## HIGHLIGHTS OF PRESCRIBING INFORMATION

PK-6681-3 111

**These highlights do not include all the information needed to use TOPICORT® Topical Spray safely and effectively. See full prescribing information for TOPICORT® Topical Spray.**

**TOPICORT® (desoximetasone) Topical Spray, 0.25%**
**Initial U.S. Approval: 1977**

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

Topicort® Topical Spray is a corticosteroid indicated for the treatment of plaque psoriasis in patients 18 years of age or older (1).

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

- Apply a thin film to the affected skin areas twice daily. Rub in gently. (2)
- Topicort® Topical Spray should be discontinued when control is achieved. (2)
- Treatment beyond 4 weeks is not recommended. (2)
- Do not use if atrophy is present at the treatment site. (2)
- Do not use with occlusive dressings, unless directed by the physician (2)
- Avoid use on the face, axilla or groin. (2)
- Topicort® Topical Spray is not for oral, ophthalmic, or intravaginal use. (2)

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

Spray, 0.25% w/w (3)

### ----------CONTRAINDICATIONS----------

None (4)

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

- Topicort® Topical Spray can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency during or after treatment. (5.1)
- Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can result from systemic absorption of topical corticosteroids. (5.1)
- Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. (5.1)
- Modify use if HPA axis suppression develops. (5.1)
- High potency corticosteroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure and young age may predispose patients to HPA axis suppression. (5.1)
- Pediatric patients may be more susceptible to systemic toxicity when treated with topical corticosteroids. (5.1, 8.4)
- Topicort® Topical Spray is flammable; keep away from heat or flame. (5.5)

### ----------ADVERSE REACTIONS----------

The most common adverse reactions (≥ 1%) are application site dryness, application site irritation and application site pruritus. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Taro at 1-866-923-4914 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

**Revised: 12/2015**

## FULL PRESCRIBING INFORMATION: CONTENTS*



* Sections or subsections omitted from the Full Prescribing Information are not listed.

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Topicort® Topical Spray is a corticosteroid indicated for the treatment of plaque psoriasis in patients 18 years of age or older.

### 2 DOSAGE AND ADMINISTRATION

Apply Topicort® Topical Spray as a thin film to the affected skin areas twice daily. Rub in gently.
The treated skin area should not be bandaged or otherwise covered or wrapped unless directed by the physician.
Topicort® Topical Spray should be discontinued when control is achieved.
Treatment beyond 4 weeks is not recommended.
Do not use if atrophy is present at the treatment site.
Avoid use on the face, axilla or groin.
Topicort® Topical Spray is for external use only. It is not for oral, ophthalmic, or intravaginal use.

### 3 DOSAGE FORMS AND STRENGTHS

Topical Spray, 0.25%. Each gram of Topicort® Topical Spray contains 2.5 mg of desoximetasone in a clear, colorless liquid.

### 4 CONTRAINDICATIONS

None

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Effect on Endocrine System

Topicort® Topical Spray is a topical corticosteroid that has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid.

In a study including 21 evaluable subjects 18 years of age or older with moderate to severe plaque psoriasis, adrenal suppression was identified in 1 out of 12 subjects having involvement of 10-15% of body surface area (BSA) and 2 out of 9 subjects having involvement of >15% of BSA after treatment with Topicort® Topical Spray twice a day for 28 days. [*see Clinical Pharmacology (12.2)*]

Because of the potential for systemic absorption, use of topical corticosteroids 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 high potency steroids, larger treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure and young age.

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 corticosteroid exposure.

Pediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids. [*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, telangiectasias, 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 Allergic Contact Dermatitis with Topical Corticosteroids

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

#### 5.4 Concomitant Skin Infections

Concomitant skin infections should be treated with an appropriate antimicrobial agent.
If the infection persists, Topicort® Topical Spray should be discontinued until the infection has been adequately treated.

#### 5.5 Flammable Contents

Topicort® Topical Spray is flammable; keep away from heat or flame.

### 6 ADVERSE REACTIONS

#### 6.1 Clinical Trials Experience

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

In randomized, multicenter, prospective vehicle-controlled clinical trials, subjects with moderate to severe plaque psoriasis of the body applied Topicort® Topical Spray or vehicle spray twice daily for 4 weeks. A total of 149 subjects applied Topicort® Topical Spray.

