PRODUCT MONOGRAPH

Pr DermOtic® Oil Ear Drops

Fluocinolone Acetonide Otic Solution, 0.01% w/v
House Standard

Anti-inflammatory, Antipruritic and Vasoconstricting Agent

Manufacturer:
Hill Dermaceuticals, Inc.
2650 South Mellonville Ave.
Sanford, Florida
32773 U.S.A.
www.hillderm.com

Canadian Distributor:
Hill Dermaceuticals, Inc.
3045 Southcreek Road, Unit #4
Mississauga, Ontario L4X 2X6
Canada

Control Number: 220228

Date of Revision:
November 27, 2018

Table of Contents

PRODUCT MONOGRAPH

Pr DermOtic® Oil Ear Drops
(Fluocinolone Acetonide Otic Solution) 0.01% w/v
House Standard

Anti-inflammatory, Antipruritic and Vasoconstricting Agent

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Topical, Otic	Otic Solution / 0.01% w/v	Refined Peanut Oil NF, Mineral Oil Light, Oleth-2, Isopropyl Myristate, Isopropyl Alcohol, Cream Fragrance, Balsam Pine Fragrance. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is a medium potency fluorinated corticosteroid indicated for:

Treatment of moderate to severe Chronic Eczematous External Otitis in adults and children 12 years of age and older.

- For use in children 12 years of age and older, see **WARNING AND PRECAUTIONS** section, "**Special populations - Paediatrics**" subsection"
- Should be used only if the tympanic membrane is intact: It is not to be used if the tympanic membrane is absent, or perforated or if a tympanostomy tube is present.

The DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v formulation is also marketed as Derma-Smoothe/FS® (Fluocinolone Acetonide Topical Oil 0.01% w/v) for the indication of atopic eczema.

CONTRAINDICATIONS

DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation. For a complete listing see **Dosage Forms, Composition and Packaging** section.

This product contains refined peanut oil NF (see **WARNINGS AND PRECAUTIONS** section)

Topical application to the eye (or around the eye) is contraindicated.

DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v should be used only if the tympanic membrane is intact: It should not be used if the tympanic membrane is absent, or perforated, or if a tympanostomy tube (ear tube) is present.

This medication should not be used if there is an untreated ear infection (bacterial or fungal or viral infections)

WARNINGS AND PRECAUTIONS

DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is formulated with 48% refined peanut oil NF. Physicians should use caution in prescribing DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for peanut-sensitive individuals. One peanut-sensitive child experienced a flare of his atopic dermatitis after 5 days of twice daily treatment with Derma-Smoothe/FS® (DermOtic® Oil Ear Drops is also marketed as Derma-Smoothe/FS® Topical Oil) (see **CLINICAL TRIALS** section).

If irritation develops, DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v 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.

General

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

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 DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v should be discontinued until the infection has been adequately controlled.

Carcinogenesis and Mutagenesis

Long term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v.

Studies have not been performed to evaluate the mutagenic potential of Fluocinolone Acetonide, the active ingredient in DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. 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).

Endocrine and Metabolism

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

Immune

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).

Neurologic

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 Hypothalamic-Pituitary-Adrenal (HPA) axis suppression. This may be done by using the ACTH (Adrenocorticotropic hormone) 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.

Ophthalmologic

Avoid contact with the eyes. In case of contact, wash eyes liberally with water.

Sensitivity/Resistance

Children may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios (see **PRECAUTIONS-Paediatrics** section). See **Adverse Drug Reactions**.

Skin

The following local adverse reactions have been reported infrequently with topical

corticosteroids, including Fluocinolone Acetonide. They may occur more frequently with the use of occlusive dressing, especially with higher potency corticosteroids. The reactions are listed in approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae and miliaria. See **Adverse Drug Reactions**.

Special Populations

Pregnant Women:

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 DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v to show teratologic effects on animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. Therefore, DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Women:

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 secreted in human milk, caution should be exercised when DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is administered to a nursing woman.

Paediatrics:

Safety and efficacy of DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for Chronic Eczematous External Otitis is not demonstrated in children 12 years and older; efficacy and safety data were extrapolated from data in adults.

Five (5) drops of DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v may be applied to the affected ear(s) twice daily for up to 7 days in paediatric patients 12 years and older with Chronic Eczematous External Otitis.

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. Children may be more susceptible to system 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, headache, and bilateral papilledema.

DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is formulated with 48% refined peanut oil NF. The peanut oil used in DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution 0.01% w/v) is tested for residual protein through amino acid analysis; the acceptance criterion for total protein is no more than 0.5 parts per million. Physicians should use caution in prescribing DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for peanut-sensitive children.

Geriatrics:

Clinical studies have not been conducted in populations >65 years of age.

Monitoring and 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

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The following local adverse reactions have been reported infrequently with topical corticosteroids, including Fluocinolone Acetonide. They may occur more frequently with the use of occlusive dressing, especially with higher potency corticosteroids. The 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 miliaria.

