HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VANOS® Cream safely and effectively. See full prescribing information for VANOS® Cream.

VANOS® (fluocinonide) cream, 0.1%
For topical use
Initial U.S. Approval: 1971

----------INDICATIONS AND USAGE----------

VANOS Cream is a corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses in patients 12 years of age or older (1.1).

Limitation of Use:

- Treatment beyond 2 consecutive weeks is not recommended and the total dosage should not exceed 60 g per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis (1.2).
- Avoid use on the face, groin, or axillae.
- Avoid use in perioral dermatitis or rosacea.

----------DOSAGE AND ADMINISTRATION----------

For topical use only. VANOS Cream is not for ophthalmic, oral, or intravaginal use. (2)

Psoriasis: apply a thin layer once or twice daily to the affected skin areas. (2)
Atopic Dermatitis: apply a thin layer once daily to the affected skin areas. (2)
Corticosteroid Responsive Dermatoses, other than psoriasis or atopic dermatitis: apply a thin layer once or twice daily to the affected areas. (2)

----------DOSAGE FORMS AND STRENGTHS----------

Cream, 0.1% (3)

----------CONTRAINDICATIONS----------

None (4)

----------WARNINGS AND PRECAUTIONS----------

- VANOS Cream has been shown to suppress the HPA axis. Systemic absorption of VANOS Cream may produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, hyperglycemia and unmask latent diabetes (5.1)
- Systemic absorption may require evaluation for HPA axis suppression (5.1)
- Modify use should HPA axis suppression develop (5.1)
- Potent corticosteroids, use on large areas, prolonged use or occlusive use may increase systemic absorption (5.3)
- Local adverse reactions with topical steroids may include atrophy, striae, irritation, acneiform eruptions, hypopigmentation and allergic contact dermatitis and may be more likely to occur with occlusive use or more potent corticosteroids (5.3)
- Children may be more susceptible to systemic toxicity when treated with topical corticosteroids. (5.1, 8.4)

----------ADVERSE REACTIONS----------

The most commonly reported adverse reactions (≥1%) were headache, application site burning, nasopharyngitis, and nasal congestion. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Medicis, The Dermatology Company at 1-800-900-6389 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

VANOS (fluocinonide) Cream, 0.1%, is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses in patients 12 years of age or older [*see Use in Specific Populations (8.4)*].

1.2 Limitation of Use

Treatment beyond 2 consecutive weeks is not recommended and the total dosage should not exceed 60 g per week because the safety of VANOS Cream for longer than 2 weeks has not been established and because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Therapy should be discontinued when control of the disease is achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary. Do not use more than half of the 120 g tube per week.

VANOS Cream should not be used in the treatment of rosacea or perioral dermatitis, and should not be used on the face, groin, or axillae.

2 DOSAGE AND ADMINISTRATION

For topical use only. VANOS Cream is not for ophthalmic, oral, or intravaginal use.

For psoriasis, apply a thin layer of VANOS Cream once or twice daily to the affected skin areas as directed by a physician. Twice daily application for the treatment of psoriasis has been shown to be more effective in achieving treatment success during 2 weeks of treatment.

For atopic dermatitis, apply a thin layer of VANOS Cream once daily to the affected skin areas as directed by a physician. Once daily application for the treatment of atopic dermatitis has been shown to be as effective as twice daily treatment in achieving treatment success during 2 weeks of treatment [*see Clinical Studies (14)*].

For corticosteroid responsive dermatoses, other than psoriasis or atopic dermatitis, apply a thin layer of VANOS Cream once or twice daily to the affected areas as directed by a physician.

3 DOSAGE FORMS AND STRENGTHS

Cream, 0.l%.

Each gram of VANOS Cream contains 1 mg of fluocinonide in a white to off-white cream base.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Effect on Endocrine System

Systemic absorption of topical corticosteroids, including Vanos Cream, can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid. In addition, the use of VANOS Cream for longer than 2 weeks may suppress the immune system [*see Nonclinical Toxicology (13.1)*].