Adverse reactions that occurred in ≥ 1% of subjects treated with Topicort® Topical Spray were application site dryness (2.7%), application site irritation (2.7%) and application site pruritus (2.0%).

Another less common adverse reaction (<1% but >0.1%) was folliculitis.

**Table 1. Number (%) of Subjects with Adverse Reactions Occurring in ≥ 1%**

| | Topicort® Topical Spray, 0.25% *b.i.d.* (N = 149) | Vehicle spray *b.i.d.* (N = 135) |
|---|---|---|
| Number of Subjects with Adverse Reactions | 13 (8.7%) | 18 (13.3%) |
| Application site dryness | 4 (2.7%) | 7 (5.2%) |
| Application site irritation | 4 (2.7%) | 5 (3.7%) |
| Application site pruritus | 3 (2.0%) | 5 (3.7%) |

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Topicort® Topical Spray 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.

Desoximetasone has been shown to be teratogenic and embryotoxic in mice, rats, and rabbits when given by subcutaneous or dermal routes of administration at doses 3 to 30 times the human dose of Topicort® Topical Spray based on a body surface area comparison.

### 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. Because many drugs are excreted in human milk, caution should be exercised when Topicort® Topical Spray is administered to a nursing woman.

If used during lactation, Topicort® Topical Spray should not be applied on the chest to avoid accidental ingestion by the infant.

### 8.4 Pediatric Use

Safety and effectiveness of Topicort® Topical Spray in patients younger than 18 years of age have not been studied; therefore use in pediatric patients is not recommended. 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 at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. [*see Warnings and Precautions (5.1)*]

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 ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema. [*see Warnings and Precautions (5.1)*]

### 8.5 Geriatric Use

Clinical studies of Topicort® Topical Spray did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

## 10 OVERDOSAGE

Topicort® Topical Spray can be absorbed in sufficient amounts to produce systemic effects. [*see Warnings and Precautions (5.1)*]

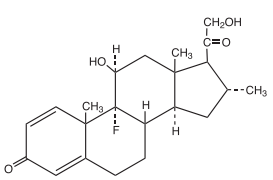
## 11 DESCRIPTION

Topicort® (desoximetasone) Topical Spray, 0.25% contains desoximetasone as the active ingredient.

Desoximetasone is a corticosteroid with the chemical name of pregna-1, 4-diene-3, 20-dione, 9-fluoro-11, 21-dihydroxy-16-methyl-, (11ß,16α)-.

Desoximetasone has the molecular formula of $C_{22}H_{29}FO_4$ and a molecular weight of 376.47. The CAS Registry Number is 382-67-2.

The structural formula is:




Each gram of Topicort® Topical Spray contains 2.5 mg of desoximetasone in a clear, colorless liquid with the following inactive ingredients: glyceryl oleate, isopropyl alcohol (23.4%), isopropyl myristate, L-menthol, and mineral oil. Topicort® Topical Spray is co-packaged with a manual spray pump for installation by the pharmacist prior to dispensing to patients.

## 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 in psoriasis is unknown.

### 12.2 Pharmacodynamics

Vasoconstrictor studies performed with Topicort® Topical Spray in healthy subjects indicate that it is in the high to super-high range of potency as compared with other topical corticosteroids.

The potential for hypothalamic-pituitary-adrenal (HPA) axis suppression was evaluated in a study of 24 adult subjects with moderate to severe plaque psoriasis. Topicort® Topical Spray was applied twice a day for 28 days. Twenty-one subjects had evaluable serum cortisol levels. The proportion of subjects demonstrating HPA axis suppression was 8.3% (1 out of 12) in subjects having psoriasis involvement of 10-15% of body surface area (BSA), and 22.2% (2 out of 9) in subjects having psoriasis involvement of > 15% of their BSA. In this study HPA axis suppression was defined as serum cortisol level ≤18 mcg/dL 30-min post cosyntropin stimulation. In the 2 subjects with available follow-up values, suppression reversed 28 days after the end of treatment.