One peanut sensitive child experienced a flare of his atopic dermatitis after 5 days of twice daily treatment with Derma-Smoothe/FS® applied to the body. (DermOtic Oil ® Ear Drops is also marketed as Derma-Smoothe/FS® Topical Oil).

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse drug 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.

Study 31

Efficacy in a placebo-controlled study for the treatment of Chronic Eczematous External Otitis on 154 patients (adults and children 2 years of age and older) treated with five drops per ear of DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v twice daily, after 7 days of treatment showed DermOtic® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v to be superior to the placebo in clearing the signs and symptoms of Chronic Eczematous External Otitis. Across all treatment groups, the large

majority of adverse events were considered to be mild or moderate, by the investigator. The incidence of adverse events at any time during the study totaled 54, where 26 of the AEs were documented as mild in intensity, 24 AEs were moderate, and 4 were recorded as severe all of which were resolved.

TABLE 1: Adverse Event Report by Incidence

System Organ Class Name:		**DermOtic® Treatment (N=139)**	**Placebo Treatment (N=79)**
Number of Subjects with at least One AE		**27 (19%)**	**10 (12.6%)**
Incidence of Adverse Events (Total = 54)			
Ear and labyrinth disorders:		**14**	**5**
Ear discomfort	Burning bilateral ear canals upon study article administration	1 1	
Ear pain	Preauricular pain – left ear	1	
Ear canal erythema	Mild erythema – right ear	1	
External ear disorder	Small amount of blood – right ear		1*
Tympanic membrane perforation	Right tympanic membrane perforation	1	
Ear pain	Bilateral ear pain		1
Deafness neurosensory	Sensorineural hearing loss – left ear		1
Otitis externa	Otitis externa – left ear	1	
Otitis media	Otitis media – right ear		1
Otitis media acute	Otitis media acute – right ear	1*	
Myringitis	Myringitis – right ear	1*	
Otitis external fungal	Fungal otitis – left ear	1	
External eczematous otitis	External eczematous otitis	1 1 1	
Rash popular, bilateral ears	Papular rash bilateral ears		1*
Worsening of external eczematous otitis	Worsening of external eczematous otitis – right ear	1	
Fungal skin infection	Fungal skin infection – left ear	1	

System Organ Class Name:		DermOtic® Treatment (N=139)	Placebo Treatment (N=79)
Number of Subjects with at least One AE		**27 (19%)**	**10 (12.6%)**
Incidence of Adverse Events (Total = 54)			
Eye disorders:		**3**	
Eye pruritus	Bilateral itching eyes	1	
Eye irritation	Bilateral burning eyes	1 1	
Gastrointestinal disorders		**4**	
Nausea	Nausea	1 1 1	
Vomiting	Vomiting	1	
General disorders and administration site conditions		**1**	
Pyrexia	Fever	1	
Injury, poisoning and procedural complications		**1**	
Open wound	Hard palate abrasion	1	
Respiratory, thoracic and mediastinal disorders		**3**	**1**
Cough	Cough	1 1	1
Wheezing	Wheezing	1	
Nervous system disorders		**4**	**5**
Headache	headache	1 1	1 1 1

System Organ Class Name:		DermOtic® Treatment (N=139)	Placebo Treatment (N=79)
Number of Subjects with at least One AE		**27 (19%)**	**10 (12.6%)**
Incidence of Adverse Events (Total = 54)			
Headache	Worsening of pre-existing intermittent headaches		1
Dizziness postural	Dizziness		1*
Dysgeusia	Metallic taste in mouth	1 1	
Metabolism and nutrition disorders		**2**	
Diabetes mellitus non-insulin dependent	Non-insulin dependent diabetes mellitus	1	
Hypoglycemia	Hypoglycemia	1	
Musculoskeletal and connective tissue disorders		**1**	
Neck pain	Mild lateral left neck pain	1	
Psychiatric disorders		**1**	
Mania	Hypermania	1	
Infections and infestations		**7**	**1**
Gastroenteritis	Acute gastroenteritis - intermittent	1	
Influenza	Influenza	1	
Sinusitis	Sinus infection	1	
Upper respiratory tract infection	URI	1 1 1	
Nasopharyngitis	Common cold		1
Skin infection	Skin infection		1
Investigations Body temperature increased	Elevated Temperature		**1** 1

***Treatment-related**

Data Source: Study 31 **INTEGRATED Study 31A and 31B and Table 22**

Most of the adverse events were not related to the study materials and were mild or moderate in intensity. When considering treatment-related adverse events, there were only seven incidence reported in five patients.

Deaths and other Serious Adverse Events

No deaths or serious adverse events were reported in any of the studies.

Withdrawals Due to Adverse Events

There were 7 withdrawals from the primary efficacy and safety study due to adverse events. Six (6) withdrawals were from the placebo group, but two of those patients were crossed over from the placebo to the open-label treatment and experienced the adverse events at or after the Derma-Smoothe/FS® open-label treatment; one of the two patients experienced a right ear myringitis, tympanic membrane perforation, and otitis media. Also, one patient from the active group was removed due to an adverse event (hypermania) considered not related to the study product.

