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**FULL PRESCRIBING INFORMATION**

SERNIVO™ Spray is indicated for the treatment of mild to moderate plaque psoriasis in patients 18 years of age or older.

**INDICATIONS AND USAGE**

SERNIVO™ Spray is a corticosteroid indicated for the treatment of mild to moderate plaque psoriasis in patients 18 years of age or older.

**DOSAGE AND ADMINISTRATION**

- Apply to the affected skin areas twice daily. Rub in gently.
- Use SERNIVO™ Spray for up to 4 weeks and not beyond.
- Discontinue treatment when control is achieved.
- Do not use on the face, scalp, axilla, groin, or other intertriginous areas.
- Do not use in the eyes, genitalia, mouth, or vagina.
- Do not use if atrophy is present at the treatment site.
- Do not bandage, cover, or wrap the treated skin area unless directed by a physician.
- Avoid use on the face, scalp, axilla, groin, or other intertriginous areas.

**DOSAGE FORMS AND STRENGTHS**

Spray: 0.05% (equivalent to 0.5 mg betamethasone dipropionate)/g

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

5.1 Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression and Other Unwanted Systemic Glucocorticoid Effects

SERNIVO™ Spray can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency during or after treatment. Corticosteroids can decrease the body’s ability to produce cortisol in times of stress. Use of systemic corticosteroids may require periodic evaluation for HPA axis suppression. If suppression occurs, gradually withdraw the drug, reduce the frequency of application, or substitute with a less potent corticosteroid. If signs and symptoms of adrenal insufficiency develop, administer cortisol as appropriate until recovery occurs. Atrophy, telangiectasia, and skin atrophy may be more susceptible to systemic toxicity when treated with topical corticosteroids. Use of topical corticosteroids may require periodic evaluation for HPA axis suppression.

5.2 Allergic Contact Dermatitis

6. ADVERSE REACTIONS

- In clinical studies of SERNIVO™ Spray in patients 18 years of age or older, the most commonly reported adverse reactions (occurring in at least 1% of subjects treated with SERNIVO™ Spray) were:

  - Application site pruritus: 2.3% to 3.9%
  - Application site burning and/or stinging: 4.5% to 10.0%
  - Application site pain: 2.3% to 3.9%
  - Application site atrophy: 1.1% to 1.7%

- Less common adverse reactions (occurring less than 1% but higher than 0.1%) included:

  - Application site redness: 0.6% to 0.9%
  - Application site burning and/or stinging: 4.5% to 10.0%
  - Application site pain: 2.3% to 3.9%
  - Application site atrophy: 1.1% to 1.7%

- Local adverse reactions included:

  - Pruritus: 2.3% to 3.9%
  - Burning and/or stinging: 4.5% to 10.0%
  - Pain: 2.3% to 3.9%
  - Application site atrophy: 1.1% to 1.7%

- Common adverse reactions included:

  - Application site redness: 0.6% to 0.9%
  - Application site burning and/or stinging: 4.5% to 10.0%

6.1 Allergic Contact Dermatitis

- Allergic contact dermatitis with SERNIVO™ Spray has been associated with the use of topical corticosteroids. If irritation develops, discontinue the use of topical corticosteroids and institute appropriate therapy.

6.2 Postmarketing Experiences

- In a study including 48 evaluable subjects 18 years of age or older with moderate to severe plaque psoriasis, abnormal ACTH stimulation test results suggestive of pituitary-adrenal insufficiency were noted in 3% of subjects treated with SERNIVO™ Spray and 18% of subjects applied vehicle spray.

Table 1: Adverse Reactions Occurring in ≥5% of Subjects Treated with SERNIVO™ Spray for up to Four Weeks

<table>
<thead>
<tr>
<th>Reaction</th>
<th>SERNIVO™ Spray A.I.D. (N=352)</th>
<th>Vehicle Spray A.I.D. (N=180)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site pruritus</td>
<td>6.0%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Application site burning</td>
<td>4.5%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Application site pain</td>
<td>2.3%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Application site atrophy</td>
<td>1.1%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

6.3 Pediatric Use

- A..4 Pediatric Use

- Pediatric patients may be more susceptible to systemic toxicity due to their larger skin surface to body mass ratio. Use of SERNIVO™ Spray is not recommended in pediatric patients.

