FLUOCINOLONE ACETONIDE- fluocinolone acetonide oil
Padagis Israel Pharmaceuticals Ltd

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FLUOCINOLONE ACETONIDE OIL safely and effectively. See full prescribing information for FLUOCINOLONE ACETONIDE OIL.
FLUOCINOLONE ACETONIDE oil (ear drops), for otic use
Initial U.S. Approval: 1988

INDICATIONS AND USAGE

Fluocinolone acetonide oil ear drops is a corticosteroid indicated for the topical treatment of chronic eczematous external otitis in adults and pediatric patients 2 years of age and older. (1)

DOSAGE AND ADMINISTRATION

- Fluocinolone acetonide oil ear drops is not for oral, ophthalmic, or intravaginal use. (2)
- Apply 5 drops of fluocinolone acetonide oil ear drops into the affected ear twice daily for 7 to 14 days. (2)
- Do not use on face or intertriginous areas. (2)

DOSAGE FORMS AND STRENGTHS

- Ear drops, containing 0.01% fluocinolone acetonide, supplied in bottles containing 20 mL. (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- Endocrine System Adverse Reactions:
  - Topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, hyperglycemia, and glucosuria. (5.1)
  - Pediatric patients may be more susceptible to systemic toxicity from equivalent doses. (5.1, 8.4)
  - Systemic absorption may require evaluation for HPA axis suppression. Potent corticosteroids use on large areas, prolonged use or occlusive use, altered skin barrier, liver failure, and young age may increase systemic absorption. Modify use should HPA axis suppression develop. (5.1)
- Local Adverse Reactions: Local adverse reactions may include atrophy, striae irritation, acneiform eruptions, hypopigmentation, and allergic contact dermatitis, and may be more likely with occlusive use or more potent corticosteroids. (5.2, 6.1)
- Ophthalmic Adverse Reactions: May increase the risks of glaucoma and posterior subcapsular cataract. Avoid contact of fluocinolone acetonide oil ear drops with eyes. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation. (5.3)

ADVERSE REACTIONS

The most commonly reported adverse reactions (≥ 1%) were headache (3%), URI (2%), cough (2%), eczematous otitis (1%). (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Padagis® at 1-866-634-9120 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Fluocinolone acetonide oil ear drops is indicated for the topical treatment of chronic eczematous external otitis in adults and pediatric patients 2 years of age and older.

2 DOSAGE AND ADMINISTRATION

Fluocinolone acetonide oil ear drops is for otic administration only. Not for oral, ophthalmic, or intravaginal use.

Apply fluocinolone acetonide oil ear drops into the affected ear using the supplied ear dropper. To apply, tilt head to one side so that the ear is facing up. Then gently pull the ear lobe backward and upward and apply 5 drops of fluocinolone acetonide oil ear drops into the ear. Keep head tilted for about a minute to allow fluocinolone acetonide oil ear drops to penetrate lower into the ear canal. Gently pat excess material dripping out of

the ear using a clean cotton ball. Follow these instructions twice each day for 7 to 14 days.

Discontinue fluocinolone acetonide oil ear drops when control of disease is achieved within 2 weeks, or contact the healthcare provider if no improvement is seen within 2 weeks.

Do not use on the face, axillae, or groin unless directed by the healthcare provider. Do not apply to intertriginous areas due to the increased risk of local adverse reactions *[see Adverse Reactions (6) and Use in Specific Populations (8.4)]*.

3 DOSAGE FORMS AND STRENGTHS

Ear drops, containing 0.01% fluocinolone acetonide supplied in bottles containing 20 mL (dropper included).

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Endocrine System Adverse Reactions

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency. Cushing's syndrome, hyperglycemia, and glucosuria can result from systemic absorption of topical corticosteroids.

HPA axis suppression and Cushing's syndrome have been reported in pediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in pediatric patients include linear growth retardation, delayed weight gain, low plasma cortisol levels, and subnormal response to ACTH stimulation. Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios *[see Use in Specific Populations (8.4)]*.

Conditions which increase systemic absorption include the use of more potent corticosteroids, use over large surface areas, use over prolonged periods, use of occlusive dressings, altered skin barrier, liver failure, and young age. Use of more than one corticosteroid-containing product at the same time may increase total systemic corticosteroid exposure. Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. The ACTH stimulation test may be helpful in evaluating patients for HPA axis suppression.

If HPA axis suppression is documented, an attempt should be made to withdraw the drug to reduce the frequency of application, or to substitute a less potent corticosteroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids.