Atopic Dermatitis Studies

Table 1: Study 25 and Study 25-S

	Derma-Smoothe/FS® N = 76 * (%)	Derma-Smoothe/FS® Vehicle N = 52 (%)
Integumentary		
Hypopigmentation	1 (1.3)	0
Erythema	2 (2.6)	0
Papules	6 (7.9)	0
Pustules	6 (7.9)	0
Burning	4 (5.3)	0
Itching	4 (5.3)	0
Irritation	4 (5.3)	0

* Combined Study 25 and Study 25-S (Open-Label)

Derma-Smoothe/FS is also marketed as DermOtic® Oil

Study 25

Study 25 was a double-blind safety and efficacy study of Derma-Smoothe/FS® versus the Derma-Smoothe/FS® vehicle in the treatment of atopic dermatitis in children 2 years and older. Derma-Smoothe/FS® was applied twice daily for 28 days. Only one adverse event was noted in Study 25. This adverse event was slight hypopigmentation, noted at the final evaluation, 2 weeks after stopping treatment with Derma-Smoothe/FS®. In Study 25, a total of 84 patients completed the study.

Study 25-S

Study 25-S was an open-label safety study of Derma-Smoothe/FS® for the treatment of atopic dermatitis (Derma-Smoothe/FS® is also marketed as DermOtic® Oil Ear Drops).

Derma-Smoothe/FS® was applied twice daily for 28 days. No adverse events were observed in Study 25-S California. Four patients in Study 25-S Chicago, Cleveland, and Miami had at least one adverse event. All patients with reported adverse events were at the Chicago site: two patients had severe papules, pustules, burning, itching, and irritation at the final visit (2 weeks after stopping study medication), and two patients had mild papules and pustules at the 4th week of treatment (the last week of treatment with study medication), and moderate erythema, papules, pustules, burning, itching, and irritation at the final visit (2 weeks after stopping study medication). All adverse events had resolved soon after the end of the study, as determined by an informal follow-up by the sponsor to each investigator after termination of the study. Seven placebo treated patients had exacerbation of the disease. In Study 25-S, a total of 25 subjects completed the study.

Study 26

Study 26 was a post-marketing (open label) safety study to evaluate the effects of Derma-Smoothe/FS® on HPA axis suppression (Derma-Smoothe/FS® is also marketed as DermOtic® Oil Ear Drops). A total of 15 people were enrolled in the safety study. One subject withdrew before week-2 evaluation and one subject was eliminated for a lack of cortisol levels at week-4. No local adverse events were reported during Study 26.

Peanut Hypersensitivity Safety Study

Chicago Peanut Allergy Study

A phase 4, controlled, open label clinical study was conducted to assess the safety of Derma-Smoothe/FS® which contains refined peanut oil NF, on subjects with known peanut allergies (Derma-Smoothe/FS® is also marketed as DermOtic® Oil Ear Drops).

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). One of the 9 peanut-sensitive patients experienced an exacerbation of atopic dermatitis after 5 days of treatment with Derma-Smoothe/FS® (see **CLINICAL TRIALS** section). In the Chicago Peanut Allergy Study, a total of 12 patients completed the study.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

Not Applicable.

Abnormal Hematologic and Clinical Chemistry Findings

Not Applicable

Post-Market Adverse Drug Reactions

The following post-marketing adverse drug reactions occurred exclusively with the Derma-Smoothe/FS® (Fluocinolone Acetonide Topical Oil 0.01% w/v) formulation. Only 41 adverse events overall have been reported to the sponsor, including (in decreasing order of frequency): allergic reaction, alopecia, skin irritation, erythema, transient corneal irritation due to accidental exposure, nausea, and vertigo.

Clinical safety studies were on the same formulation of Fluocinolone Acetonide 0.01%, marketed as Derma-Smoothe/FS® Topical Oil. 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 a baseline body surface area involvement greater than 75% in 18 patients and 50% to 75% in 15 patients, were treated with Derma-Smoothe/FS® Topical Oil 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 the 18 subjects, ages 2 to 5 years, showed low pre-stimulation cortisol levels (3.2 μg/dL to 6.6 μg/dL; normal: cortisol > 7 μg/dL) but all had normal responses to 0.25 mg of Cortrosyn stimulation (cortisol > 18 μg/dL). No local adverse events were reported in the open-label safety study.

DRUG INTERACTIONS

Overview

There are no known genetic differences in response to DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for treatment of Chronic Eczematous External Otitis, and there are no known clinically relevant interactions with other medicinal products. There are no known genetic differences in response to Derma-Smoothe/FS® Topical Oil for treatment of atopic dermatitis, and there are no known clinically relevant interactions with other medicinal products. There were insufficient numbers of patients in the clinical trials of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v to examine potential drug-drug, drug-demographic, or drug-disease interactions.

Drug-Drug Interactions

There have been no clinical studies conducted to assess the safety of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v used in combination therapy. It is recommended that DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v be used without the use of other medications.

