PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrSYNALAR®

Fluocinolone Acetonide
Ointment 0.025% w/w

Topical Corticosteroid

Bausch Health, Canada Inc.
2150 St-Elzear Blvd. West
Laval, Quebec
H7L 4A8

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RECENT MAJOR LABEL CHANGES

Not applicable

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PrSYNALAR®
Fluocinolone Acetonide
Ointment 0.025% w/w

PART I: HEALTH PROFESSIONAL INFORMATION

1. INDICATIONS

SYNALAR (fluocinolone acetonide) possesses anti-inflammatory, anti-pruritic and vasoconstrictive properties.

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

1.1 Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use**.**

2. CONTRAINDICATIONS

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

3. DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

SYNALAR ointments are suitable when an emollient effect is desired.

3.2 Recommended Dose and Dosage Adjustment

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

3.3 Administration

A small amount of SYNALAR ointments 0.025% should be applied gently on the affected skin area, 2 or 3 times daily, as needed.

4. OVERDOSAGE

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

5. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Active ingredients
Ointment 0.025% w/w: Fluocinolone Acetonide.
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Nonmedicinal ingredients
Ointment 0.025% w/w:White Petrolium.

SYNALAR ointment 0.025% is available in 60g collapsible tubes.

6. WARNINGS AND PRECAUTIONS

Avoid contact of the medicinal product with eyes.

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

This product is not for ophthalmic use.

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

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

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

If a symptomatic response is not noted within a few days to a week, the local applications of corticosteroids should be discontinued, and the patient re-evaluated.

During the use of topical corticosteroids secondary infections may occur. Although hypersensitivity reactions have been rare with topically applied steroid products, the drug should be discontinued, and appropriate therapy instituted if there are signs of reaction.
In cases of bacterial infections of the skin, appropriate antibacterial agents should be used as

primary therapy. If it is considered necessary, the topical corticosteroid product may be used as an adjunct to control inflammation, erythema and itching.

Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

Significant systemic absorption may result when steroids are applied over large areas of the body. To minimize the possibility, when long-term therapy is anticipated, interrupt treatment periodically or treat one area of the body at a time.

Laboratory Tests

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

7. ADVERSE REACTIONS

The following adverse skin reactions have been reported with the use of topical steroids: rebound eczema, dermatitis contact, dryness, burning itching, local irritation, striae, skin atrophy, atrophy of subcutaneous tissues, telangiectasia, hypertrichosis change in pigmentation and secondary infection.

Adrenal suppression has also been reported following topical corticosteroid therapy. Posterior subcapsular cataracts have been reported following systemic use of corticosteroids.

8. DRUG INTERACTIONS

Interactions with other drugs, foods, herbal products or with laboratory tests have not been established.

9. CLINICAL PHARMACOLOGY

The vasoconstrictor activity assay has been used to estimate the anti-inflammatory potential of topical corticosteroids in humans. In this assay fluocinolone acetonide showed 100 times the activity of hydrocortisone acetate.

It was shown by Holden & Adams (1959) and by Ruhman & Berliner (1965) that corticosteroids inhibit fibroblast growth and by Dougherty & Berliner that fibroblasts are directly involved in the inflammatory process. In the fibroblast inhibitory effect on fibroblast multiplication in a tissue culture system, fluocinolone acetonide was 440 times more potent than cortisol (hydrocortisone).

Corticosteroids stabilize lysosomal membranes, thus preventing the liberation of digestive and lytic enzymes which are released in response to certain noxious stimuli. It has been suggested that this protective effect of corticoids may be a basis for their therapeutic action.

Orally, as measured by the oesinopenic assay in man, fluocinolone acetonide is equipotent to prednisolone. Administered intravenously, it is more potent than prednisolone on a mg/mg basis.

The effect of oral fluocinolone acetonide in the suppression of the standard croton oil inflammatory insult assay was assessed in human volunteers. In 5 subjects, triamcinolone was consistently more potent than fluocinolone acetonide. In 4 of 6 subjects, fluocinolone acetonide did have an anti-inflammatory effect exceeding that of a control placebo, but in 2 of 6 subjects it was equal to the control. Utilizing stable strontium as a tracer for studying calcium metabolism in man, it was found that fluocinolone acetonide had a negligible effect. In human subjects 20mg of fluocinolone acetonide per os per day 18-24 days produced a negative nitrogen balance and parallel weight loss. At this dose level there was no effect on calcium balance nor on the excretion of 17-hydroxycorticosteroids or 17-ketosteroids.

9.1 Pharmacokinetics

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

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

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

Human systemic absorption studies have been conducted by various researchers. McNall and Melby (data on file) have studied the effect of applying large amounts of fluocinolone acetonide cream 30-60g /day (7.5 to 15mg of active material) to the skin of normal subjects and one patient with severe exfoliative dermatitis. In the normal patients, urine volume, sodium and potassium excretions were also measured in addition to the 17-ketosteroids and 17-hydroxycorticosteroids.

No abnormal values were reported. In a similar study, Myerson (1964) reported that there were no appreciable changes in these parameters which could be attributed to absorption of fluocinolone acetonide.