6.4 Pediatric Use

- Safety and effectiveness of SERNIVO™ Spray in patients younger than 18 years of age have not been studied; therefore use in pediatric patients is not recommended.

6.5 Postmarketing Reports

- Postmarketing reports for SERNIVO™ Spray have not been associated with any unexpected adverse reactions.

6.6 Pregnancy

- Pregnancy Category: C

7. CLINICAL PHARMACOLOGY

- SERNIVO™ Spray contains betamethasone dipropionate, a high-potency corticosteroid, which has anti-inflammatory and immunosuppressive activity.

7.1 Pharmacokinetics

- SERNIVO™ Spray is absorbed through the skin and may suppress the HPA axis.

7.2 Pharmacodynamics

- SERNIVO™ Spray is absorbed through the skin and may suppress the HPA axis.

7.3 Nonclinical Toxicology

- SERNIVO™ Spray is absorbed through the skin and may suppress the HPA axis.

7.4 Carcinogenesis, Mutagenesis, Impairment of Fertility

- SERNIVO™ Spray is absorbed through the skin and may suppress the HPA axis.

7.5 Clinical Studies

- SERNIVO™ Spray is absorbed through the skin and may suppress the HPA axis.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

- Use of SERNIVO™ Spray in pregnant women has not been studied; therefore use in pregnant women is not recommended.

8.2 Lactation

- Use of SERNIVO™ Spray is not recommended in nursing mothers.

8.3 Pediatric Use

- Use of SERNIVO™ Spray is not recommended in pediatric patients.

8.4 Geriatric Use

- Use of SERNIVO™ Spray is not recommended in older adults.

8.5 Allergic Contact Dermatitis

- Use of SERNIVO™ Spray is not recommended in patients with a history of allergic contact dermatitis.

8.6 Hypersensitivity

- Use of SERNIVO™ Spray is not recommended in patients with a history of hypersensitivity.

8.7 Local Adverse Reactions

- Use of SERNIVO™ Spray is not recommended in patients with a history of local adverse reactions.

8.8 Other Conditions

- Use of SERNIVO™ Spray is not recommended in patients with a history of other conditions.

9. PATIENT COUNSELING INFORMATION

- Inform patients of the possible side effects of SERNIVO™ Spray and instruct them to report any adverse reactions to their healthcare provider.

10. DOSAGE FORMS AND STRENGTHS

Spray: 0.05% (equivalent to 0.5 mg betamethasone dipropionate)/g

**PATIENT INFORMATION**

SERNIVO™ Spray is for use on the skin only. Do not get SERNIVO Spray near or in your eyes, mouth, or vagina.

What is SERNIVO Spray?

- SERNIVO™ Spray is a prescription corticosteroid medicine used to treat mild to moderate plaque psoriasis in people 18 years of age and older.

- It is not known if SERNIVO™ Spray is safe and effective in children under 18 years of age.

Before you use SERNIVO Spray, tell your doctor about all of your medical conditions, including if you:

- are allergic to any of the ingredients in SERNIVO™ Spray.
- have thining of the skin (atrophy) at the treatment site.
- are pregnant or plan to become pregnant. It is not known if SERNIVO™ Spray will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if SERNIVO™ Spray passes into breast milk.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal products. Especially tell your doctor if you take other corticosteroid medicines by mouth or use other products on your skin that contain corticosteroids.

How should I use SERNIVO Spray?

- See the “Instructions for Use” for detailed information about the way to apply SERNIVO™ Spray.
- Use SERNIVO™ Spray exactly as your doctor tells you to use it.
- Your doctor should tell you how much SERNIVO™ Spray to use and where to apply it.
- Apply SERNIVO™ Spray 2 times a day.
- Use SERNIVO™ Spray for the shortest amount of time needed to treat your plaque psoriasis. Tell your doctor if your skin condition is not getting better after 4 weeks of using SERNIVO™ Spray. Do not use SERNIVO™ Spray for longer than 4 weeks.
- Wash your hands after applying SERNIVO™ Spray.
- Do not use SERNIVO™ Spray on your face, scalp, underarms (armpits), groin, or areas where your skin may touch or rub together.
- Do not bandage, cover, or wrap the treated skin area, unless your doctor tells you to.