5.2 Local Adverse Reactions

Local adverse reactions may occur with use of topical corticosteroids, including fluocinolone acetonide oil ear drops, and may be more likely to occur with occlusive use, prolonged use, or use of higher potency corticosteroids. Some local adverse reactions may be irreversible. Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria *[see Adverse Reactions (6.1)]*.

5.3 Ophthalmic Adverse Reactions

Use of topical corticosteroids may increase the risks of glaucoma and posterior subcapsular cataract. Glaucoma and cataracts have been reported in postmarketing experience with the use of topical corticosteroid products. Avoid contact of fluocinolone acetonide oil ear drops with eyes. Advise patients to report any visual symptoms and consider referral to an ophthalmologist for evaluation.

5.4 Allergic Contact Dermatitis

Use of topical corticosteroids can cause allergic contact dermatitis. Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

5.5 Concomitant Skin Infections

Use of topical corticosteroids may delay healing or worsen concomitant skin infections. Treat concomitant skin infections with an appropriate antimicrobial agent. If the infection persists unchanged, discontinue fluocinolone acetonide oil ear drops until the infection has been adequately treated.

5.6 Use in Peanut Sensitive Individuals

Use caution in prescribing fluocinolone acetonide oil ear drops for peanut sensitive individuals *[see Description (11)]*.

Should signs of hypersensitivity present (wheal and flare reactions, pruritus, or other manifestations), or should disease exacerbations occur, discontinue fluocinolone acetonide oil ear drops immediately and institute appropriate therapy.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in more detail in other sections of the labeling:

- Endocrine System Adverse Reactions *[see Warnings and Precautions (5.1), Use in Specific Populations (8.4)]*
- Local Adverse Reactions *[see Warnings and Precautions (5.2)]*
- Ophthalmic Adverse Reactions *[see Warnings and Precautions (5.3)]*

6.1 Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In trials that enrolled 154 subjects (adults and pediatric subjects 2 years and older) with chronic eczematous external otitis who were treated with five drops per ear of fluocinolone acetonide oil ear drops twice daily for a maximum 14 days of treatment, the following adverse reactions were reported:

Table 1: Adverse Reactions in ≥ 1% of Fluocinolone Acetonide Oil Ear Drops-Treated Adult and Pediatric Subjects 2 Years of Age and Older with Chronic Eczematous External Otitis, N=154

Adverse Reaction	n (%)
Headache	4 (3)
URI	3 (2)
Cough	3 (2)
Eczematous otitis	2 (1)

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of products containing topical corticosteroids. Because postmarketing adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Endocrine Disorders:* HPA axis suppression and Cushing's syndrome *[see Use in Specific Populations (8.4)]*
- *Eye Disorders:* glaucoma and cataracts *[see Warnings and Precautions (5.3)]*
- *Nervous System Disorders:* intracranial hypertension including bulging fontanelles, headaches, and bilateral papilledema *[see Use in Specific Populations (8.4)]*

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from case reports, case series, and observational studies on fluocinolone acetonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Observational studies suggest maternal use of high to super-high potency topical steroids may be associated with an increased risk of low birthweight infants. Advise pregnant women to use fluocinolone acetonide oil ear drops on the smallest area of skin and for the shortest duration possible.

Corticosteroids can cause fetal malformations in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids cause fetal malformations after dermal application in laboratory animals.

The background risk of major birth defects and miscarriage for the indicated population

is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of fluocinolone acetonide in breast milk or its effects on the breastfed infant or on milk production. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for fluocinolone acetonide oil ear drops and any potential adverse effects on the breastfed infant from fluocinolone acetonide oil ear drops or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of fluocinolone acetonide oil ear drops for the topical treatment of chronic eczematous external otitis have been established in pediatric patients aged 2 years and older.

Safety and effectiveness of fluocinolone acetonide oil ear drops in pediatric patients with chronic eczematous external otitis below the age of 2 years have not been established.

Systemic Adverse Reactions in Pediatric Patients

HPA Axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in pediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in pediatric patients include linear growth retardation, delayed weight gain, low plasma cortisol levels, and subnormal response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk for systemic adverse reactions than are adults when treated with topical corticosteroids *[see Warnings and Precautions (5.1)]*.

