because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. (1)
Avoid use on the face, groin, or anal area. (1.2)
Avoid concomitant use of VaniGard® and other corticosteroids. Reactions may include atrophy, striae, acneiform eruptions, hypertrichosis, and development of acne inversa. Children are more susceptible to these reactions than adults. (1.2)
DOSE AND ADMINISTRATION
For topical use only. VANOS Cream is not for oral, nasal, or intranasal use. (2)
For atopic dermatitis: apply a thin layer once daily to the affected skin areas. (2)
Corticosteroid Responsive Dermatoses, other than atopic dermatitis: apply a thin layer once or twice daily to the affected skin areas. (2)
DOSE FORMS AND STRENGTHS
Cream, 0.1% (3)
VANOS® (fluocinonide) Cream, 0.1%
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1.1 Indications
1.2 Limitation of Use
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINdications
5 WARNINGS AND PRECAUTIONs
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5.2 Local Adverse Reactions with Topical Corticosteroids
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16 PATIENT COUNSELING INFORMATION

FULL PRESCRIBING INFORMATION
1 INDICATIONS AND USAGE
1.1 Indications
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. (1)
1.2 Limitation of Use
Topical use only. Treatment for 2 consecutive weeks is not recommended, and the total dosage should not exceed 60 g per week because the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. (1)
Avoid use on the face, groin, or anal area. (1.2)
Avoid concomitant use of VaniGard® and other corticosteroids. Reactions may include atrophy, striae, acneiform eruptions, hypertrichosis, and development of acne inversa. Children are more susceptible to these reactions than adults. (1.2)
DOSE AND ADMINISTRATION
For topical use only. VANOS Cream is not for oral, nasal, or intranasal use. (2)
For atopic dermatitis: apply a thin layer once daily to the affected skin areas. (2)
Corticosteroid Responsive Dermatoses, other than atopic dermatitis: apply a thin layer once or twice daily to the affected skin areas. (2)

VANOS® (fluocinonide) Cream, 0.1%

CONTRAINdications
None (4)

WARNINGS AND PRECAUTIONs
• VANOS Cream has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Systemic absorption of topical corticosteroids may produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing’s syndrome, hyperglycemia, and glucocorticoid unmasking of Cushing’s syndrome. (5.1)
• Systemic absorption may require evaluation for HPA-axis suppression. (5.1)
• Modify use if HPA-axis suppression develops. (5.1)
• Potent corticosteroids, use on large areas, prolonged use or use in conjunction with other corticosteroids may produce systemic effects (5.3)
• Children may be more susceptible to systemic toxicity when treated with topical corticosteroids. (5.6)

ADVERSE REACTIONS
The most commonly reported adverse reactions (1.1%) were headache, application site burning, nasopharyngitis, and nasal congestion. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Vances Pharmaceuticals North America LLC at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 05/2017

USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use

2 DOSAGE AND ADMINISTRATION
For topical use only. VANOS Cream is not for oral, nasal, or intranasal use. (2)
For atopic dermatitis: apply a thin layer once daily to the affected skin areas. (2)
Corticosteroid Responsive Dermatoses, other than atopic dermatitis: apply a thin layer once or twice daily to the affected skin areas. (2)

3 CONTRAINdications
None (4)

4 WARNINGS AND PRECAUTIONs
• VANOS Cream has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Systemic absorption of topical corticosteroids may produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing’s syndrome, hyperglycemia, and glucocorticoid unmasking of Cushing’s syndrome. (5.1)
• Systemic absorption may require evaluation for HPA-axis suppression. (5.1)
• Modify use if HPA-axis suppression develops. (5.1)
• Potent corticosteroids, use on large areas, prolonged use or use in conjunction with other corticosteroids may produce systemic effects (5.3)
• Children may be more susceptible to systemic toxicity when treated with topical corticosteroids. (5.6)