What are the possible side effects of SERNIVO™ Spray?

- SERNIVO™ Spray can pass through your skin. Too much SERNIVO™ Spray passing through your skin can cause your adrenal glands to stop working. Your doctor may do blood tests to check for adrenal gland problems.

- The most common side effects of SERNIVO™ Spray include itching, burning, stinging, pain, and thinning of skin (atrophy) at the treated site.

- These are not all the possible side effects of SERNIVO™ Spray.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store SERNIVO Spray?

- Store SERNIVO™ Spray at room temperature between 68°F to 77°F (20°C to 25°C).
- Throw away (discard) any unused SERNIVO™ Spray after 4 weeks.

Keep SERNIVO™ Spray and all medicines out of the reach of children.

General information about the safe and effective use of SERNIVO™ Spray.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SERNIVO™ Spray for a condition for which it was not prescribed. Do not give SERNIVO™ Spray to other people even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or doctor for information about SERNIVO™ Spray that is written for health professionals.
What are the ingredients in SERNIVO Spray?

Active ingredient: betamethasone dipropionate

Inactive ingredients: butylated hydroxytoluene, cetostearyl alcohol, hydroxyethyl cellulose, methylparaben, mineral oil, oleyl alcohol, polyoxyl 20 cetostearyl ether, propylparaben, purified water, and sorbitan monostearate.

Manufactured by: DPT Laboratories, Ltd., San Antonio, TX 78215
Distributed by: Promius Pharma, LLC., Princeton, NJ 08540

Issued: 02/2016

11 DESCRIPTION

SERNIVO Spray contains 0.045%, betamethasone dipropionate (equivalent to 0.05% betamethasone), a synthetic, fluorinated corticosteroid.

The chemical name for betamethasone dipropionate is 9-fluoro-11(β), 17, 21-trihydroxy-16(β)-methylpregna-1,4-diene-3,20-dione-17,21-dipropionate. The empirical formula is C_{28}H_{37}FO_{7} and the molecular weight is 504.6. The structural formula is shown below.

Each gram of SERNIVO Spray contains 0.043 mg of betamethasone dipropionate USP (equivalent to 0.05 mg betamethasone) in a slightly thickened, white to off-white, oil-water, non-sterile emulsion with the following inactive ingredients: butylated hydroxytoluene, cetostearyl alcohol, hydroxyethyl cellulose, methylparaben, mineral oil, oleyl alcohol, polyoxyl 20 cetostearyl ether, propylparaben, purified water, and sorbitan monostearate. SERNIVO 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 of SERNIVO Spray in psoriasis is unknown.

12.2 Pharmacodynamics

Vasoconstrictor studies performed with SERNIVO Spray in healthy subjects indicate that it is in the mid-range of potency as compared with other topical corticosteroids; however, similar blanching scores do not necessarily imply therapeutic equivalence. The potential for HPA axis suppression by SERNIVO Spray was evaluated in a study randomizing 52 adult subjects with moderate to severe plaque psoriasis. SERNIVO Spray was applied twice daily for 15 or 29 days, in subjects with psoriasis involving a mean of 29.0% and 28.5% body surface area at baseline across the 2 treatment duration arms, respectively. Forty-eight (48) subjects were evaluated for HPA axis suppression at the end of treatment. The proportion of subjects with HPA suppression was 20.8% (5 out of 24) in subjects treated with SERNIVO Spray for 15 days. No subjects (0 out of 24) treated with SERNIVO Spray for 29 days had HPA axis suppression. In this study HPA axis suppression was defined as serum cortisol level <16 mcg/dL 10 minutes post-corticotropin stimulation. In the 4 subjects with available follow-up values, all subjects had normal ACTH stimulation tests at follow-up.