DOSAGE AND ADMINISTRATION

Dosing Considerations

- Children have a larger surface to body mass area leading to a higher susceptibility to HPA axis suppression; however, there have been no reported cases during clinical studies or post-marketing experience of HPA axis suppression. DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is for otic use. DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v are not for oral, ophthalmic, or intravaginal use. DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v should not be used on the face or diaper area.

- Geriatrics: Clinical studies have not been conducted in population ages >65 years of age.

Recommended Dose and Dosage Adjustment

- Chronic eczematous external otitis in Adults: using the supplied ear-dropper, apply 5 drops of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v into the affected ear. 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 DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v into the ear. Keep head tilted for about a minute to allow DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v to penetrate into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice daily for 7 to 14 days.

- Chronic eczematous external otitis in children 12 years and older: DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v may be used for up to 7 days in children 12 years or of age and older: follow the same instructions as for adults, however, if no improvement is seen within 7 days, or if symptoms worsen, contact the physician.

- Do not use DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v with occlusion (i.e. ear plugs or cotton dressing) as this may increase absorption across the skin.

Missed Dose

If a dose of this medication is missed, it is not necessary to make up the missed dose. Skip the missed dose and continue with the next scheduled dose.

Reconstitution:

Not Applicable.

OVERDOSAGE

The possibility of overdose, using DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for the treatment of Chronic Eczematous External Otitis is very unlikely following topical administration of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v, even if it were applied to most of the body. Pediatric studies with patients suffering from atopic dermatitis on >50% of the body did not demonstrate any signs of overdosing or HPA axis suppression while using Derma-Smoothe/FS® Topical Oil, which is also marketed as DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. If an overdose should occur, there is no antidote.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Like other topical corticosteroids, Fluocinolone Acetonide has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 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 A_2.

Pharmacodynamics

The pathways by which topical steroids improve atopic dermatitis are not clearly understood. No studies involving the pharmacodynamics of the active Fluocinolone Acetonide or the drug product DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v have been performed.

Pharmacokinetics

No studies in pharmacokinetics, absorption, distribution, excretion, or metabolism involving the active Fluocinolone Acetonide or the drug product DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v have been performed. Pharmacokinetic properties of the drug class of topically applied corticosteroids remain incompletely understood.

Absorption:

Topically applied corticosteroids may be absorbed percutaneously; percutaneous absorption of topical steroids is determined by many factors including the vehicle, thickness of the stratum corneum, presence of skin disease, skin hydration, and integrity of the epidermal barrier. Topical corticosteroids can be absorbed through normal skin.

Distribution:

Dermally applied corticosteroids are distributed throughout the skin, although the distribution in the skin depends on their percutaneous absorption. Percutaneously absorbed corticosteroids can also be distributed throughout the body, entering the systemic circulation via the dermal microcirculation.

Metabolism:

The viable epidermis is known to be metabolically active and contains many of the enzymes also found in the liver, including a cytochrome P450 system which may be inducible. Steroids may undergo hydrolysis within the epidermis; sulphate conjugation also occurs. The importance of dermal metabolism of steroids to their mechanism of action is unknown.

Systemically, 90% or more of glucocorticoids is reversibly bound to protein under normal circumstances. Corticosteroid-binding globulin and albumin account for most of the plasma steroid-binding capacity. Topically applied corticosteroids undoubtedly undergo further systemic metabolic processes. All of the biologically active adrenocortical steroids and their synthetic congeners have a double bond in the 4,5 position and a ketone group at C3. Reduction of the 4,5 double bond occurs at both hepatic and extrahepatic sites, yielding inactive compounds. Reduction of the 3-ketone constituent occurs only in the liver.

Excretion:

Systemically distributed steroids are excreted in the urine as water-soluble esters and glucuronides. Neither biliary nor fecal excretion is of quantitative importance in humans. Topical steroids may also remain on the surface of the skin and may be eliminated by washing them off the skin.

Special Populations and Conditions

Paediatrics:

Safety and efficacy of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v for Chronic Eczematous External Otitis is not demonstrated in children; efficacy and safety were extrapolated from data in adults. Children have a larger surface to body mass area leading to a higher susceptibility to HPA axis suppression; however, there have been no reported cases during clinical studies or post-marketing experience of HPA axis suppression.

Geriatrics:

Clinical Studies have not been conducted in populations >65 years of age.

Gender:

No gender-related differences of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v have been observed.

Race:

DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is not race specific.

STORAGE AND STABILITY

Recommended storage condition for DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is at controlled room temperature of approximately 25^{o} C. DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v has a full shelf life of 18 months under the required storage conditions.

SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions when using DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms: Oil

Composition:

Peanut Oil Refined NF
Mineral Oil Light NF
Oleth-2
Isopropyl Myristate NF
Isopropyl Alcohol USP
Cream Fragrance # 362411
Balsam Pine Fragrance # 5124

Packaging:

DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is supplied in 1 fl. oz. bottles containing 20 mL of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. A dropper is supplied in each package.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

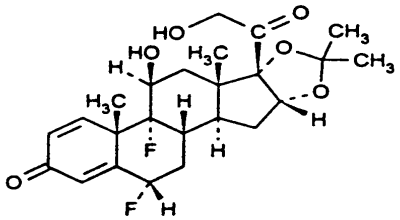
Drug Substance

Proper Name: Fluocinolone acetonide

Chemical Name: 6α,9α-Difluoro-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone

Molecular Formula and Molecular Mass: $C_{24}H_{30}F_2O_6$, 452.50

Structural Formula:



Physicochemical Properties:

Physical Form: White, crystalline powder that is odorless; stable in light.
Solubility: Fluocinolone Acetonide is soluble in alcohol, acetone and methanol; slightly soluble in chloroform; insoluble in water.
Melting Point: Melts at about 270°C, with decomposition.
Storage: Store in well-closed containers, protected from light, at temperatures not exceeding 25°C

CLINICAL TRIALS

Efficacy and Safety of Derma-Smoothe/FS® (Fluocinolone Acetonide Topical Oil 0.01% w/v) in the Treatment of Patients with Chronic Eczematous External Otitis

The primary efficacy parameter used in the two pivotal studies was the assessment of the proportion of subjects that cleared, score = 0, on the signs/symptoms of chronic eczematous external otitis, using a grading scale of 0 (cleared) to 3 (severe). Primary treatment success was defined in the protocols as a severity score of zero at Day 7 for each signs/symptom (erythema, scaling, erosion with oozing and crusting, debris, and pruritus). The secondary efficacy parameters are: i) the proportion of patients in each treatment group who have a score = 0 or 1 at Day 7 for erythema, scaling, erosion, debris, and pruritus. The difference between active and Placebo treatment were tested using Fisher's Exact test; ii) the physician and patient global assessments of improvement from baseline, tested between treatment groups by the chi-square test; and, iii) the global severity at the time of the patient's visit.

DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v was applied to the affected ear(s) 5 drops twice daily for 7 to 14 days. Fourteen days of treatment is based on the additional seven days of treatment which occurred beyond the initial seven days of blinded treatment. After the additional 7 days of open-label treatment with DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v (total of 14 days), there was no statistically significant difference between the two treatment groups.

Table 2: Demographics

Study Population	**All Enrolled Subjects N = 154**			**ITT Population N = 151**			**PP Population N = 140**		
Characteristics	Active (N=75)	Vehicle (N=79)	p-Value	Active (N=75)	Vehicle (N=76)	p-Value	Active (N=70)	Vehicle (N=70)	p-Value
Gender†:									
Male	31	31	0.87	31	29	0.74	29	25	0.60
Female	44	48		44	47		41	45	
Race†:									
Caucasian	62	69		62	66		57	60	
Black	7	4	0.67	7	4	0.71	7	4	0.72
Asian	2	1		2	1		2	1	
Other	4	5		4	5		4	5	
Age* (yrs)	47.3 ± 24.3	46.7 ± 24.7	0.86	47.3 ± 24.3	46.1 ± 24.9	0.76	47.5 ± 24.2	45.6 ± 25.0	0.65
Weight* (lbs)	163.9 ± 62.6	155.7 ± 54.2	0.39	163.9 ± 62.6	155.7 ± 55.0	0.40	162.9 ± 63.3	154.2 ± 56.0	0.39
Height* (in)	64.1 ± 8.2	64.6 ± 6.9	0.68	64.1 ± 8.2	64.5 ± 7.1	0.75	64.0 ± 8.4	64.3 ± 7.1	0.84

†Chi Square test *t-test

Data Source: Study 31 INTEGRATED STUDY 31 Table 1

Table 3: Discontinued Patients

Reason for Discontinuation From the Study Combined Studies 31A and 31B All Patients		
	Treatment Group	
	Active Treatment Group	Placebo Treatment Group
	Number of Patients	
Number Randomized	75	79
ITT population	75	76
PP population	70	70
Completed Study	71 (94.6%)	64 (84.2%)
Discontinued:	4 (5.3%)	12 (15.8%)
Patient request	0	4 (5.3%)
Adverse event	1 (1.3)	6 (7.9%)
Treatment failure	1 (1.3)	2 (2.6%)
Non-compliance	2 (2.6%)	0

Data Source: Study 31 INTEGRATED STUDY 31 Table 14

Of the 151 patients in the ITT population, the majority, 135 (89.4%) completed the study. Twelve of the 16 patients who did not complete the study were in the Placebo treated group.

Out of the 16 patients that were discontinued, seven patients were withdrawn due to adverse events (6 placebo, 1 active). Majority of the adverse events were unrelated to the study drug. Two of those 6 patients were crossed over from the placebo to the open-label treatment and experienced the adverse events at or after the DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v open-label treatment; one of the two patients experienced a right ear myringitis, tympanic membrane perforation, and otitis media. Also, one patient from the active group was removed due to an adverse event (hypermania) considered not related to the study product. Three patients were discontinued due to treatment failure. Two patients discontinued due to non-compliance, from use of interfering medication and from missed doses greater than 2 consecutive applications. Those who requested to be discontinued from the studies (4) gave the reasons of scheduling conflicts.

