

NEO-SYNALAR- neomycin sulfate and fluocinolone acetonide
Medimetriks Pharmaceuticals

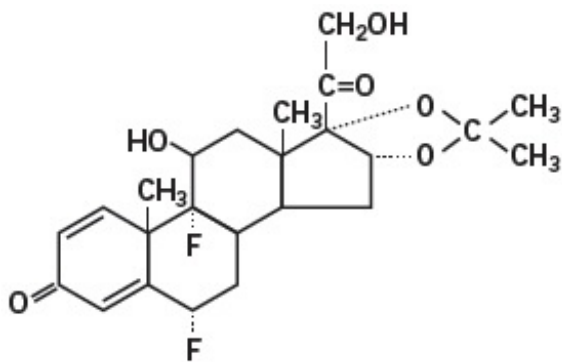
NEO-SYNALAR®

[neomycin sulfate 0.5% (0.35% neomycin base), fluocinolone acetonide 0.025%] Cream

Rx Only

DESCRIPTION

NEO-SYNALAR® cream is intended for topical administration. The active component is the corticosteroid fluocinolone acetonide, which has the chemical name pregna-1,4-diene-3,20-dione,6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis (oxy)]-, (6 α ,11 β ,16 α)-, and the antibacterial neomycin sulfate. Fluocinolone acetonide has the following chemical structure:



The cream contains neomycin sulfate 5 mg/g (3.5 mg/g neomycin base) and fluocinolone acetonide 0.25 mg/g in a water-washable aqueous base of butylated hydroxytoluene, cetyl alcohol, citric acid, edetate disodium, methylparaben and propylparaben (preservatives), mineral oil, polyoxyl 20 cetostearyl ether, propylene glycol, simethicone, stearyl alcohol, water (purified) and white wax.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetics

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

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

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. Corticosteroids 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.

INDICATIONS AND USAGE

NEO-SYNALAR[®] cream is indicated for the treatment of corticosteroid-responsive dermatoses with secondary infection. It has not been demonstrated that this steroid-antibiotic combination provides greater benefit than the steroid component alone after 7 days of treatment (*see WARNINGS section*).

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation. This product should not be used in the external auditory canal if the eardrum is perforated.

WARNINGS

If local infection should continue or become severe, or in the presence of systemic infection, appropriate systemic antibacterial therapy, based on susceptibility testing, should be considered.

Because of the concern of nephrotoxicity and ototoxicity associated with neomycin, this combination product should not be used over a wide area or for extended periods of time.

There are articles in the current medical literature that indicate an increase in the prevalence of persons sensitive to neomycin.

PRECAUTIONS

General

It is recommended that NEO-SYNALAR[®] cream not be used under occlusive dressings. Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (*see PRECAUTIONS—Pediatric Use*).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

As with any topical corticosteroid product, prolonged use may produce atrophy of the skin and subcutaneous tissues. When used on intertriginous or flexor areas, or on the face, this may occur even with short-term use.

Information for the Patient

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions, especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests

The following tests may be helpful in evaluating the HPA axis suppression:

Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy Category C

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities *not* likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

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

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently with topical corticosteroids. These reactions are listed in an approximate decreasing order of occurrence:

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	Miliaria

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

Ototoxicity	Nephrotoxicity
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OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (*see PRECAUTIONS*).

DOSAGE AND ADMINISTRATION

NEO-SYNALAR[®] cream is generally applied to the affected area as a thin film from two to four times daily depending on the severity of the condition.

Since NEO-SYNALAR[®] cream is a water-washable vanishing cream, it is easily applied and leaves no traces.

HOW SUPPLIED

NEO-SYNALAR[®] [neomycin sulfate 0.5% (0.35% neomycin base), fluocinolone acetonide 0.025%]
Cream is supplied in

15 g Tube – NDC 43538-940-15

60 g Tube – NDC 43538-940-60

STORAGE

Store at room temperature 15-25°C (59-77°F); avoid freezing and excessive heat above 40°C (104°F).

To report SUSPECTED ADVERSE REACTIONS, contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured for:

MEDIMETRIKS
PHARMACEUTICALS, INC.

