

PRODUCT MONOGRAPH

CAPEX™ SHAMPOO

**Fluocinolone Acetonide Shampoo
0.01%**

Synthetic corticosteroid

**Galderma Pharmaceuticals Inc.
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**Date of Preparation:
2000.08.14**

**Revision Date:
April 25, 2002**

Control # 067736

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Synthetic corticosteroid with anti-inflammatory, antipruritic, and vasoconstrictive properties

THERAPEUTIC/PHARMACOLOGIC CLASSIFICATION

Fluocinolone acetonide is a synthetic fluorinated corticosteroid with anti-inflammatory, antipruritic, and vasoconstrictive properties.

ACTION AND CLINICAL PHARMACOLOGY

PHARMACODYNAMICS. Like other topical corticosteroids, fluocinolone acetonide has anti-inflammatory, anti-pruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids in general is unclear. Various laboratory methods, including skin blanching assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is evidence of recognizable correlation between vasoconstrictor potency and therapeutic efficacy in man. Generally, fluocinolone acetonide is considered to be in the low range of corticosteroid potency.

PHARMACOKINETICS. The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings. 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 the same metabolic and elimination pathways as after systemic administration.

INDICATIONS AND CLINICAL USE

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is indicated for the treatment of seborrheic dermatitis of the scalp. Capex™ Shampoo has not been proven, by clinical trials, to be effective in other corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation. Topical application to the eye is absolutely contraindicated, especially in the presence of ophthalmological infections.

WARNINGS

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is considered an eye irritant. If the product is accidentally introduced into the eyes, liberal rinsing with water should be immediately performed.

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 receiving a large dose of a higher potency topical steroid applied to a large surface area or 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.

Patients receiving superpotent corticosteroids should not be treated for more than two weeks at a time, and only small areas should be treated at any one time due to the increased risk of HPA suppression.

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 and complete upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids.

Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios.

If irritation develops, Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) 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 test.

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 Capex™ Shampoo should be discontinued until the infection has been adequately controlled.

PEDIATRIC USE. Safety and effectiveness in children and infants have not been established. Because of a higher ratio of skin surface area to body mass, children are at a greater risk than adults of HPA-axis-suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of glucocorticosteroid insufficiency after withdrawal of treatment, and of Cushing's syndrome while on treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

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

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. No studies have been done on Capex™ Shampoo to show teratologic effects on animals.

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 CAPEX_{TM} Shampoo is administered to a nursing woman.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of CapexTM Shampoo (0.01% Fluocinolone Acetonide).

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. In case of contact, wash eyes liberally with water.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated 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 reaction.
5. CAPEXTM Shampoo mixture is to be discarded after three (3) months.

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

DRUG INTERACTION. No studies have been done on CapexTM Shampoo (Fluocinolone Acetonide, 0.01%) to show any drug interaction. Generally, there are known drug interactions caused by glucocorticoids, not necessarily from topical application.

Glucocorticoids decrease the hypoglycemic activity of insulin and oral hypoglycemics, so that a change in dose of the antidiabetic drugs may be necessitated. The usual doses of mineralocorticoids and large doses of some glucocorticoids cause hypokalemic and may exaggerate the hypokalemic effects of thiazides and high-cleaning diuretics.

In combination with amphotericin-B, they also may cause hypokalemia. Glucocorticoids appear to enhance the ulcerogenic effects of non-steroidal anti-inflammatory drugs. They decrease the plasma levels of salicylates, and salicylism may occur on discontinuing steroids. Glucocorticoids may increase or decrease the effects of prothrombopenic anticoagulants. Estrogens, phenobarbital, phenytoin and rifampin increase the metabolic clearance of adrenal steroids and hence necessitate dose adjustments.

ADVERSE REACTIONS

In controlled clinical trials, the total incidence of adverse reactions associate with the use of Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) was less than 1%. There was no evidence of skin atrophy or increased irritation in patients treated in the controlled clinical trials.

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

OVERDOSAGE

Topically applied Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) can be absorbed in sufficient amounts to produce systemic effects (refer to PRECAUTIONS).

DOSAGE AND ADMINISTRATION

The pharmacist must empty the contents of the Fluocinolone acetonide capsule into the shampoo base prior to dispensing to the patient. This product should be shaken well prior to use. **No more than approximately 30 ml (one ounce) of the medicated shampoo should be applied to the scalp area once daily, worked into a lather and allowed to remain on the scalp for about 5 minutes.** The hair and scalp should then be rinsed completely twice. It has been found, through patient responses, that the shampoo lathers better if the hair is fully wet before applying the shampoo.

