

FLUCINOLONE ACETONIDE- fluocinolone acetonide oil
Amneal Pharmaceuticals LLC

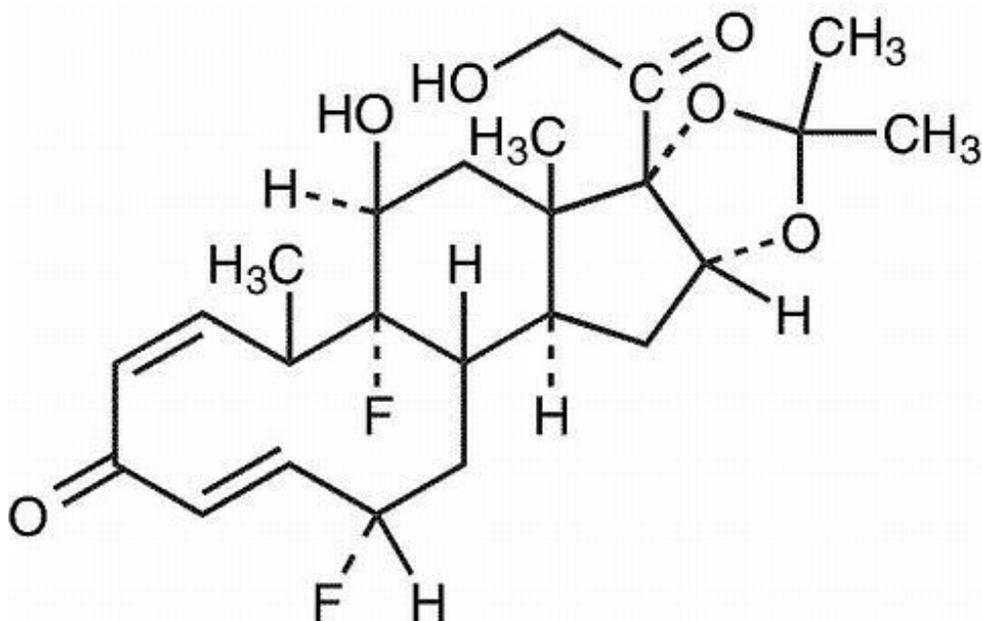
Fluocinolone Acetonide 0.01% Topical Oil (Scalp Oil)

For Topical Use Only-

Not for Oral, Ophthalmic, or Intravaginal Use

DESCRIPTION

Fluocinolone Acetonide 0.01 % Topical Oil contains fluocinolone acetonide {(6 α , 11 β , 16 α)-6,9-difluoro-11,21-dihydroxy-16,17[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione, cyclic 16,17 acetal with acetone}, a synthetic corticosteroid for topical use dermatologic use. This formulation is also marketed as Fluocinolone Acetonide 0.01% Topical Oil for use as body oil for atopic dermatitis in adults and for moderate to severe atopic dermatitis in pediatric patients 2 years and older, and as fluocinolone acetonide oil, 0.01% for chronic eczematous external otitis. Chemically, fluocinolone acetonide is C₂₄H₃₀F₂O₆. It has the following structural formula:



Fluocinolone acetonide in Fluocinolone Acetonide 0.01% Topical Oil has a molecular weight of 452.50. It is a white crystalline powder that is odorless, stable in light, and melts at 270°C with decomposition; soluble in alcohol, acetone and methanol; slightly soluble in chloroform; insoluble in water.

Each gram of Fluocinolone Acetonide 0.01% Topical Oil contains approximately 0.11 mg of fluocinolone acetonide in a blend of oils, which contains isopropyl alcohol, isopropyl myristate, light mineral oil, oleth-2, and refined peanut oil NF.

Each packaged product contains 2 shower caps. The shower cap is made of low density

polyethylene material with rubber elastic.

CLINICAL PHARMACOLOGY

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

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusion of topical corticosteroids can enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Also, inflammation and/or other disease processes in the skin can increase percutaneous absorption.