HPA axis suppression has been observed with VANOS Cream, 0.1% applied once or twice daily in 2 out of 18 adult patients with plaque-type psoriasis, 1 out of 31 adult patients with atopic dermatitis and 4 out of 123 pediatric patients with atopic dermatitis [*see Use in Specific Population (8.4) and Clinical Pharmacology (12.2)]*.

Because of the potential for systemic absorption, use of topical corticosteroids, including Vanos Cream, may require that patients be periodically evaluated for HPA axis suppression. Factors that predispose a patient using a topical corticosteroid to HPA axis suppression include the use of more potent steroids, use over large surface areas, use over prolonged periods, use under occlusion, use on an altered skin barrier, and use in patients with liver failure.

An 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 gradually withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroids. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids.

Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids.

Use of more than one corticosteroid-containing product at the same time may increase the total systemic absorption of topical corticosteroids.

Studies conducted in pediatric patients demonstrated reversible HPA axis suppression after use of VANOS Cream. Pediatric patients may be more susceptible than adults to systemic toxicity from equivalent doses of VANOS Cream due to their larger skin surface-to-body-mass ratios [*See Use in Specific Populations (8.4)*].

5.2 Local Adverse Reactions with Topical Corticosteroids

Local adverse reactions may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Reactions may include atrophy, striae, telangiectasis, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria. Some local adverse reactions may be irreversible.

5.3 Concomitant Skin Infections

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 VANOS Cream should be discontinued until the infection has been adequately controlled.

5.4 Allergic Contact Dermatitis

If irritation develops, VANOS Cream 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 testing.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

In clinical trials, a total of 443 adult subjects with atopic dermatitis or plaque-type psoriasis were treated once daily or twice daily with VANOS Cream for 2 weeks. The most commonly observed adverse reactions in these clinical trials were as follows:

Table 1: Most Commonly Observed Adverse Reactions (≥1%) in Adult Clinical Trials

Adverse Reaction	VANOS Cream, *once daily* (n=216)	VANOS Cream, *twice daily* (n=227)	Vehicle Cream, *once or twice daily* (n=211)
Headache	8 (3.7%)	9 (4.0%)	6 (2.8%)
Application Site Burning	5 (2.3%)	4 (1.8%)	14 (6.6%)
Nasopharyngitis	2 (0.9%)	3 (1.3%)	3 (1.4%)
Nasal Congestion	3 (1.4%)	1 (0.4%)	0

Safety in patients 12 to 17 years of age was similar to that observed in adults.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of VANOS Cream:

Administration Site Conditions: discoloration, erythema, irritation, pruritis, swelling, pain and condition aggravated.

Immune System Disorders: hypersensitivity.

Nervous System Disorders: headache and dizziness.

Skin and Subcutaneous Tissue Disorders: acne, dry skin, rash, skin exfoliation and skin tightness.

Because these 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Therefore, VANOS Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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.

8.3 Nursing Mothers

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Nevertheless, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and efficacy of VANOS Cream in pediatric patients younger than 12 years of age have not been established; therefore use in pediatric patients younger than 12 years of age is not recommended.

HPA axis suppression was studied in 4 sequential cohorts of pediatric patients with atopic dermatitis covering at least 20% of the body surface area, treated once daily or twice daily with VANOS Cream. The first cohort of 31 patients (mean 36.3% BSA) 12 to < 18 years old; the second cohort included 31 patients (mean 39.0% BSA) 6 to < 12 years old; the third cohort included 30 patients (mean 34.6% BSA) 2 to < 6 years old; the fourth cohort included 31 patients (mean 40.0% BSA) 3 months to < 2 years old. VANOS Cream caused HPA-axis suppression in 1 patient in the twice daily group in Cohort 1, 2 patients in the twice daily group in Cohort 2, and 1 patient in the twice daily group in Cohort 3. Follow-up testing 14 days after treatment discontinuation, available for all 4 suppressed patients, demonstrated a normally responsive HPA axis. Signs of skin atrophy were present at baseline and severity was not determined making it difficult to assess local skin safety. Therefore, the safety of VANOS Cream in patients younger than 12 years of age has not been demonstrated [*see Warnings and Precautions (5.1)*].