Evaluation in Peanut-Sensitive Pediatric Patients

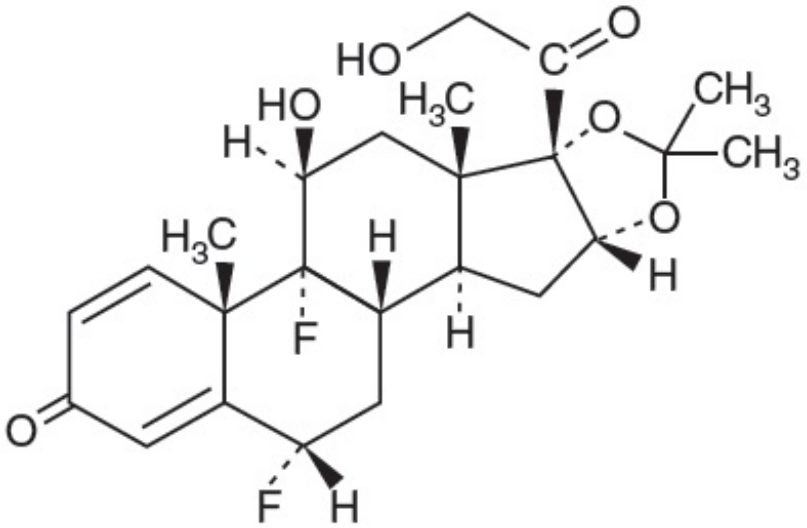
A clinical trial was conducted to assess the safety of the formulation of fluocinolone acetonide oil ear drops, which contains refined peanut oil, in patients with known peanut allergies. The trial enrolled 13 pediatric subjects with atopic dermatitis, 6 to 17 years of age. Fluocinolone acetonide oil ear drops is not approved for the treatment of atopic dermatitis. Of the 13 subjects, 9 were Radioallergosorbent Test (RAST) positive to peanuts and 4 had no peanut sensitivity (controls). The trial evaluated the subjects' responses to both prick test and patch test utilizing refined peanut oil, the formulation of fluocinolone acetonide oil ear drops and histamine/saline controls. Subjects were also treated with the formulation of fluocinolone acetonide oil ear drops twice daily for 7 days. Prick test and patch test results for all 13 subjects were negative to the formulation of fluocinolone acetonide oil ear drops and the refined peanut oil. One of the 9 peanut-sensitive subjects experienced an exacerbation of atopic dermatitis after 5 days of use on the formulation of fluocinolone acetonide oil ear drops.

Evaluation in Pediatric Patients 2 to 6 years old

Use of the formulation of fluocinolone acetonide oil ear drops in pediatric patients 2 to 6 years old is supported by open-label safety trials conducted in 33 pediatric subjects (20 subjects ages 2 to 6 years, 13 subjects ages 7 to 12 years) with moderate to severe stable atopic dermatitis. Baseline body surface area involvement was 50% to 75% in 15 subjects and greater than 75% in 18 subjects. Subjects were treated with the formulation of fluocinolone acetonide oil ear drops twice daily for 4 weeks. Morning pre-stimulation cortisol and post-ACTH stimulation cortisol levels 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 µg/dL; normal: cortisol > 7µg/dL) but all had normal responses to 0.25 mg of ACTH stimulation (cortisol > 18 µg/dL) *[see Clinical Pharmacology (12.2)]*.

11 DESCRIPTION

Fluocinolone Acetonide Oil, 0.01% Ear Drops contains fluocinolone acetonide [(6α, 11β, 16α)-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 dermatologic use. Chemically, fluocinolone acetonide is $C_{24}H_{30}F_2O_6$. It has the following structural formula:



Fluocinolone acetonide 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 oil ear drops 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.

Fluocinolone acetonide oil ear drops is formulated with 48% refined peanut oil. The bulk refined peanut oil, used in fluocinolone acetonide oil ear drops is heated just below 232°C (450°F) for at least 15 minutes.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Corticosteroids play a role in cellular signaling, immune function, inflammation, and protein regulation; however, the precise mechanism of action in eczematous external otitis is unknown.

12.2 Pharmacodynamics

Vasoconstrictor Assay

Fluocinolone acetonide oil ear drops is in the low to medium range of potency as compared with other topical corticosteroids in vasoconstrictor studies. However, similar blanching scores do not necessarily imply therapeutic equivalence.

Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression

HPA axis suppression was evaluated in 33 pediatric subjects 2 to 12 years old (20 subjects ages 2 to 6 years, 13 subjects ages 7 to 12 years) with moderate to severe stable atopic dermatitis. Subjects were treated with the formulation of fluocinolone acetonide oil ear drops twice daily for 4 weeks. Baseline body surface area involvement was 50% to 75% in 15 subjects and greater than 75% in 18 subjects. Morning pre-stimulation cortisol and post-ACTH stimulation cortisol levels 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 µg/dL; normal cortisol >7 µg/dL) but all had normal responses to 0.25 mg of ACTH stimulation (cortisol > 18 µg/dL) *[see Warnings and Precautions (5.1)]*.