Table 4: Day 7 Efficacy Evaluation (ITT Population)

Efficacy Parameter Day 7	Proportion of Subjects Classified as Success		p-Value	
	Active (N=75)	Placebo (N=76)	Chi Sq	CMH*
Erythema	53.3	32.9	0.014	0.010
Scaling	73.3	47.4	0.002	0.001
Erosion/Oozing/Crusting	80.0	64.5	0.045	0.032
Debris	66.7	43.4	0.005	0.006
Pruritus (Subject Assessment)	49.3	9.2	<0.0001	<0.0001

*CMH – stratified across study centers

Data Source: Study 31 INTEGRATED STUDY 31 Table 3.1

Table 5: Day 7 Efficacy Evaluation (PP Population)

Efficacy Parameter	Proportion of Subjects Classified as Success		p-Value	
	Active (N=70)	Placebo (N=70)	Chi Sq	CMH*
Erythema	51.4	32.9	0.040	0.029
Scaling	72.9	47.1	0.003	0.002
Erosion/Oozing/Crusting	81.4	64.3	0.036	0.040
Debris	67.1	41.4	0.004	0.003
Pruritus (Subject Assessment)	50.0	8.6	<0.0001	<0.0001

*CMH – stratified across study centers

Data Source: Study 31 INTEGRATED STUDY 31 Table 3.2

Table 6: Day 7 Secondary Efficacy Parameter Results

Subjects with Score = 0 or 1

Efficacy Parameter	Proportion of Subjects Classified as Success		p-Value	
	Active (N=75)	Placebo (N=76)	Chi Sq	CMH*
Erythema	92.0	72.1	0.001	0.001
Scaling	97.3	80.3	0.001	0.001
Erosion/Oozing/Crusting	94.7	86.8	0.159	0.093
Debris	96.0	80.3	0.005	0.003
Pruritus (Subject Assessment)	89.3	55.3	<0.0001	<0.0001

*CMH – stratified across study centers

Data Source: Study 31 INTEGRATED STUDY 31 Table 4.1

Study 25-S Open-Label Safety Study on Derma-Smoothe/FS® Topical Oil on Pediatric Patients with Atopic Dermatitis

Suppression of the hypothalamic-pituitary-adrenal (HPA) axis was assessed in several studies for the indication of atopic dermatitis involving pediatric populations. No evidence of suppression of the HPA axis was observed in Study 25-S following treatment with the Fluocinolone Acetonide 0.01% formulation marketed as Derma-Smoothe/FS® Topical Oil. Derma-Smoothe/FS® Topical Oil was applied twice daily for 4 weeks.

Table 7: Cortisol Concentrations

Cortisol Concentrations (ug/dL) Before and After Adrenal Stimulation: Start of Study and After 4 Weeks of Treatment with Derma-Smoothe/FS® Study 25-S California			
	At Start of Study (N=11)	After 4 Weeks of Treatment (N=11)	Week 0 vs. Week 4[c] p value[a]
Cortisol Concentration at Baseline (SD)[b]	12.09 (3.87)	10.73 (1.96)	0.185
Cortisol Concentration Following Stimulation (SD)	25.30 (3.60)	24.51 (1.93)	0.408
Increase in Cortisol After Stimulation	13.21 (5.00)	13.78 (2.25)	0.742

[a] p-value from paired t-test
[b] Baseline value is value prior to stimulation
Data Source: Study 25 Statistical Report, Table 11
[c] Day 28: 7 day post-treatment evaluation

Table 8: Cortisol Concentrations

Cortisol Concentrations (ug/dL) Before and After Adrenal Stimulation: Start of Study and After 4 Weeks of Treatment with Derma-Smoothe/FS® Study 25-S Chicago, Cleveland, and Miami			
	At Start of Study (N=10)	After 4 Weeks of Treatment (N=10)	Week 0 vs. Week 4[c] p value[a]
Cortisol Concentration at Baseline (SD)[b]	11.00 (3.95)	11.76 (3.28)	0.444
Cortisol Concentration Following Stimulation (SD)	28.84 (6.74)	26.07 (5.20)	0.056
Increase in Cortisol After Stimulation	17.84 (9.67)	14.28 (5.60)	0.091

[a] p-value from paired t-test
[b] Baseline value is value prior to stimulation
Data Source: Study 25 Statistical Report, Table 12
[c] Day 28: 7 day post-treatment evaluation

Study 26 HPA Axis Open-Label Safety Study on Derma-Smoothe/FS® on Pediatric Patients with Atopic Dermatitis (2 to 5 years)

Derma-Smoothe/FS® Topical Oil was used twice daily for 28 days. No HPA axis suppression was observed following treatment of Derma-Smoothe/FS® Topical Oil.