HPA axis suppression has not been evaluated in patients with psoriasis who are less than 18 years of age.

Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA-axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

HPA-axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to cosyntropin ($ACTH_{1-24}$) stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

8.5 Geriatric Use

Clinical studies of VANOS Cream did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

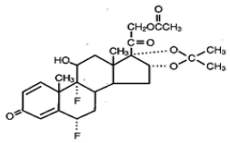
10 OVERDOSAGE

Topically applied VANOS Cream can be absorbed in sufficient amounts to produce systemic effects [*see Warnings and Precautions (5.1)*].

11 DESCRIPTION

VANOS (fluocinonide) Cream, 0.1% contains fluocinonide, a synthetic corticosteroid for topical dermatologic use. The corticosteroids constitute a class of primarily synthetic steroids used topically as anti-inflammatory and antipruritic agents. Fluocinonide has the chemical name 6 alpha, 9 alpha-difluoro-11 beta, 21-dihydroxy-16 alpha, 17 alpha-isopropylidenedioxypregna-1, 4-diene-3,20-dione 21-acetate. Its chemical formula is $C_{26}H_{32}F_2O_7$ and it has a molecular weight of 494.58.

It has the following chemical structure:



Fluocinonide is an almost odorless white to creamy white crystalline powder. It is practically insoluble in water and slightly soluble in ethanol.

Each gram of VANOS Cream contains 1 mg micronized fluocinonide in a cream base of propylene glycol USP, dimethyl isosorbide, glyceryl stearate (and) PEG-100 stearate, glyceryl monostearate NF, purified water USP, carbopol 980 NF, diisopropanolamine, and anhydrous citric acid USP.

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 of VANOS Cream in corticosteroid responsive dermatoses is unknown.

12.2 Pharmacodynamics

Vasoconstrictor studies performed with VANOS Cream in healthy subjects indicate that it is in the super-high range of potency as compared with other topical corticosteroids; however, similar blanching scores do not necessarily imply therapeutic equivalence.

Application of VANOS Cream twice daily for 14 days in 18 adult subjects with plaque-type psoriasis (10–50% BSA, mean 19.6% BSA) and 31 adult subjects (17 treated once daily; 14 treated twice daily) with atopic dermatitis (2-10% BSA, mean 5% BSA) showed demonstrable HPA-axis suppression in 2 subjects with psoriasis (with 12% and 25% BSA) and 1 subject with atopic dermatitis (treated once daily, 4% BSA) where the criterion for HPA-axis suppression is a serum cortisol level of less than or equal to 18 micrograms per deciliter 30 minutes after stimulation with cosyntropin ($ACTH_{1-24}$) [*see Warnings and Precautions (5.1)*].

HPA-axis suppression following application of VANOS Cream, 0.1% (once or twice daily) was also evaluated in 123 pediatric patients from 3 months to < 18 years of age with atopic dermatitis (mean BSA range 34.6 % - 40.0 %). HPA-axis suppression was observed in 4 patients in the twice daily groups. Follow-up testing 14 days after treatment discontinuation demonstrated a normally responsive HPA axis in all 4 suppressed patients [see *Warnings and Precautions (5.1) and Use in Specific populations (8.4)*].

12.3 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 may increase percutaneous absorption.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of VANOS Cream because of severe

immunosuppression induced in a 13-week dermal rat study. The effects of fluocinonide on fertility have not been evaluated.

Fluocinonide revealed no evidence of mutagenic or clastogenic potential based on the results of two *in vitro* genotoxicity tests (Ames test and chromosomal aberration assay using human lymphocytes). However, fluocinonide was positive for clastogenic potential when tested in the *in vivo* mouse micronucleus assay.