383 Route 46 West, Fairfield, NJ 07004-2402 USA • www.medimetriks.com

Manufactured by: IGI Laboratories, Inc., Buena, NJ 08310

IP026

Iss. 4/14

PRINCIPAL DISPLAY PANEL - Kit Carton

NDC 43538-941-60

For Topical Use Only
Not For Ophthalmic Use

60 g

R_x Only

NEO-SYNALAR[®]

[neomycin sulfate 0.5% (0.35% neomycin base),
fluocinolone acetonide 0.025%] Cream

Cream KIT

KIT CONTAINS:

- 1 - **NEO-SYNALAR[®]**
[neomycin sulfate 0.5% (0.35% neomycin base),
fluocinolone acetonide 0.025%] Cream
60 g Tube
- 1 - Keradan[®] Cream
Net wt. 9 oz. (255 g) Tube

MEDIMETRIKS
PHARMACEUTICALS, INC.

NDC 43538-941-60

For Topical Use Only
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Rx Only



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 **MEDIMETRIKS**
PHARMACEUTICALS, INC.

Medimetrics Pharmaceuticals guarantees that this product was manufactured with the highest pharmaceutical control standards, the most desirable ingredients, under strict demands for quality and safety, ensuring batch-to-batch quality and use-to-use consistency.

For Topical Use Only
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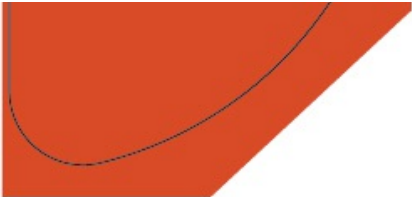
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[neomycin sulfate 0.5% (0.35% neomycin base),
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Cream KIT

NDC 43538-941-60

 **MEDIMETRIKS**
PHARMACEUTICALS, INC.



Directions: Apply daily as needed, especially after using soaps and detergents.
 Caution: For external use only. Avoid contact with eyes, lips and mucous membranes.
 Storage: Store at 15°C-30°C (59°F-86°F). KEEP OUT OF REACH OF CHILDREN.
 No Animal Testing • Made in USA

Keradan[®] CREAM

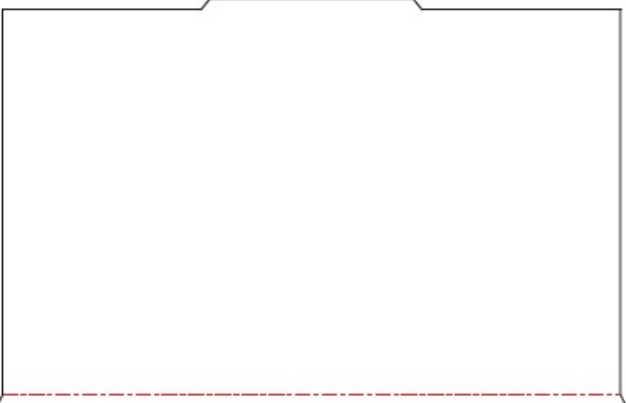


Usual Dose: A small amount should be gently massaged into the affected area two to four times daily, as needed.
 See package insert for full prescribing information.
 Store at room temperature 15-25°C (59-77°F);
 avoid freezing and excessive heat above 40°C (104°F).

NEO-SYNALAR[®]
 [neomycin sulfate 0.5% (0.35% neomycin base),
 fluocinolone acetonide 0.025%] Cream



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NDC 43538-941-60

For Topical Use Only
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60 g



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Cream KIT



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[neomycin sulfate 0.5% (0.35% neomycin base),
fluocinolone acetonide 0.025%] Cream

Manufactured for: Medimetriks Pharmaceuticals, Inc.
383 Route 46 West, Fairfield, NJ 07004-2402 USA
Manufactured by: Teligent Pharma, Inc., Buena, NJ 08310



Manufactured for: Medimetriks Pharmaceuticals, Inc.
383 Route 46 West, Fairfield, NJ 07004-2402 USA

IC170-R1



NO VARNISH AREA

Serialization code, Lot # and
Expiration Date imprint goes here



Cream KIT

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[neomycin sulfate 0.5% (0.35% neomycin base),
fluocinolone acetonide 0.025%] Cream

60g

Rx Only

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[neomycin sulfate 0.5% (0.35% neomycin base),
fluocinolone acetonide 0.025%] Cream
60 g Tube
- 1 - Keradan® Cream
Net wt. 9 oz. (255 g) Tube

NEO-SYNALAR

neomycin sulfate and fluocinolone acetonide kit

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:43538-941
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Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43538-941-60	1 in 1 CARTON; Type 1: Convenience Kit of Co-Package	07/15/2014	

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 TUBE	60 g
Part 2	1 TUBE	255 g

