PRESCRIBING MONOGRAPH

LIDEMOL®

(fluocinonide)

0.05% Emollient

Topical Corticosteroid

Valeant Canada LP
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Date of Preparation
October 15, 2014

Control No.: 178720

® Registered Trade Mark

NAME OF DRUG

LIDEMOL®

(fluocinonide)

Emollient, 0.05%

THERAPEUTIC CLASSIFICATION

Topical Corticosteroid

ACTION

Lidemol (fluocinonide) possess anti-inflammatory, anti-pruritic and vasoconstrictor actions.

INDICATIONS

Lidemol (fluocinonide) is indicated for topical therapy of corticosteroid responsive acute and chronic skin eruptions where an anti-inflammatory, anti-allergenic and anti-pruritic activity in the topical management is required.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in untreated bacterial, tubercular, fungal and most viral lesions of the skin (including herpes simplex, vaccinia and varicella). They are also contraindicated in individuals with a history of hypersensitivity to its components.

WARNINGS

The safety of topical corticosteroids during pregnancy or lactation has not been established. The potential benefit of topical corticosteroids, if used during pregnancy or lactation, should be weighed against possible hazard to the fetus or the nursing infant.
These products are not for ophthalmic use.

PRECAUTIONS

These products are not recommended for use under occlusive dressings.
Apply cautiously on lesions close to the eye. Severe irritation is possible if these formulations contact the eye. Should this occur, immediate flushing of the eye with a large volume of water is recommended.

Prolonged use of topical corticosteroid products may produce atrophy of the skin and of subcutaneous tissues, particularly on flexor surfaces and on the face. If this is noted, discontinue the use of this product.

The products should be used with caution in patients with stasis dermatitis and other skin diseases associated with impaired circulation.

If a symptomatic response is not noted within a few days to a week, the local application of corticosteroids should be discontinued and the patient reevaluated.

During the use of topical corticosteroids secondary infections may occur.

Although hypersensitivity reactions have been rare with topically applied steroid products, the drug should be discontinued and appropriate therapy instituted if there are signs of reaction.

In cases of bacterial infections of the skin, appropriate antibacterial agents should be used as primary therapy. If it is considered necessary, the topical corticosteroid product may be used as an adjunct to control inflammation, erythema and itching.
Patients should be advised to inform subsequent physicians of the prior use of corticosteroids. Significant systemic absorption may result when steroids are applied over large areas of the body. To minimize the possibility, when long-term therapy is anticipated, interrupt treatment periodically or treat one area of the body at a time.

Laboratory Tests
Urinary free cortisol test and ACTH stimulation test may be helpful in evaluating HPA axis suppression.

ADVERSE REACTIONS

The following adverse skin reactions have been reported with the use of topical steroids: dryness, burning, itching, local irritation, striae, skin atrophy, atrophy of subcutaneous tissues, telangiectasia, hypertrichosis, change in pigmentation and secondary infection. Adrenal suppression has also been reported following topical corticosteroid therapy. Posterior subcapsular cataracts have been reported following systemic use of corticosteroids.

TREATMENT OF OVERDOSAGE

There is no specific antidote, but gastric lavage should be performed.
In case of hypercorticism and/or adrenal suppression, discontinue therapy.

DOSAGE AND ADMINISTRATION

Lidemol (fluocinonide) is suitable when an emollient effect is desired.

A small amount of Lidemol should be applied gently on the affected skin area, two to four times daily, depending on the severity of the condition.

It is recommended that Lidemol, ointment not be used under occlusive conditions.

AVAILABILITY

Lidemol (fluocinonide) emollient, 0.05% is available in 30g collapsible tubes and in 100g plastic jars.