5 WARNINGS AND PRECAUTIONs
5.1 Effect on Endocrine System
Systemic absorption of topical corticosteroids may produce a suppression of the HPA-axis. Topical corticosteroids, like glucocorticoids and other corticosteroids, may produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression which may affect the rates observed in placebo controlled studies. (5.1)
As many as 15% of patients receiving topical corticosteroids may show HPA-axis suppression (40-50% for hydrocortisone) (5.1)
HPA-axis suppression has not been evaluated with VANOS Cream. 0.1% cream once or twice daily in 2 out of 3 adult patients with atopic dermatitis, and 4 out of 12 pediatric patients with atopic dermatitis (see Use in Specific Populations (8.4) and Clinical Pharmacology (12.2)).
Because of the potential for the systemic absorption of corticosteroids, the systemic absorption of VANOS Cream may require that patients be periodically evaluated for HPA-axis suppression. Factors that prompt a patient using a topical corticosteroid to HPA-axis suppression include the use of more potent steroids, use over large body areas during periods, use under occlusion, use on an altered skin barrier, and use in patients with liver failure. (5.1)
An adrenocorticotropic hormone (ACTH) stimulation test may be helpful in evaluating patients for HPA-axis suppression. It is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. (5.1)

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
The following adverse reactions have been identified during the use of VANOS Cream: Headache, Application Site Burning, Nasopharyngitis, and Nasal congestion. (6)

6.2 Postmarketing Experience
The following adverse reactions have been identified during the use of VANOS Cream: Headache, Application Site Burning, Nasopharyngitis, Nasal congestion, and Nasal irritation. (6)

7 CLINICAL STUDIES
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) and Clinical Pharmacology (12.2)).

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. (8.1)
Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dose levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. (8.1)

8.2 Lactation
Nursing Mothers

8.4 Pediatric Use
Systemically administered corticosteroids appear in human milk and could suppress, interfere with adequate milk production, or to discontinue the drug, taking into account the importance of the drug to the mother. (8.4)
Pediatric use is not recommended. 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 four sequential cohorts of corticosteroid naive dermatitis covering at least 20% of the body surface area (BSA), treated once daily or twice daily with VANOS Cream. The first cohort of 31 patients (mean 50.6% ± 12.9 years old; the second cohort included 31 patients (mean 50.2% ± 12.3 years old; the third cohort included 30 patients (mean 48.3% ± 12.1 years old); the fourth cohort included 31 patients (mean 40.0% ± 8.3 years old) for at least 2 years of equivalent HPA-axis suppression. Hypothyroidism, hyperglycemia, and unmasking of latent diabetes. (5.1)
renal function impairment have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to short synacthen stimulation. Manifestations of intracranial hypertension include headaches, blurred vision, and papilledema. (8.1)

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 systemic amounts to produce systemic effects (see Warnings and Precautions (5.1)).

11 DESCRIPTION
VANOS (fluocinonide) Cream, 0.1% contains fluorocorticosteroids of the corticosteroid topical for dermatologic use. The corticosteroids constitute a class of primary synthetic steroids used topically as anti-inflammatory and antipruritic agents. (11.1)
Fluocinonide is almost odorless while white to creamy while crystalline and 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 anhydrous citric acid USP, carbopol 980 NF, disopropylamine, dimethyldialkylamine, isoboride, glycerin monostearate NF, glycerin stearate (and) PEG-100 stearate, propylene glycol USP, and purified water USP.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Corticosteroids in general exert multiple actions on 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 activity observed with VANOS Cream in healthy subjects indicate that it is in the super-high corticosteroid responsive range.

Application of VANOS Cream twice daily for 14 days in 18 adult subjects resulted in clearance completed, one in adult subjects with plaque-type psoriasis (10–50% BSA, mean 19.6% BSA) and 21 adult subjects (treated once daily, 14 treated twice daily) with atopic dermatitis (10%–100% BSA, mean 53.5% BSA) showed demonstrable HPA-axis suppression in 2 subjects with plaque (with 12% and 25% BSA) and 1 subject with atopic dermatitis (treated once daily, 4% BSA) where HPA-axis suppression is a serum cortisol level of less than or equal to 10 mcg/dl. Treatment with topically applied fluocinonide was not associated with an adverse effect in this study. The results of this study suggest that topical treatment with VANOS Cream would not enhance photosensitization.