12.3 Pharmacokinetics

Topical corticosteroids can be absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the product formulation and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may increase percutaneous absorption. The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids may be necessary due to the fact that circulating levels are often below the level of detection. Once absorbed through the skin, topical corticosteroids are metabolized, primarily in the liver, and are then excreted by the kidneys. Some corticosteroids and their metabolites are also excreted in the bile.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity, genotoxicity, or fertility studies were conducted with fluocinolone acetonide oil ear drops. However, some corticosteroids are 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).

14 CLINICAL STUDIES

In two vehicle-controlled trials (Trial 1 and Trial 2), 154 subjects (adults and pediatric subjects 2 years of age and older) with chronic eczematous external otitis were treated with 5 drops per ear of fluocinolone acetonide oil ear drops twice daily for 7 days. Efficacy was assessed on Day 7 by clearance of the signs and symptoms of eczematous external otitis, and the results are presented in the following table:

Table 2: Efficacy Results at Day 7 in Subjects with Chronic Eczematous External Otitis in Trial 1 and 2*

	Fluocinolone Acetonide Oil Ear Drops	**Vehicle**
Study 1	30% (14/47)	7% (3/46)
Study 2	32% (9/28)	3% (1/30)

* Erythema, scaling, pruritus, erosion/oozing/crusting and debris

16 HOW SUPPLIED/STORAGE AND HANDLING

Fluocinolone Acetonide Oil, 0.01% Ear Drops is supplied in bottles containing 20 mL, (dropper included) (NDC 45802-**009**-10).

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

Discard fluocinolone acetonide oil ear drops 2 months after initial use.

17 PATIENT COUNSELING INFORMATION

Administration Instructions

Advise patients that fluocinolone acetonide oil ear drops is for otic administration only and not for oral, ophthalmic, or intravaginal use *[see Dosage and Administration (2)]*.

Advise patients to avoid use of fluocinolone acetonide oil ear drops on the face, axillae, or groin unless directed by their healthcare provider *[see Dosage and Administration (2)]*.

Advise patients to discontinue therapy when control of disease is achieved. Instruct patients to contact their healthcare provider if no improvement is seen within 2 weeks *[see Dosage and Administration (2)]*.

Endocrine System Adverse Reactions

Instruct patients not to use other corticosteroid-containing products while using fluocinolone acetonide oil ear drops without first consulting their healthcare provider *[see Warnings and Precautions (5.1)]*.

Ophthalmic Adverse Reactions

Advise patients to avoid contact with the eyes and in case of contact, wash eyes liberally with water. Instruct patients to tell their healthcare provider if they develop any visual symptoms *[see Warnings and Precautions (5.3)]*.

Pregnancy and Lactation

Advise patients to use fluocinolone acetonide oil ear drops on the smallest area of skin and for the shortest duration possible while pregnant or breastfeeding. Advise patients that are breastfeeding not to apply fluocinolone acetonide oil ear drops directly to the nipple and areola to avoid direct infant exposure *[see Use in Specific Populations (8.1 and 8.2)]*.

Manufactured by Padagis®, Yeruham, Israel
www.padagis.com
Rev 07-25
0N300 RC PH5

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 45802-009-10

Rx Only

Fluocinolone Acetonide Oil, 0.01%

(Ear Drops)

For Otic Use Only

Not For Ophthalmic Use

NET CONTENTS

20 mL

The following image is a placeholder representing the product identifier that is either affixed or imprinted on the drug package label during the packaging operation.

S/N [insert product's serial number]
Lot [insert product's lot number]
Exp [insert product's expiration date]

FLUOCINOLONE ACETONIDE

fluocinolone acetonide oil

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:45802-009
Route of Administration	AURICULAR (OTIC)		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
FLUOCINOLONE ACETONIDE (UNII: 0CD5FD6S2M) (FLUOCINOLONE ACETONIDE - UNII:0CD5FD6S2M)	FLUOCINOLONE ACETONIDE	0.11 mg in 1 mL

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

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:45802-009-10	1 in 1 CARTON	10/04/2017	
1		20 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	ANDA202849	10/04/2017	

Labeler - Padagis Israel Pharmaceuticals Ltd (600093611)

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Padagis Israel Pharmaceuticals Ltd