Fluocinolone Acetonide 0.01% Topical Oil is in the low to medium range of potency as compared with other topical corticosteroids.

CLINICAL STUDIES

In a vehicle-controlled study for the treatment of psoriasis of the scalp in adults, after 21 days of treatment, 60% of patients on active treatment and 21% of patients on the drug vehicle had excellent to cleared clinical response.

Open-label safety studies on 33 children (20 subjects ages 2 to 6 years, 13 subjects ages 7 to 12 years) with moderate to severe stable atopic dermatitis, and baseline body surface area involvement greater than 75% in 18 patients, and 50% to 75% in 15 patients, were treated with fluocinolone acetonide oil 0.01% twice daily for 4 weeks. Morning pre-stimulation cortisol level and post-Cortrosyn stimulation cortisol level were obtained in each subject at the beginning of the trial and at the end of 4 weeks of treatment. At the end of treatment, 4 out of 18 subjects aged 2 to 5 years showed low pre-stimulation cortisol levels (3.2 to 6.6 mcg/dL; normal: cortisol > 7 mcg/dL) but all had normal responses to 0.25 mg of Cortrosyn stimulation (cortisol > 18 mcg/dL).

A clinical study was conducted to assess the safety of fluocinolone acetonide oil 0.01%, which contains refined peanut oil, on subjects with known peanut allergies. The study enrolled 13 patients with atopic dermatitis, 6 to 17 years of age. Of the 13 patients, 9 were Radioallergosorbent Test (RAST) positive to peanuts and 4 had no peanut sensitivity (controls). The study evaluated the responses to both prick test and patch test utilizing refined peanut oil NF, fluocinolone acetonide topical oil 0.01% and histamine/saline controls, on the 13 individuals. These subjects were also treated with fluocinolone acetonide 0.01% topical oil twice daily for 7 days. Prick test and patch test results for all 13 patients were negative to fluocinolone acetonide 0.01% topical oil and the refined peanut oil. One of the 9 peanut-sensitive patients experienced an exacerbation of atopic dermatitis after 5 days of fluocinolone acetonide 0.01% topical oil use. Importantly, the bulk peanut oil NF, used in fluocinolone acetonide 0.01% topical oil is heated at 475°F for at least 15 minutes, which should provide for adequate

decomposition of allergenic proteins.

INDICATIONS AND USAGE

Fluocinolone Acetonide 0.01% Topical Oil is a low to medium potency corticosteroid indicated:

In adult patients for the treatment of psoriasis of the scalp (Scalp Oil).

CONTRAINDICATIONS

Fluocinolone Acetonide 0.01% Topical Oil is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

This product contains refined peanut oil NF (see PRECAUTIONS section).

PRECAUTIONS

General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

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

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. Infrequently, signs and symptoms of glucocorticoid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

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

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a *failure to heal* rather than noting a clinical exacerbation, which may occur with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic testing. One peanut sensitive child experienced a flare of his atopic dermatitis after 5 days of twice daily treatment with fluocinolone acetonide 0.01% topical oil (see CLINICAL STUDIES section).

If wheal and flare type reactions (which may be limited to pruritus) or other manifestations of hypersensitivity develop, Fluocinolone Acetonide 0.01% Topical Oil should be discontinued immediately and appropriate therapy instituted.

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 Fluocinolone Acetonide 0.01% Topical Oil should be discontinued until the infection has been adequately controlled.

Fluocinolone Acetonide 0.01% Topical Oil is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide 0.01% Topical Oil for peanut-sensitive individuals.