Absorption studies utilizing fluocinolone acetonide cream 0.2% in quantities of 2 to 3 g per day with occlusion (4 to 6 mg of active material) have failed to show any evidence of corticosteroid effect. Additional studies utilizing fluocinolone acetonide cream 0.2% in quantities of 10 g per day without occlusion have also shown no evidence of corticosteroid effect.

Transient suppression of adrenal activity has been noted after application of corticosteroids to moderately large body areas under occlusive therapy. The adrenal suppression depends on several factors: percentage of body surface treated, concentration of the corticosteroid in the topical preparation, and most important, the integrity of the skin barrier. The adrenals apparently revert to normal function within 48 hours after cessation of therapy.

Administered orally, clinical evaluation of fluocinolone acetonide resulted in a surprisingly variable response in patients with corticosteroid responsive disease. Most investigators found it to be effective and about equipotent to prednisolone but in at least one group of patients with rheumatic disease previously shown to be corticoid responsive there was negligible benefit in 11 of 18 subjects from administered doses of up to 8 mg per day.

SYNALAR (fluocinolone acetonide) used topically has been shown to be an effective agent in the treatment of inflammatory and pruritic dermatoses. It is significantly more effective than hydrocortisone, and in many instances, was effective when other available topical corticosteroids gave inadequate therapeutic responses.

PHARMACOLOGY

SYNALAR (fluocinolone acetonide) is a chemical modification of prednisolone which possesses greater anti-inflammatory and gluconeogenic properties than the parent compound when compared on an equivalent basis.

Fluocinolone acetonide has been reported to posses 263 times the glucocorticoid activity of cortisol (hydrocortisone) as measured by the thymolitic activity assay in the rat; 446 times assay in the rat; 446 times that of cortisol in the antigranuloma activity assay in the rat; and also in the same animal 138 times that of cortisol in the liver glycogen deposition assay.

In similar test in rats, data indicated that fluocinolone acetonide has 500 times the glucocorticoid activity of cortisol (hydrocortisone) as measured by the thymolitic and antigranuloma activity assays. Fluocinolone acetonide showed minimal effects on sodium and potassium excretion as studied in the adrenalectomized rat.

10. STORAGE AND STABILITY

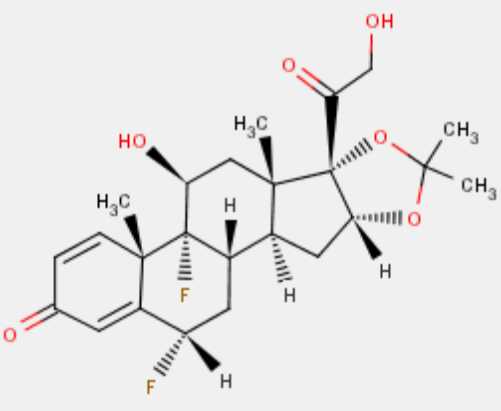
Store at room temperature, 15°C - 30°C.

11. PHARMACEUTICAL INFORMATION

Drug Substance

Chemical name: 6a, 9a-difluoro-16-hydroxyprednisolone-16, 17-acetonide.

Structural formula:



Molecular formula: $C_{24}H_{30}F_2O_6$

Molecular weight: 452.48 g/mol

Physicochemical Properties

Description: Fluocinolone acetonide, the active ingredient in SYNALAR, is a chemical modification of prednisolone and occurs as a white to creamy-white crystalline powder. It is odorless and stable in air.

Melting Point: Melting range between 268°C - 280°C.

12. CLINICAL TRIAL

The efficacy of fluocinolone acetonide, the active ingredient in SYNALAR, is well documented in over 4,000 patients for the indications listed below. Table I summarizes some of the representative accumulated clinical data.

Table I

	No. of publications	No. of patients	Significant Improvement**
contact dermatitis	27	750	713
eczematous dermatitis	21	472	409
seborrheic dermatitis	18	442	426
atopic dermatitis	24	460	426
psoriasis	36	1699	1510
neurodermatitis	18	351	324
TOTAL	**144**	**4174**	**3808**

**Expressed by authors as excellent, very good, good, improved, complete remission of inflammation, etc.

TOXICOLOGY

Acute toxicity studies with fluocinolone acetonide, the active ingredient in SYNALAR, have been done in rats, cats, and dogs. In rats, the LD_{50} intraperitoneal dose ranged from 79 mg/kg to 126 mg/kg. Administered orally, the LD_{50} dose was 1000 mg/kg. Administered orally, the LD_{50} in cats and dogs is greater than 1 g/kg. Subacute toxicity studies with fluocinolone acetonide have been done in monkeys. Six months of oral administration of fluocinolone acetonide to monkeys resulted in no significant deviation from control observations except for weight loss at the high dosages. The dosage was 0.5 mg/kg for 14 weeks with an increase to 2 mg/kg for the remainder of the six months.