Topical (dermal) application of 0.0003%-0.03% fluocinonide cream to rats once daily for 13 weeks resulted in a toxicity profile generally associated with long term exposure to corticosteroids including decreased skin thickness, adrenal atrophy, and severe immunosuppression. A NOAEL could not be determined in this study. In addition, topical (dermal) application of 0.1% fluocinonide cream plus UVR exposure to hairless mice for 13 weeks and 150-900 mg/kg/day of 0.1% fluocinonide cream to minipigs (a model which more closely approximates human skin) for 13 weeks produced glucocorticoid-related suppression of the HPA axis, with some signs of immunosuppression noted in the dermal minipig study. Although the clinical relevance of the findings in animals to humans is not clear, sustained glucocorticoid-related immune suppression may increase the risk of infection and possibly the risk for carcinogenesis.

14 CLINICAL STUDIES

Two adequate and well-controlled efficacy and safety studies of VANOS Cream have been completed, one in adult subjects with plaque-type psoriasis (Table 2), and one in adult subjects with atopic dermatitis (Table 3). In each of these studies, subjects with between 2% and 10% body surface area involvement at baseline treated all affected areas either once daily or twice daily with VANOS Cream for 14 consecutive days. The primary measure of efficacy was the proportion of subjects whose condition was cleared or almost cleared at the end of treatment. The results of these studies are presented in the tables below as percent and number of patients achieving treatment success at Week 2.

Table 2: Plaque-type Psoriasis in Adults

	VANOS Cream, *once daily* (n=107)	Vehicle, *once daily* (n=54)	VANOS Cream, *twice daily* (n=107)	Vehicle, *twice daily* (n=55)
Subjects cleared	0 (0)	0 (0)	6 (6%)	0 (0)
Subjects achieving treatment success*	19 (18%)	4 (7%)	33 (31%)	3 (5%)

*Cleared or almost cleared

Table 3: Atopic Dermatitis in Adults

	VANOS Cream, *once daily* (n=109)	Vehicle, *once daily* (n=50)	VANOS Cream, *twice daily* (n=102)	Vehicle, *twice daily* (n=52)
Subjects cleared	11 (10%)	0 (0)	17 (17%)	0 (0)
Subjects achieving treatment success*	64 (59%)	6 (12%)	58 (57%)	10 (19%)

*Cleared or almost cleared

No efficacy studies have been conducted to compare VANOS (fluocinonide) Cream, 0.1% with any other topical corticosteroid product, including fluocinonide cream 0.05%.

16 HOW SUPPLIED/STORAGE AND HANDLING

VANOS Cream is white to off-white in color and is supplied in tubes as follows:

30 g (NDC 99207-525-30)
60 g (NDC 99207-525-60)
120 g (NDC 99207-525-10)

Store at controlled room temperature: 15° to 30°C (59° to 86°F).

17 PATIENT COUNSELING INFORMATION

Patients using VANOS Cream should receive the following information and instructions. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or unintended effects:

- VANOS Cream is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes. It should not be used on the face, groin, and underarms.
- VANOS Cream should not be used for any disorder other than that for which it was prescribed.
- The treated skin area should not be bandaged or otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
- Patients should report to their physician any signs of local adverse reactions.
- Other corticosteroid-containing products should not be used with VANOS Cream without first talking to the physician.
- As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen in 2 weeks, the patient should be instructed to contact a physician. The safety of the use of VANOS Cream for longer than 2 weeks has not been established.
- Patients should be informed to not use more than 60 g per week of VANOS Cream. Do not use more than half of the 120 g tube per week.
- Patients should inform their physicians that they are using VANOS Cream if surgery is contemplated.
- Patients should wash their hands after applying medication.

Manufactured for:
Medicis, The Dermatology Company
Scottsdale, AZ 85256

Manufactured by:
Contract Pharmaceuticals Ltd.
Mississauga, Ontario
Canada L5N 6L6

Made in Canada

U.S. Patents 6,765,001; 7,217,422; 7,220,424 and Patents Pending