Part 1 of 2

NEO-SYNALAR

neomycin sulfate and fluocinolone acetonide cream

Product Information

Item Code (Source) NDC:43538-940

Route of Administration TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
neomycin sulfate (UNII: 057Y626693) (neomycin - UNII:I16QD7X297)	neomycin	3.5 mg in 1 g
fluocinolone acetonide (UNII: 0CD5FD6S2M) (fluocinolone acetonide - UNII:0CD5FD6S2M)	fluocinolone acetonide	0.25 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
butylated hydroxytoluene (UNII: 1P9D0Z171K)	
cetyl alcohol (UNII: 936JST6JCN)	
citric acid monohydrate (UNII: 2968PHW8QP)	
edetate disodium (UNII: 7FLD91C86K)	
propylparaben (UNII: Z8IX2SC1OH)	
methylparaben (UNII: A218C7HI9T)	
mineral oil (UNII: T5L8T28FGP)	
polyoxyl 20 cetostearyl ether (UNII: YRC528SWUY)	
propylene glycol (UNII: 6DC9Q167V3)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
water (UNII: 059QF0KO0R)	
white wax (UNII: 7G1J5DA97F)	

Product Characteristics

Color	WHITE	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43538-940-60	1 in 1 CARTON		
1		60 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA060700	06/13/1963	

KERADAN

moisturizing cream

Product Information

Route of Administration

TOPICAL

Other Ingredients

Ingredient Kind	Ingredient Name	Quantity
INGR	water (UNII: 059QF0KO0R)	
INGR	cetostearyl alcohol (UNII: 2DMT128M1S)	
INGR	medium-chain triglycerides (UNII: C9H2L21V7U)	
INGR	glycerin (UNII: PDC6A3C0OX)	
INGR	cetyl alcohol (UNII: 936JST6JCN)	
INGR	petrolatum (UNII: 4T6H12BN9U)	
INGR	polyoxyl 20 cetostearyl ether (UNII: YRC528SWUY)	
INGR	caprylyl trisiloxane (UNII: Q95M2P1KJL)	
INGR	cyclomethicone 5 (UNII: 0THT5PCI0R)	
INGR	cyclomethicone 4 (UNII: CZ227117JE)	
INGR	stearic acid (UNII: 4ELV7Z65AP)	
INGR	paraffin (UNII: I9O0E3H2ZE)	
INGR	poly sorbate 20 (UNII: 7T1F30V5YH)	
INGR	phenoxyethanol (UNII: HIE492ZZ3T)	
INGR	xanthan gum (UNII: TTV12P4NEE)	
INGR	cholesterol (UNII: 97C5T2UQ7J)	
INGR	allantoin (UNII: 344S277G0Z)	
INGR	yellow wax (UNII: 2ZA36H0S2V)	
INGR	methylparaben (UNII: A2I8C7HI9T)	
INGR	linoleic acid (UNII: 9KJL21T0QJ)	
INGR	trolamine (UNII: 9O3K93S3TK)	
INGR	edetate disodium (UNII: 7FLD91C86K)	
INGR	squalane (UNII: GW89575KF9)	
INGR	.alpha.-tocopherol acetate (UNII: 9E8X80D2L0)	
INGR	microcrystalline wax (UNII: XOF597Q3KY)	
INGR	olive oil (UNII: 6UYK2W1W1E)	
INGR	aluminum acetate (UNII: 80EHD8I43D)	
INGR	aluminum sulfate (UNII: 34S289N54E)	
INGR	calcium acetate (UNII: Y882YXF34X)	
INGR	sodium lauroyl lactylate (UNII: 7243K85WFO)	
INGR	linolenic acid (UNII: 0RBV727H71)	
INGR	hyaluronate sodium (UNII: YSE9PPT4TH)	
INGR	CERAMIDE NP (UNII: 4370DF050B)	
INGR	CERAMIDE AP (UNII: F1X8L2B00J)	
INGR	tocopherol (UNII: R0ZB2556P8)	
INGR	ceramide 1 (UNII: 5THT33P7X7)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 in 1 CARTON		
1		255 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Cosmetic		06/15/2011	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA060700	07/15/2014	

Labeler - Medimetriks Pharmaceuticals (019903816)**Establishment**

Name	Address	ID/FEI	Business Operations
Teligent Inc		011036910	MANUFACTURE(43538-941)

Revised: 11/2017

Medimetriks Pharmaceuticals