### 12.3 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.

Plasma concentrations of desoximetasone were measured at two single random time points in the HPA axis suppression trial in 24 subjects with psoriasis [*see Clinical Pharmacology (12.2)*]. The mean (% Coefficient of Variation) concentration of desoximetasone was 449 pg/mL (86%) at Day 14 and 678 pg/mL (135%) at Day 28. The concentration time profile following application of Topicort® Topical Spray is not known.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of Topicort® Topical Spray.

In a 13-week repeat-dose toxicity study in rats, topical administration of desoximetasone spray at concentrations of 0.001, 0.005 and 0.02% BID (which corresponds to dose levels of 0.01, 0.05, or 0.2 mg/kg/dose BID, respectively) resulted in a toxicity profile consistent with long-term exposure to corticosteroids, including adrenal atrophy and histopathological changes in several organ systems indicative of severe immune suppression. A no observable adverse effect level (NOAEL) could not be determined in this 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.

Desoximetasone revealed no evidence of mutagenic or clastogenic potential based on the results of two *in vitro* genotoxicity tests (Ames assay and Chinese hamster ovary cell chromosome aberration assay) and one *in vivo* genotoxicity test (mouse bone marrow micronucleus assay).

No evidence of impairment of male or female fertility was observed at subcutaneous desoximetasone doses up to 0.1 mg/kg/day (0.6 mg/m$^2$/day) in Sprague-Dawley rats.

## 14 CLINICAL STUDIES

Two multi-center, randomized, double-blind, vehicle-controlled clinical trials were conducted in 239 subjects aged 18 years and older with moderate to severe plaque psoriasis of the body. In both trials, randomized subjects applied Topicort® Topical Spray or vehicle spray to the affected areas twice daily for 4 weeks. Enrolled subjects had a minimum body surface area of involvement of 10%, and a Physician's Global Assessment score (PGA) of 3 (moderate) or 4 (severe).

Efficacy was assessed at Week 4 as the proportion of subjects who were considered a Clinical Success ("clear" (0) or "almost clear" (1) according to the PGA scale). Table 2 presents the efficacy results.

**Table 2. Number of Subjects (%) with Clinical Success (scored as clear or almost clear) at Week 4.**

| Parameter | Trial 1 | | Trial 2 | |
|---|---|---|---|---|
| | Topicort® N=59 | Vehicle N=60 | Topicort® N=60 | Vehicle N=60 |
| Clinical Success | 18 (30.5%) | 3 (5.0%) | 32 (53.3%) | 11 (18.3%) |

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied/Storage

Topicort® (desoximetasone) Topical Spray, 0.25% is a clear colorless liquid supplied in white, opaque bottles with white, opaque screw caps in the following sizes:

- 30 mL (NDC 51672-5281-3)
- 50 mL (NDC 51672-5281-4)
- 100 mL (2-50 mL bottles) (NDC 51672-5281-6)
- 100 mL (NDC 51672-5281-7)

Store at controlled room temperature between 20°C to 25°C (68°F to 77°F), excursions permitted to 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature] Spray is flammable; avoid heat, flame or smoking when using this product.

Each unit is co-packaged with a manual spray pump for installation by the pharmacist.

### 16.2 Instructions for the Pharmacist

1. Remove the spray pump from the wrapper
2. Remove and discard the cap from the bottle
3. Keeping the bottle vertical, insert the spray pump into the bottle and turn clockwise until well-fastened
4. Dispense the bottle with the spray pump inserted
5. Label the bottle with "discard the product 30 days after dispensing"

## 17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use)

Inform patients of the following:

- Use this medication as directed by the physician.
- Topicort® Topical Spray is for external use only. Avoid use on the face, axilla or groin.
- Do not to use this medication for any disorder other than that for which it was prescribed.
- Do not bandage or otherwise cover or wrap the treated skin so as to be occlusive.
- Report any signs of local or systemic adverse reactions to the physician.
- Do not use other corticosteroid-containing products with Topicort® Topical Spray without first consulting with the physician.
- Discontinue therapy when control is achieved. If no improvement is seen within 4 weeks, contact the physician.
- This medication is flammable; avoid heat, flame, or smoking when applying this product.
- Discard this product 30 days after dispensed by pharmacist.

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