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 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. Patients should promptly report to their physician any worsening of their skin condition.
4. Parents of pediatric patients should be advised not to use Fluocinolone Acetonide 0.01% Topical Oil in the treatment of diaper dermatitis. Fluocinolone Acetonide 0.01% Topical Oil should not be applied to the diaper area, as diaper or plastic pants may constitute occlusive dressing.
5. This medication should not be used on the face, underarm, or groin unless directed by the physician.
6. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

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

ACTH stimulation test

A.M. plasma cortisol test

Urinary free cortisol test

Carcinogenesis, mutagenesis, and impairment of fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of Fluocinolone Acetonide 0.01% Topical Oil. Studies have not been performed to evaluate the mutagenic potential of fluocinolone acetonide, the active ingredient in Fluocinolone Acetonide 0.01% Topical Oil. Some corticosteroids have been found to be genotoxic in various genotoxicity tests (i.e. the *in vitro* human peripheral blood lymphocyte chromosome aberration assay with metabolic activation, the *in vivo* mouse bone marrow micronucleus assay, the Chinese hamster micronucleus test and the *in vitro* mouse lymphoma gene mutation assay).

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.

There are no adequate and well-controlled studies in pregnant women on teratogenic effects from Fluocinolone Acetonide 0.01% Topical Oil. Therefore, Fluocinolone Acetonide 0.01% Topical Oil should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and

could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when Fluocinolone Acetonide 0.01% Topical Oil is administered to a nursing woman.

Pediatric Use: Fluocinolone Acetonide 0.01% Topical Oil may be used twice daily for up to 4 weeks in pediatric patients 2 years and older with moderate to severe atopic dermatitis. Fluocinolone Acetonide 0.01% Topical Oil should not be applied to the diaper area.

Application to intertriginous areas should be avoided due to the increased possibility of local adverse events such as striae, atrophy, and telangiectasia, which may be irreversible. The smallest amount of drug needed to cover the affected areas should be applied. Long term safety in the pediatric population has not been established.

Fluocinolone Acetonide 0.01% Topical Oil is not recommended for use on the face (see ADVERSE REACTIONS section).

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 (see PRECAUTIONS).

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. 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 fontanelles, headaches, and bilateral papilledema.

Fluocinolone Acetonide 0.01% Topical Oil is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing Fluocinolone Acetonide 0.01% Topical Oil for peanut-sensitive individuals.

ADVERSE REACTIONS

The following local adverse reactions have been reported infrequently with topical corticosteroids. 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: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and malaria. One peanut sensitive child experienced a flare of his atopic dermatitis after 5 days of twice daily treatment with fluocinolone acetonide oil 0.01%.

A post marketing (open-label) safety study was conducted in 58 children to evaluate the local safety of fluocinolone acetonide 0.01% topical oil when applied twice daily for 4 weeks to the face in children (2 to 12 years) with moderate to severe atopic dermatitis (see Table of Incidence of Adverse Events).

Incidence of Adverse Events (%)

N=58

Adverse Event (AE)*	# of patients (%)	Day 14	Day 28**	Day 56***
Any AE	15 (25.9)	6 (10.3)	7 (12.1)	7 (12.1)
Telangiectasia	5 (8.6)	3 (5.2)	4 (6.9)	2 (3.5)
Erythema	3 (5.2)			3 (5.2)
Itching	3 (5.2)			3 (5.2)
Irritation	3 (5.2)			3 (5.2)
Burning	3 (5.2)			3 (5.2)
Hypopigmentation	2 (3.5)	2 (3.5)		
Shiny skin	1 (1.7)		1 (1.7)	
Secondary atopic dermatitis	1 (1.7)			1 (1.7)
Papules and pustules	1 (1.7)			1 (1.7)
Keratosis pilaris	1 (1.7)			1 (1.7)
Folliculitis	1 (1.7)		1 (1.7)	
Facial herpes simplex	1 (1.7)	1 (1.7)		
Acneiform eruption	1 (1.7)		1 (1.7)	
Ear infection	1 (1.7)		1 (1.7)	

***The number of individual adverse events reported does not necessarily reflect the number of individual subjects, since one subject could have multiple reporting of an adverse event.**