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 are absorbed through normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

A plasma concentration following a single adminstration of betamethasone dipropionate (0.05%) in 34 subjects with plaque psoriasis (mean body surface area involvement 49%) at a dose concentrations of 0.05% and 0.1% (providing 0.05% and 0.1% betamethasone) were detected in the majority of subjects (Table 2). The majority of subjects had no measurable plasma cortisol level ≤18 mcg/dL 30-minutes post-cosyntropin stimulation. In the 4 subjects who had measurable cortisol levels, the mean (±SD) percentage suppression of baseline cortisol levels was 31.1 ± 16.3% at 15 minutes post-cosyntropin stimulation.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of betamethasone dipropionate. In a 90-day repeat-dose toxicity study in rats, topical administration of betamethasone dipropionate spray formulation at dose concentrations of 0.05% and 0.1% (providing dose levels of up to 0.5 mg/kg/day in males and 0.25 mg/kg/day in females) resulted in a toxicity profile consistent with long-term exposure to corticosteroids including reduced body weight gain, adrenal atrophy, and histological changes in bone marrow, thymus and spleen 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 of carcinogenesis.

Betamethasone was negative in the bacterial mutagenicity assay (Salmonella typhimurium and Escherichia coli), and in the mammalian cell mutagenicity assay (CHO/HGPRT). It was positive in the in vitro human lymphocyte cytokine stimulation assay, and equivocal in the in vivo mouse bone marrow micronucleus assay.

Studies in rabbits, mice, and rats using intramuscular doses up to 1,33, and 2 mg/kg, respectively, resulted in dose-related increases in fetal resorptions in rabbits and mice.

14 CLINICAL STUDIES

Two multi-center, randomized, double-blind, vehicle-controlled clinical trials were conducted in subjects aged 18 years and older with moderate plaque psoriasis. In both trials, randomized subjects applied SERNIVO Spray or vehicle spray to the affected areas twice daily for 28 days. Emolllent subjects had body surface area of involvement between 15% to 20%, and an Investigator Global Assessment (IGA) score of 3 (moderate). Efficacy was assessed as the proportion of subjects who were considered a treatment success (defined as having an IGA score of 0 or 1 [clear or almost clear] and at least a 2-grade reduction from baseline). Table 3 presents the efficacy results at Day 15 and Day 29.

<table>
<thead>
<tr>
<th>Table 2: Mean (±SD) Maximum Plasma Concentrations (pg/mL) of Betamethasone Dipropionate Metabolites after 15 or 29 Days of Treatment with SERNIVO Spray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analyte (pg/mL)</td>
</tr>
<tr>
<td>Betamethasone-17-propionate</td>
</tr>
<tr>
<td>Betamethasone</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3: Proportion of Subjects with Plaque Psoriasis with Treatment Success after 14 Days and 28 Days of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
</tr>
<tr>
<td>SERNIVO Spray</td>
</tr>
<tr>
<td>Spray</td>
</tr>
<tr>
<td>N=142</td>
</tr>
<tr>
<td>Treatment Success at Day 15</td>
</tr>
<tr>
<td>Treatment Success at Day 29</td>
</tr>
</tbody>
</table>

- Treatment success is defined as an IGA of 0 or 1 (clear or almost clear) and at least a 2-grade reduction from baseline.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied/Storage

SERNIVO Spray is a slightly thickened, white to off-white, non-sterile emulsion supplied in high density polyethylene bottles with a heat induction seal lined polypropylene cap. The drug is supplied in the following volumes:

- 60 mL (NDC 67857-808-17)
- 120 mL (NDC 67857-808-04)

Store at controlled room temperature of 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]. Each unit is co-packaged with a manual spray pump for installation by the pharmacist prior to dispensing.

16.2 Handling/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 upright, insert the spray pump into the bottle and turn clockwise until it is closed tightly.
4. Disperse the bottle with the spray pump inserted.
5. Include the date dispensed in the space provided on the carton.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Inform patients of the following:

- Discontinue therapy when control is achieved, unless directed otherwise by the physician.
- Do not use for longer than 4 consecutive weeks.
- Avoid contact with the eyes.
- Avoid use of SERNIVO Spray on the face, scalp, underarms, groin or other intertriginous areas, unless directed by the physician.
- Do not occlude the treatment area with bandage or other covering, unless directed by the physician.
- Local reactions and skin atrophy are more likely to occur with occlusive use, prolonged use, or use of higher potency corticosteroids.

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

- Store at controlled room temperature of 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].