Patch Test, (C86-005-01), Mometasone Furoate Lotion 0.1% Health Registration Dossier, Schering International; 1988.
71. Data on file, Merck Canada Inc.
72. Belsito DV, Baer RL, Schultz JM, Thorbecke GJ. Relative lack of systemic effects of mometasone furoate on Langerhans Cells of mice after topical administration as compared with other glucocorticosteroids. *J Invest Dermatol* 1988 91:219-23.
73. Bressinck R, Williams J, Peets E. Comparison of the effect of mometasone furoate ointment 0.1%, and hydrocortisone ointment 1%, on adrenocortical function in psoriasis patients. *Today's Therapeutic Trends* 5:25-34, 1988.
74. Medansky RS, Brody NI, Kanof NB, Russo GJ, Peets EA. Clinical investigations of mometasone furoate - a novel nonfluorinated, topical corticosteroid. *Topical Corticosteroid Seminars in Dermatology*. 1987 6(2):94-100.
75. Medansky RS, Bressinck R, Cole GW, Deeken JH, Ellis CN, Guin JD, et al. Mometasone furoate ointment and cream 0.1 percent in treatment of psoriasis: comparison with ointment and cream formulations of fluocinolone acetonide 0.025 percent and triamcinolone acetonide 0.1 percent. *1988 Cutis* 41:480-5.
76. Rosenthal D, Duke E. A clinical investigation of the efficacy and safety of mometasone furoate ointment 0.1% vs betamethasone valerate ointment 0.1% in the treatment of psoriasis. *1988 Curr Ther Res* 44(5):790-801.

PART III: CONSUMER INFORMATION

ELOCOM

- Mometasone furoate Cream, 0.1%**
- Mometasone Furoate Ointment, 0.1%**
- Mometasone Furoate Lotion, 0.1%**

This leaflet is part III of a three-part "Product Monograph" published when ELOCOM was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ELOCOM. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ELOCOM (mometasone furoate) Cream, Ointment and Lotion 0.1% provide:

- the relief of swelling and itching caused by skin conditions like psoriasis and atopic dermatitis. The lotion may be applied to scalp lesions.

What it does:

ELOCOM, has anti-inflammatory and vasoconstrictive actions (makes blood vessels constrict) to help relieve swelling and itching. The exact mechanism of action is not known.

When it should not be used:

Do not use ELOCOM Cream, Ointment or Lotion 0.1%

- if you are allergic to mometasone furoate, to other corticosteroids or to any of the ingredients included in these products. (*See section, What the important nonmedicinal ingredients are*).
- if you presently have a skin infection of fungal, bacterial or viral origin (i.e. herpes simplex, chicken pox and vaccinia).

What the medicinal ingredient is:

Mometasone furoate

What the important nonmedicinal ingredients are:

Cream:

- aluminum starch octenylsuccinate
- cetareth-20

- hexylene glycol
- phosphoric acid
- propylene glycol monostearate
- purified water
- stearyl alcohol
- titanium dioxide
- white petrolatum
- white wax

Ointment:

- hexylene glycol
- phosphoric acid
- propylene glycol monostearate
- purified water
- white petrolatum
- white wax

Lotion:

- hydroxypropylcellulose
- isopropyl alcohol
- phosphoric acid
- propylene glycol
- purified water
- sodium phosphate monobasic

What dosage forms it comes in:

- ELOCOM Cream 0.1% is supplied in 15 g, and 50 g tubes
- ELOCOM Ointment 0.1% is supplied in 15 g, and 50 g tubes
- ELOCOM Lotion 0.1% is supplied in 30 mL and 75 mL plastic bottles

WARNINGS AND PRECAUTIONS

BEFORE you use ELOCOM talk to your doctor or pharmacist if:

- you have had any side effects caused by previous use of other topical corticosteroids (anti-inflammatory medicine to apply to the skin). Side effects may include:
 - Allergic reaction
 - Irritation
 - Adrenal suppression (characterized by darkening of the skin, fatigue, low blood pressure, diarrhea, and digestive disturbance).
- you are currently treating an infection using an antifungal or antibacterial agent.
- You are pregnant or nursing
- You have used steroid hormone medication in

- the past
- You have poor circulation due to stasis dermatitis (an inflammation of the skin) or other skin diseases

For external use on skin or scalp only.

Do not use in or nears the eyes.

INTERACTIONS WITH THIS MEDICATION

It is **NOT** known whether ELOCOM interacts with other medication.

PROPER USE OF THIS MEDICATION

Usual dose:

ELOCOM Cream/Ointment: Apply a thin film to the affected skin areas once daily or as directed by your doctor; massage gently and thoroughly.

ELOCOM Lotion: Apply a few drops of the lotion to the affected skin areas (which may include scalp sites) once daily, or as directed by your doctor; massage gently and carefully until medication disappears.

Do **NOT** cover the affected skin or scalp areas with airtight bandages.

Use ELOCOM only as directed by your health care provider. **Do NOT use more of it, do NOT take it more often and do NOT take it for a longer period of time than your health care provider recommended.** Using too much ELOCOM may increase your chances of unwanted and sometimes dangerous side effects.

This medication has been prescribed specifically for you. Do NOT give it to anyone else. It may harm them, even if their symptoms seem to be similar to yours.

Overdose:

Symptoms: fatigue, weakness, decreased appetite, constipation, nausea, vomiting, diarrhea, abdominal pain, skin colour darkening (especially on scars, elbows, knees, knuckles, toes, lips, and mucous membranes).

Treatment: **In case of overdose, contact your doctor or poison control center immediately.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Along with desirable effects, Elocom may cause undesirable effects.

Side effects that may occur with the use of this medication include: skin sensation such as burning or tingling, or stinging strong itching sensation and signs of skin atrophy (thinning of the skin), as well as inflammation of hair follicles, and acne-like reactions.

Very rarely the following may occur: aggravation of the disease, dry skin, abnormal redness, appearance of boils, aggravated allergy, dermatitis (swelling of the skin), increased lesion size and nausea.

Additionally, the following side effects have been found to occur with the use of other topical corticosteroids: infection or signs of infection, irritation, unwanted hair, lightening of skin color, dermatitis (swelling of the skin) near or around the mouth, allergic contact dermatitis, stretch marks as well as kidney suppression, demonstrated by decreased urine, increased blood pressure, heart palpitations, shortness of breath, itching, nausea, loss of appetite, upset stomach, and joint inflammation.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Un-common	Allergic reaction to the medication (chills, fever, muscle aches or pains or other flu-like symptoms occurring with or before a skin rash)			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Rare	Symptoms associated with Kidney suppression (see symptoms listed above)			✓
Rare	Symptoms associated with Adrenal suppression (see symptoms listed in <i>WARNINGS</i> and <i>PRECAUTIONS</i> section)			✓

*This is not a complete list of side effects. For any unexpected effects while taking **ELOCOM cream, ointment or lotion** contact your doctor or pharmacist.*

HOW TO STORE IT

Store between 15°and 30°C

Do **NOT** use if past expiry date on the label.

Keep out of reach of children

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: **866-234-2345**
 toll-free fax **866-678-6789**
 By email: cadtmp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness
Information Division
Marketed Health Products Directorate
Tunney’s Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Merck Canada Inc. at: 1-800-463-5442

This leaflet was prepared by Merck Canada Inc.

Last revised: December 14, 2011