Table 9: Cortisol Concentrations

Cortisol Concentrations (ug/dL) Before and After Adrenal Stimulation: Start of Study and After 4 Weeks of Treatment with Derma-Smoothe/FS® Study 26			
	At Start of Study (N=13)	After 4 Weeks of Treatment (N=13)	Week 0 vs. Week 4 p value[a]
Cortisol Concentration at Baseline (SD)[b]	10.73 (5.01)	9.35 (3.82)	0.376
Cortisol Concentration Following Stimulation (SD)	26.12 (2.97)	24.20 (3.79)	0.153
Increase in Cortisol After Stimulation	15.39 (4.81)	14.85 (3.10)	0.647

[a] p-value from paired t-test
[b] Baseline value is value prior to stimulation
Data Source: Study 26 Report, Table 2

DETAILED 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. One factor may be the ability of the glucocorticoids to inhibit the recruitment of neutrophils and monocyte-macrophages into the affected area. Glucocorticoid also decreases the adherence of neutrophils to nylon fibers, indicating decreased tendency of neutrophils to adhere to capillary endothelial cells in areas of inflammation. Although steroids do not affect the production of macrophage migratory inhibitory factor (MIF), it blocks the effect of MIF on macrophages so that the movements of these cells are no longer restricted hence they do not accumulate locally. Evidence also show that glucocorticoids induce the production of a protein that inhibits phospholipase A_2, reducing the release of arachidonic acid from phospholipids, in turn decreasing the formation of prostaglandins, leukotrienes, endoperoxides and thromboxane which plays an important role in chemotaxis and inflammation.

MICROBIOLOGY

Investigative studies showing pharmacokinetic, toxicology and microbiological aspects have not been carried out for Derma-Smoothe/FS®, which is also marketed as DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v.

TOXICOLOGY

No nonclinical studies were performed to assess the toxicology, genotoxicity, carcinogenicity, reproductive or developmental toxicity, or local tolerance of Fluocinolone Acetonide or DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. However, some corticosteroids are associated with several toxic effects; they are summarized below.

- Genotoxicity
  Some corticosteroids have been found to be genotoxic in various genotoxicity tests (e.g., 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).
- Reproductive and Developmental Toxicity
  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. The relationship between corticosteroid use and teratogenicity in humans is unclear.
- Local Tolerance
  Skin thinning (atrophy) has been shown after Fluocinolone Acetonide administration on mouse tail epidermis and on the dorsal skin of hairless dogs. This activity may correlate with the activity of Fluocinolone Acetonide in treating atopic dermatitis.

REFERENCES

1. Balow JE. Glucocorticoid suppression of macrophage migration inhibitory factor. J. Exp. Med. 1973; 137(4): 1031-41
2. Blackwell GJ. Macrocortin: a polypeptide causing the anti-phospholipase effect of glucocorticoids. Nature 1980; 287(5778):147-9.
3. Burks AW, Stanley JS. Food allergy. Curr Opin Pediatr 1998; 10: 588-93.
4. Carmichael SL, Shaw GM. Maternal corticosteroid use and risk of selected congenital anomalies. Am J Med Genet 1999; 86:242-4.
5. Fauci AS. Immunosupressive and anti-inflammatory effects of glucocorticoids. Monographs on Endocrinology 1979; 12:449-65.
6. Goa KL. Clinical pharmacology and pharmacokinetic properties of topically applied corticosteroids. A review. Drugs 1988; 36:51-61.
7. Hirata F. A phospholipase A2 inhibitory protein in rabbit neutrophils induced by glucocorticoids. Proc Natl Acad Sci USA 1980; 77(5): 2533-6.
8. Hoffman DR, Collins-Williams C. Cold-pressed peanut oils may contain peanut allergen. J Allergy Clin Immunol 1994; 93:801-802.
9. Hourihane JO, Bedwanie SJ, Dean TP, Warner JO. Randomized, double-blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts. BMJ 1997; 314:1084-1088.
10. Kimura T, Doi K. Dorsal skin reactions of hairless dogs to topical treatment with corticosteroids. Toxicol Pathol 1999; 27:528-35.
11. McKenzie AW, Stoughton RB. Method for comparing percutaneous absorption of steroids. Arch Dermatol 1962; 86:608-10.
12. Nordlee JA, Taylor SR, Jones RT, Yunginger JW. Allergenicity of various peanut products as determined by RAST inhibition. J Allergy Clin Immunol 1981; 68:376-382.
13. Schimmer BP, Parker KL. Adrenocorticotropic hormone; adrenocortical steroids and their synthetic analogs; inhibitors of the synthesis and actions of adrenocortical hormones. In Goodman & Gilman's the pharmacological basis of therapeutics. New York: The Mc Graw-Hill Companies; 2001. p. 1649-77.
14. Spearman RIC, Jarrett A. Bio-assay of corticosteroids for topical application. Br J Dermatol 1975; 92:581-4.
15. Stoughton RB. Vasoconstrictor assay-specific applications. In: Maibach HI, Surber C (eds). Topical corticosteroids. Basel: S Karger AG; 1992. p. 42-52.
16. Taylor SL, Busse WW, Sachs MI, Parker JL, Yunginger JW. Peanut oil is not allergenic to peanut-sensitivity individuals. J Allergy Clin Immunol 1981; 68:372-375.
17. Wester RC, Bucks DAW, Maibach HI. In vivo percutaneous absorption of hydrocortisone in psoriatic patients and normal volunteers. J Amer Acad Dermatol 1983; 8:645-7.
18. Yunginger JW, Calobrisi SD. Investigation of the allergenicity of a refined peanut oil-containing topical dermatologic agent in persons who are sensitive to peanuts. Cutis 2001; 68:153-5.
19. Gilman AG, Goodman LS, Rall TW, Murad F (eds). Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan Publishing Company; 1985.
20. Maibach HI, Surber C (eds). Topical corticosteroids. Basel: S Karger AG; 1992.