12 CLINICAL STUDIES
Two adequate and well-controlled efficacy and safety studies have been conducted. VANOS Cream has been compared, 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 once daily or twice daily with VANOS Cream for 14 consecutive days. The primary efficacy measure was the proportion of subjects whose condition was cleared or almost cleared at the end of the treatment. The results of these studies are presented in percent and number of patients achieving treatment success at Week 2.

Table 2: Plaque-type Psoriasis in Adults

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vehicle, once daily</th>
<th>Vehicle, twice daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects cleared</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Subjects achieving treatment success</td>
<td>19 (88%)</td>
<td>33 (51%)</td>
</tr>
</tbody>
</table>

*Table 2: Plaque-type Psoriasis in Adults

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vehicle, once daily</th>
<th>Vehicle, twice daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects cleared</td>
<td>11 (100%)</td>
<td>17 (100%)</td>
</tr>
<tr>
<td>Subjects achieving treatment success</td>
<td>64 (49%)</td>
<td>58 (157%)</td>
</tr>
</tbody>
</table>

*Table 3: Atopic Dermitis in Adults

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 the severe local irritancy associated with topical steroids 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 0.003%–0.03% fluocinonide cream to rats once daily for 2 years resulted in a toxicity profile generally associated with long-term exposure to corticosteroids including increased 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 ultraviolet radiation (UVR) exposure to hairless mice for 13 weeks and 150–300 mg/kg/day of 0.1% fluocinonide cream to minipigs (a model which more closely approaches the human skin) resulted in a significant reduction in body weight, produced glucocorticoid-related supression of the HPA axis, and some signs of immunosuppression noted in the dermal minipig study. Although the clinical relevance of the findings in animals to humans remains unclear, sustained glucocorticoid-related immune suppression may increase the risk of infection and may contribute to the risk for malignancy.

Topical doses of 0% (fluocinonide cream vehicle), 0.003%, 0.005%, and 0.01% fluocinonide cream were evaluated in a 52-week dermal photosensitogenicity study (40 weeks of treatment followed by 12 weeks of observation) conducted in hairless mice with concurrent exposure to low level ultraviolet radiation. Topical treatment with moderate-to-high concentrations of fluocinonide cream did not have an adverse effect in this study. The results of this study suggest that topical treatment with VANOS Cream would not enhance photosensitization.

13.2 Mechanism of Action
VANOS Cream contains micronized fluocinonide in a cream base of anhydrous citric acid USP, carbopol 980 NF, disopropylamine, dimethyldialkylamine, isoboride, glycerin monostearate NF, glycerin stearate (and) PEG-100 stearate, propylene glycol USP, and purified water USP.

The mechanism of action of VANOS Cream is burning of the skin treated with VANOS Cream. Tell your doctor about any side effect that bothers you or that does not go away. These are not all the side effects with VANOS Cream. Ask your doctor or pharmacist for more information. Keep VANOS Cream and all other medicines out of reach of children.

14.1 Mechanism of Action
Corticosteroids in general exert multiple actions on cellular signaling, immune function, inflammation, and protein regulation; however, the precise mechanism of action of VANOS Cream in corticosteroid responsive dermatoses is unknown.

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Vasoconstrictor activity observed with VANOS Cream in healthy subjects indicate that it is in the super-high corticosteroid responsive range.

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14.3 Pharmacokinetics
The extent of percutaneous absorption of topical corticosteroids is influenced by many factors including the vehicle and the integrity of the epidermal barrier. Topical corticosteroids may be absorbed from intact normal skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

14 NONCLINICAL TOXICOLOGY
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