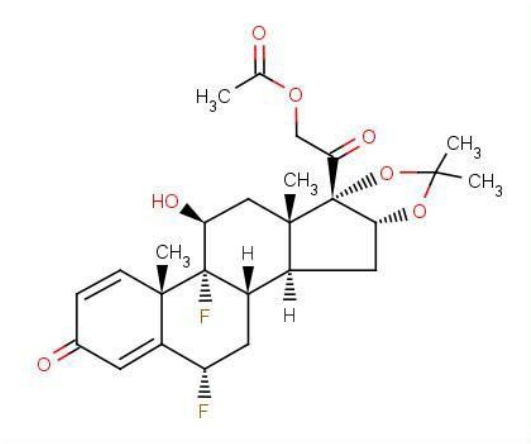
Store at room temperature, 15°C - 30°C.

CHEMISTRY

Chemical Name

6α, 9-difluoro-11β, 16α , 17, 21-tetrahydroxypregna-1, 4-diene-3, 20-dione, cyclic 16, 17-acetonide-21 acetate.

Structural Formula



Molecular Formula
$C_{26}H_{32}O_7F_2$
Molecular Weight
494.52
Description
Fluocinonide is a white to creamy white, odorless, crystalline powder which melts at about 300° C with decomposition. It is sparingly soluble in acetone and chloroform, slightly soluble in ethanol and methanol, very slightly soluble in ether and practically insoluble in water.

Composition
Lidemol (0.05%) emollient contain fluocinonide in a water washable aqueous emollient base consisting of cetyl alcohol, citric acid, mineral oil, polysorbate 60, propylene glycol, sorbitan monostearate, stearyl alcohol. These formulations do not contain lanolin, parabens or phenolic compounds.

PHARMACOLOGY

Fluocinonide demonstrated 310 and 160 times the subcutaneous and oral thymolytic activity of cortisol respectively. Its anti-granuloma activity in relation to cortisol was of the same magnitude as its thymolytic activity. The composite results of seven assays demonstrates that fluocinonide has 350 times the topical anti-inflammatory activity of cortisol when tested utilizing the croton oil-inflamed ear. The glucocorticoid activity of fluocinonide to cortisol was determined in adrenalectomized male rats. The results demonstrate that fluocinonide has approximately 50 times the glucocorticoid activity of cortisol.

Fluocinonide has approximately 400 times the adrenal suppressive activity of cortisol when given subcutaneously to female rats. In adrenalectomized mice, fluocinonide has approximately 100 times the activity of cortisol with regard to the effect on the white blood count and depletion of eosinophils.

The sodium and potassium retaining activity of fluocinonide using desoxycorticosterone as a positive control was determined by subcutaneous injection in adrenalectomized male rats with a dosage range of 1 to 16 mcg/rat. When no sodium load is given, there was a significant ($P<0.01$) increase in potassium excretion with the 16 mcg dose only. Significant ($P<0.05$) increase in potassium excretion was observed at all doses studied. When fluocinonide is given along with a sodium load, it produces only a slight elevation of urinary sodium, whereas a dose as low as 1 mcg/kg significantly ($P<0.01$) increases potassium excretion.

Vasoconstrictor Tests
Vasoconstrictor assay has proved to be a reliable human bioassay for the screening of compounds with topical corticosteroid activity, and for the comparative evaluation of biologic effects relative to existing standards.

Although the results of this standardized assay method cannot be directly equated with topical efficacy in dermatologic therapy, they appear to have definite predictive value, and to correlate well with clinical activity and potency. According to McKenzie, "the most powerful vasoconstrictors are those substances which clinical studies have shown to be the most effective topical anti-inflammatory agents". Vasoconstrictor tests were performed comparing fluocinonide creams and ointments to betamethasone17-valerate, and hydrocortisone. Results of the alcoholic vasoconstrictor assay, demonstrate the relative activity of fluocinonide to be of the order of 400 times the activity of hydrocortisone and 4 times the activity of betamethasone 17-valerate.