Fluocinolone acetonide applied topically in rabbits at a dose of 2 g/kg body weight over a 13-week period produced weight loss and slight decrease in the size of adrenals. Ten human adult males received per os 4 mg of fluocinolone acetonide daily for 90 days. Complete blood counts, urinalysis, liver function tests, serum sodium, potassium, calcium and stool examinations were done during the control period, at 45 and 90 days. No significant alterations of these parameters from control levels were noted.

No significant eye irritation was observed in rabbits during a 15-day period in which 0.1ml of either the vehicle of fluocinolone acetonide ophthalmic solution with antibiotics or the vehicle without antibiotics was instilled twice daily into eyes of rabbits. Daily doses of fluocinolone acetonide ranging from 0.062 to 0.083 mg/kg/day delivered by nasal spray to rabbits for 24 consecutive days produced no significant gross pathology of the respiratory tract.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

SYNALAR
Fluocinolone Acetonide
Ointment 0.025% w/w

Read this carefully before you start taking **SYNALAR** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **SYNALAR**.

What is SYNALAR used for?

- SYNALAR is used to treat acute and chronic skin eruptions.

How does SYNALAR work?

SYNALAR (fluocinolone acetonide) is a topical corticosteroid, which reduces inflammation, itching and possesses blood vessel constriction properties.

What are the ingredients in SYNALAR?

Medicinal ingredients:
Ointment 0.025% w/w: Fluocinolone Acetonide.

Non-medicinal ingredients:
Ointment 0.025% w/w:White Petrolium.

SYNALAR comes in the following dosage forms:

Ointment: 0.025% w/w

Do not use SYNALAR if you have:

- untreated bacterial, tubercular and fungal lesions of the skin
- viral lesions of the skin (including herpes simplex, vaccinia and varicella)
- Have, or have ever had, an unusual or allergic reaction to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SYNALAR. Talk about any health conditions or problems you may have, including if you:

- have stasis dermatitis (inflammation, ulcers, and itchy skin on your lower legs)
- Other skin diseases caused by poor blood circulation.

Other warnings you should know about:

Avoid contact of the medicinal product with eyes.

It has not been determined if SYNALAR is safe for use during pregnancy or lactation. If you are pregnant or breastfeeding, talk to your healthcare profession. Your healthcare professional will determine if SYNALAR is right for you.

Do not apply SYNALAR in your eyes. Apply SYNALAR carefully on lesions close to your eyes. If you get any SYNALAR in your eyes, flush out your eyes with lots of water.

Using SYNALAR for a long time may cause thinning of the skin and tissues. Your healthcare professional will tell you exactly how long to use SYNALAR for.

If you have to use SYNALAR for a long time, your healthcare professional may stop your treatment for a short period. Your healthcare professional may also treat only one area of your body at a time. Your healthcare professional will tell you exactly how to use SYNALAR. Your healthcare professional will also tell you how long you should be using SYNALAR for.

If you do not see any improvements in your skin within in a few days to a week after using SYNALAR, talk to your healthcare professional. Your healthcare professional may stop your treatment with SYNALAR.

During the use of SYNALAR, you may develop other skin infections or an allergic reaction. If this happens, stop using SYNALAR and let your healthcare professional know.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take SYNALAR:

Do not use this medication if it looks cloudy or is leaking.

You should not cover the treated skin area with a bandage or other covering unless your healthcare professional tells you to.

Usual dose:
Apply a small amount of SYNALAR ointments 0.025% gently on the affected skin area. Apply SYNALAR 2 or 3 times daily, as needed.

Overdose:

If you think you, or a person you are caring for, have taken too much SYNALAR, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using SYNALAR?

The following adverse skin reactions have been reported with the use of topical steroids:

- rebound eczema
- contact dermatitis (red, itchy, skin rash)
- dryness
- burning itching
- local irritation
- striae (stretch marks that are red, pink or purple)
- skin atrophy (thinning of the skin)
- atrophy of subcutaneous tissues (thinning of the skin's tissues)
- telangiectasia (spider veins)
- hypertrichosis change in pigmentation (excessive hair growth over the body)
- secondary infection

Serious Side effects and what to do about them			
Symptom / effect	**Talk with your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Common			
Subcapsular cataracts (clouding of the normally clear lens of your eyes): blurred or decrease vision (difficulties in seeing clearly), increasing difficulty with vision at night, sensitivity to light and glare, need for brighter light for reading and other activities, seeing "halos" around lights		✓	
Adrenal suppression (adrenal glands do not produce enough hormones): fatigue, muscle and joint pain, psychiatric symptoms (psychosis, depression, mania, memory impairment, mild to moderate organic brain syndrome), hypoglycemia (low blood sugar), hyponatremia (low levels of sodium), hypotension (low blood pressure), gastrointestinal complaints (nausea vomiting, abdominal pain, diarrhea, constipation)		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

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.

Storage:

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

Do not use this medicine after the date shown on the container.

Keep out of the reach and sight of children.

If you want more information about SYNALAR:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (http://hc-sc.gc.ca/index-eng.php); can be found by contacting the sponsor, Bauschhealth, Canada inc. at 1-800-553-5340.

Last Revised: June 25, 2021