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is supplied as a two-component package: a capsule containing the active ingredient, fluocinolone acetonide; and 118 milliliters (4 fluid ounces) of the shampoo base in a 180 ml (6 oz.) bottle. The pharmacist must mix the capsule contents into the shampoo base at the time of dispensing; hence, is supplied to patients as mixed Capex™ Shampoo.

ADDITIONAL INFORMATION

Local Treatment - Topical Application. Topical efficacy depends on the inherent glucocorticoid activity (or potency) of the steroid, the concentration in the preparation, permeability coefficient, the vehicle and excipients and local metabolic processes. Except for serious conditions, low-potency glucocorticoids are preferred by many authorities because adverse effects on the skin appear to be less severe than with high potency agents, even if the latter are used at appropriately lower concentrations. Only hydrocortisone and its acetate are available for non-prescription topical use.

Drugs with a high lipid-water distribution coefficient penetrate well from absorbable or non-oleaginous vehicles and tend to remain longer in the skin than water-soluble agents, exerting a more extended local action but lesser systemic side effects, especially if the drug is metabolized rapidly systemically. However, it is desirable that the agents be metabolized in the skin so that less is delivered to the systemic circulation.

Steroids that have the 17-OH group substituted and/or which are fluorinated are metabolized poorly locally and hence may have a significant potential for systemic effects; for this reason, special caution is urged when such compounds are used in children.

Occlusive dressings may be used, especially for low-potency, poorly penetrant steroids. The stratum corneum under the dressing becomes macerated and more permeable. However, such dressings increase absorption into the bloodstream and hence favor systemic effects.

Anti-inflammatory Properties. Cortisol and the synthetic analogs of cortisol have the capacity to prevent or suppress the development of the local heat, redness, swelling, and tenderness by which inflammation is recognized. At the microscopic level, they inhibit not only the early phenomena of the inflammatory process (edema, fibrin deposition, capillary dilation, migration of leukocytes into the inflamed area, and phagocytic activity) but also the later manifestations (capillary proliferation, fibroblast proliferation, deposition of collagen, and, still later, cicatrization).

Although understanding of these effects is unsatisfactory, many observations have been made that have therapeutic relevance and that must be taken into account in explanatory formulations. Perhaps the most important of these for the physician is that corticosteroids inhibit the inflammatory response whether the inciting agent is radiant, mechanical, chemical, infectious, or immunological. In clinical terms, the administration of corticosteroids for their anti-inflammatory effects is palliative therapy; the underlying cause of the disease remains; the inflammatory manifestations are merely suppressed.

It is this suppression of inflammation and its consequences that has made the corticosteroids such valuable therapeutic agents - indeed, at times lifesaving. It is also this property that gives them a nearly unique potential for therapeutic disaster. The signs and symptoms of inflammation are expressions of the disease process that are often used by the physician in diagnosis and in evaluating the effectiveness of treatment. These may be missing in patients treated with corticosteroids.

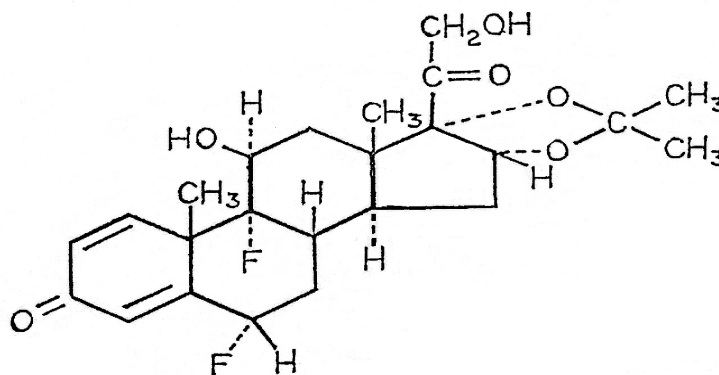
Anti-inflammatory effects depend upon the direct local action of the steroids. Topical or systemic glucocorticoids often markedly improve certain skin diseases, such as pruritus, psoriasis, dermatitis herpetiformis and eczema; pemphigus; erythema multiforme, exfoliative dermatitis and mycosis fungoides usually require systemic treatment, which may be life-saving.

PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

PROPER NAME:	Fluocinolone Acetonide
CHEMICAL NAME:	Pregna-1,4-diene-3,20-dione,6,9-difluoro-11,21-dihydroxy-16,17-[(1 methyl-ethylidene)bis(oxy)], (6a,11B,16a)-,
I.U.P.A.C. NAME:	6A,9-Difluoro-11B,16a,17,21-tetrahydroxypregna-1,4-diene-3,20-dione, cyclic 16,17-acetal with Acetone (67-73-2).
MOLECULAR FORMULA:	$C_{24}H_{30}F_2O_6$

STRUCTURAL FORMULA:



PHYSICAL FORM:	White, crystalline powder that is odorless; stable in light.
SOLUBILITY:	1 g in > 100ml water, 45 ml alcohol, 25 ml chloroform or 350 ml ether.
MELTING POINT:	Melts at about 270° , with decomposition.
STORAGE:	Store in well-closed containers, protected from light, at temperature not exceeding 25° C.

DOSAGE FORM

(Capex™ Shampoo, 0.01%)

Fluocinolone Acetonide Capsule PLUS Shampoo Base

COMPOSITION

Fluocinolone Acetonide Capex™ SHAMPOO CAPSULE **Quantity**

Fluocinolone Acetonide USP (ACTIVE).....12mg
Dibasic Calcium Phosphate Dihydrate USP
Talc USP # 114

Capex™ Shampoo BASE

Magnesium Aluminum Silicate NF
Oat Flour
Aluminum Acetate Basic
Boric Acid NF Powder
Propylene Glycol USP
Methylparaben NF
Propylparaben NF
Citric Acid USP Anhydrous
D&C Yellow #10
FD&C Blue #1
Herbal Fragrance # 10396
Lauramide DEA
Cocamido-Ether-Sulfate Complex
Cocoamine Oxide
Benzalkonium Chloride 50% Solution, NF
Purified Water USP

STABILITY AND STORAGE RECOMMENDATIONS

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is dispensed to the patient as the mixture form in 180 ml bottles (capsule mixed into the shampoo base by the pharmacist). It is recommended that the (mixed) dispensed dosage form be kept at room temperature, approximately 15° - 30° C (59° - 86° F) and shaken well before each use.

Storage conditions for unmixed dosage form of Capex™ Shampoo capsule is at controlled room temperature of 15° - 30° C (59° - 86° F).

DIRECTIONS FOR MIXING

The contents of the capsule is mixed into the shampoo base prior to dispensing to the patients. The mixed form, when dispensed to the patient, should be disposed of after three (3) months.

AVAILABILITY OF DOSAGE FORMS

Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is marketed as a two-component product: capsule and shampoo base. Each capsule contains 12 mg of the active ingredient, Fluocinolone Acetonide. The shampoo base, quantity 118.28 ml, is packaged in a 180 ml bottle. The mixed dosage form Capex™ Shampoo has a concentration of 0.01% Fluocinolone Acetonide.

INFORMATION FOR THE CONSUMER

1. Capex™ Shampoo (Fluocinolone Acetonide, 0.01%) is considered an eye irritant. If accidentally introduced into the eyes, the eyes should be liberally rinsed with tap water.
2. Capex™ Shampoo is to be used only as directed by the physician. It is for external use only.
3. Capex™ Shampoo should not be used for any other disorder other than that for which it is indicated (prescribed) for.
4. To get better lather, the hair should be totally wet before applying Capex™ Shampoo. Once applied to the scalp, this is worked into a lather and let to stand for approximately 5 minutes, after which it should be rinsed off completely. It is recommended that the hair and scalp be rinsed twice with water.
5. The treated scalp should not be bandaged or covered in any way, unless directed by the physician.
6. The contents of Capex™ Shampoo (mixed) is to be discarded after three (3) months.

TOXICOLOGY

There were three studies done to show toxicologic and/or tolerance effects of Capex™ Shampoo (Fluocinolone Acetonide, 0.01%).

1. Primary Eye Irritation Study in White Rabbits.
Animal species: New Zealand White Rabbits.
Route of administration: Topical
Form and Dosage regime: Liquid Capex™ Shampoo at dose of 0.1 ml per eye.

Study description: Nine animals were treated with 0.1 ml of the test material in one eye and the other eye left untreated to serve as control. Three of the 9 rabbits had their eyes rinsed off with water 5 seconds after the application of the test material. The other 6 rabbits were not rinsed at all.

Findings: The rabbits that had the eyes rinsed did not present any kind of irritation. Those that did not have their eyes rinsed showed evidence of positive corneal, iris, or conjunctival changes. Although all irritation had cleared by day 4 in 5 of the 6 non-rinsed rabbits, low grade corneal opacity persisted in the remaining animal at the final day 10 reading.

2. Repeat-Insult Patch Test in Humans.
3. Photocontact Allergenicity Study of Capex™ Shampoo in Humans.

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