Stoughton reports fluocinonide to be five times as potent as betamethasone 17-valerate in inducing vasoconstriction. The in vitro penetration* of fluocinonide and betamethasone is shown in the following table:

	Human* Skin	Hairless* Mouse Skin
Betamethasone 17-valerate	1.7	2.1
Fluocinonide	9.1	13.0

*Agent showing least in vitro penetration (fluocinolone alcohol) and least activity in vasoconstrictor bioassay (betamethasone alcohol and fluocinolone alcohol) listed as one (1.0). All other agents listed in the numerical ratio of their abilities to penetrate skin in vitro or induce vasoconstriction, respectively.

These data demonstrate that fluocinonide penetrates both human skin and hairless mouse skin better than betamethasone 17-valerate in this test system.

Place, V. A. et al., with a recent modification of the Stoughton-McKenzie Assay, demonstrated fluocinonide to have approximately five times the potency of betamethasone 17-valerate as determined by vasoconstriction in normal skin.

Pharmacokinetics
The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption.

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. They are metabolized primarily in the liver and are then excreted by the kidneys. Some of the

topical corticosteroids and their metabolites are also excreted into the bile.

Absorption studies utilizing fluocinonide cream and ointment 0.05% in quantities of 30 to 60g/day (15 to 30 mg/day of active material) were done in 13 patients during 10 days. Transient suppression of adrenal activity has been noted in 3 out of 4 patients receiving 30 g/day of the cream under occlusion and in 2 out of 6 patients without occlusion. Transient adrenal suppression was noted with the application of 60 g/day of the cream in 2 patients out of 3 without occlusive therapy. Adrenal suppression can be expected in a number of patients with such large quantities since it is known that it depends on several factors such as the percentage of body surface treated, the concentration of the corticosteroid in the topical preparation, and most important, the integrity of the skin barrier. The adrenals apparently revert to normal function within 48 hours after cessation of therapy.

A similar study was done on 3 patients with a 0.01% solution of fluocinonide in propylene glycol using 15 ml/day. No adrenal suppression was observed.

Laboratory results for fasting blood sugar, SGPT or SGOT, blood urea nitrogen, serum potassium and serum sodium were determined in the patients entered in the above absorption studies. Examination of the data shows values to be in normal range.

A Draize test was performed on 213 healthy adult volunteers, none of whom had previous exposure to fluocinonide, the cream base or the ointment. There was no evidence of contact hypersensitivity to the cream or ointment formulation. However, in a few volunteers, a slight degree of erythema was noted which rapidly disappeared after removing the patch and it represented a very mild degree of irritation.

CLINICAL STUDIES

Forty-seven investigators completed a large-scale double-blind, paired comparison clinical trial utilizing a common protocol. Seven hundred and seventeen patients were studied on the cream formulation, and 731 patients on the ointment formulation.

The results of these studies were analyzed statistically utilizing both the truncated sequential method and the student t-tests. Fluocinonide in the cream and ointment formulation, when tested in steroid-responsive dermatoses, gave significant therapeutic results. The low incidence and mild severity of adverse reactions noted by the patients and the investigators indicate that the drug is safe and effective when used as directed.

TOXICOLOGY

Fluocinonide is an active synthetic corticosteroid. As judged by animal tests, the compound can be absorbed through the skin to produce systemic effects similar to those observed following oral, parenteral or aerosol administration.

In some cases, the LD50 of fluocinonide, when administered as a single intraperitoneal dose to rats, is of the same order of magnitude as that seen with other synthetic corticosteroids. In other cases, the LD50 value of this compound is lower. As with previously studied corticoids, the toxic effects include reduction in adrenal weight, liver changes, lung consolidation, septicemia, and gastrointestinal effects.

When deaths occurred, time after dosing with fluocinonide was about the same as that reported for other corticosteroids.

Subacute and chronic administration of fluocinonide to various species of laboratory animals produced typical corticosteroid effects, which included hyperglycemia, lymphopenia and changes in liver structure. These effects were generally not severe and were reversible with cessation of treatment.

No cleft palates or other skeletal anomalies were observed in pups from rabbits dosed with the compound during organogenesis.

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