III: CONSUMER INFORMATION

Pr DermOtic ® Oil Ear Drops
(Fluocinolone Acetonide Otic Solution), 0.01% w/v

This leaflet is part III of a three-part "Product Monograph" published when DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is indicated for moderate to severe Chronic Eczematous External Otitis (inflammatory condition of the external ear) in adults and children 12 years and older. Not to be used on the face.

What it does:
DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v is a topical corticosteroid. When applied to the affected area, corticosteroid, DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v, has anti-inflammatory action and is believed to interfere in the production of important mediators of inflammation, the prostaglandins and leucokotrienes, to help reduce the ear inflammation (swelling), redness, and itching.

When it should not be used:
- **Do not use if hypersensitive (allergic) to any of the ingredients in this formulation. (See What the nonmedicinal ingredients are).**
- **This product contains refined peanut oil.**
- Do not apply in the eye or eye area.
- This medication should not be used if you have a perforated eardrum, or ear tubes, or untreated ear infection (bacterial or fungal or viral infections). Contact your doctor if you are not sure about an ear infection.

What the medicinal ingredient is:
Fluocinolone Acetonide

What the important nonmedicinal ingredients are:
Refined Peanut Oil NF, Mineral Oil Light, Oleth-2, Isopropyl Myristate, Isopropyl Alcohol, Cream Fragrance, and Balsam Pine Fragrance. The peanut oil used in DermOtic® Oil Ear Drops is tested for residual protein through amino acid analysis; the acceptance criterion for total protein is no more than 0.5 parts per million.

What dosage forms it comes in:
Oil, for Otic Use Only. Strength 0.01% w/v
A dropper is supplied with the package.

WARNINGS AND PRECAUTIONS

BEFORE you use DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v, talk to your doctor or pharmacist if:
- Do not use on the eye (or eye area), face, underarm or groin. In case of accidental eye contact, rinse thoroughly with water."
- This medication should not be used for any condition other than that for which it was prescribed.
- If you develop any allergic reaction during product use, such as rash, intense itching (flare), raised skin area (wheal) or any other skin reaction, stop use of the product and contact your doctor.

INTERACTIONS WITH THIS MEDICATION

There are no known drug interactions with DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v. No drug interaction studies have been conducted with this product.

PROPER USE OF THIS MEDICATION

Usual dose:
Chronic Eczematous External Otitis in Adults and Children 12 Years and Older:

Using the supplied ear-dropper, apply 5 drops of DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v into the affected ear. 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 DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v into the ear. Keep head tilted for about a minute to allow DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v to penetrate into the ear canal. Gently pat excess material dripping out of the ear using a clean cotton ball. Follow these instructions twice daily for 7 days in children, and 7 to 14 days in adults. If no improvement is seen within 1 week in your child, contact your child's doctor.
Do not use an ear plug, cotton or any other dressing in the ear while using this medication.

Overdose:
If swallowed, contact your doctor.

Missed Dose:
If a dose of this medication is missed, it is not necessary to make up the missed dose. Skip the missed dose and continue with the next scheduled dose. Do not double dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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: (common) burning, itching, irritation, dryness, (uncommon) hair follicle infection, acne, skin lightening, rash around the mouth, allergic contact dermatitis, (rare) secondary infection, skin thinning, stretch mark, and bumps. If a raised area and flare type reactions (which may be limited to intense itching) or other manifestations of allergic reaction develop, DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v should be discontinued immediately and appropriate therapy instituted. If side effects persist please contact your doctor or pharmacist.

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	
There have been no reported Serious Side Effects during clinical trials or post-marking experience. If a serious side effect does occur, discontinue the drug and call your doctor or pharmacist.			
Allergic Reaction: Flare up of existing condition			v

This is not a complete list of side effects. For any unexpected effects while taking DermOtic ® Oil Ear Drops (Fluocinolone Acetonide Otic Solution), 0.01% w/v, contact your doctor or pharmacist.

HOW TO STORE IT

Keep tightly closed. Store at 25°C (77°F). Keep out of reach of children.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor:
Hill Dermaceuticals, Inc.
At: 1-800-344-5707

This leaflet was prepared by Hill Dermaceuticals, Inc.

Last revised: November 27, 2018