****End of Treatment**

*****Four Weeks Post Treatment**

OVERDOSAGE

Topically applied Fluocinolone Acetonide 0.01% Topical Oil can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION

Fluocinolone Acetonide 0.01% Topical Oil for scalp psoriasis in adults (Scalp Oil):

For the treatment of scalp psoriasis, wet or dampen hair and scalp thoroughly. Apply a thin film of Fluocinolone Acetonide 0.01% Topical Oil on the scalp, massage well and cover scalp with the supplied shower cap. Leave on overnight, or for a minimum of 4 hours before washing off. Wash hair with regular shampoo and rinse thoroughly.

HOW SUPPLIED

Fluocinolone Acetonide 0.01% Topical Oil is supplied in a 4 fluid ounce bottle with a net content of 118.28 mL. It is labeled as Scalp Oil (NDC 65162-703-86). Scalp Oil is supplied with 2 shower caps.

Keep tightly closed. Store upright at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or www.amneal.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

CAUTION: Rx only

Distributed by:

Amneal Pharmaceuticals

Bridgewater, NJ 08807

Rev. 08-2015-00

PACKAGE LABEL PRINCIPAL DISPLAY PANEL

NDC 65162-703-86
FLUOCINOLONE ACETONIDE
0.01% Topical Oil
SCALP OIL

SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION.
Contains: fluocinolone acetonide (0.01%), isopropyl alcohol (1.6%), in a base containing isopropyl myristate, light mineral oil, oleyl-2 and refined peanut oil NF.
Contents of Package: 4 fl. oz. bottle/2 shower caps.
Storage: Keep tightly closed. Store upright at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].
For questions or to report suspected adverse reactions, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088.

Rx only
Distributed by:
Amneal Pharmaceuticals
Bridgewater, NJ 08807 Rev. 08-2015-00

NDC 65162-703-86
FLUOCINOLONE ACETONIDE
0.01% Topical Oil
SCALP OIL

FOR TOPICAL USE ONLY
NOT FOR ORAL, OPHTHALMIC
or INTRAVAGINAL USE
SHAKE WELL BEFORE USE

Keep Out of Reach of Children
DOSAGE AND ADMINISTRATION: For the treatment of scalp psoriasis, wet or dampen hair and scalp thoroughly. Apply a thin film of Fluocinolone Acetonide 0.01% Topical Oil on the scalp, massage well and cover scalp with one of the supplied shower caps. Leave on overnight or for a minimum of 4 hours before washing off. Wash hair with regular shampoo and rinse thoroughly.

Rx only Net Contents 118.28 mL (4 fl. oz.)

LOT
EXP



FLUOCINOLONE ACETONIDE

fluocinolone acetonide oil

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:65162-703
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FLUOCINOLONE ACETONIDE (UNII: 0CD5FD6S2M) (FLUOCINOLONE ACETONIDE - UNII:0CD5FD6S2M)	FLUOCINOLONE ACETONIDE	0.11 mg in 118.28 mL

Inactive Ingredients

Ingredient Name	Strength
ISOPROPYL ALCOHOL (UNII: ND2M416302)	
ISOPROPYL MYRISTATE (UNII: 0RE8K4LNJS)	
LIGHT MINERAL OIL (UNII: N6K5787QVP)	
PEANUT OIL (UNII: 5TL50QU0W4)	
OLETH-2 (UNII: 7L6R1SQ6M0)	

Product Characteristics

Color	yellow	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65162-703-86	1 in 1 CARTON	09/22/2015	
1		118.28 mL in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA201759	09/22/2015	

Labeler - Amneal Pharmaceuticals LLC (123797875)**Establishment**

Name	Address	ID/FEI	Business Operations
Amneal Pharmaceuticals, LLC		963900878	analysis(65162-703) , label(65162-703) , manufacture(65162-703) , pack(65162-703)