HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use XHANCE® safely and effectively. See full prescribing information for XHANCE®.

XHANCE® (fluticasone propionate) nasal spray, for intranasal use
Initial U.S. Approval: 1994

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

XHANCE is a corticosteroid indicated for the treatment of nasal polyps in patients 18 years of age or older. (1)

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

- For intranasal use only. XHANCE is delivered into the nose by actuating the pump spray into one nostril while simultaneously blowing into the mouthpiece of the device. (2.2)
- Recommended adult dosage: One spray per nostril twice daily (total daily dose of 372 mcg). Two sprays per nostril twice daily may also be effective in some patients (total daily dose of 744 mcg). (2.1)

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

Nasal spray: 93 mcg of fluticasone propionate in each 106-mg spray. (3)

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

Hypersensitivity to any ingredient in XHANCE. (4)

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

- Local Nasal Effects: epistaxis, erosion, ulceration, septal perforation, *Candida albicans* infection, and impaired wound healing. Monitor patients periodically for signs of adverse effects on the nasal mucosa. Avoid use in patients with recent nasal ulcerations, nasal surgery, or nasal trauma. (5.1)
- Close monitoring for glaucoma and cataracts is warranted. (5.2)
- Hypersensitivity reactions (e.g., anaphylaxis, angioedema, urticaria, contact dermatitis, rash, hypotension, and bronchospasm) have been reported after administration of fluticasone propionate. Discontinue XHANCE if such reactions occur. (5.3)
- Immunosuppression: potential increased susceptibility to or worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients. (5.4)
- Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue XHANCE slowly. (5.5)
- Assess for decrease in bone mineral density initially and periodically thereafter. (5.7)

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

The most common adverse reactions (incidence ≥ 3%) are epistaxis, nasal septal ulceration, nasopharyngitis, nasal mucosal erythema, nasal mucosal ulcerations, nasal congestion, acute sinusitis, nasal septal erythema, headache, and pharyngitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact OptiNose US, Inc. at 1-833-678-6673 and safety@optinose.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

Strong cytochrome P450 3A4 inhibitors (e.g., ritonavir, ketoconazole): Use not recommended. May increase risk of systemic corticosteroid effects. (7.1)

----------USE IN SPECIFIC POPULATIONS----------

- Hepatic impairment: Monitor patients for signs of increased drug exposure. (8.6)

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

Revised: 09/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

XHANCE® nasal spray is indicated for the treatment of nasal polyps in patients 18 years of age or older.

2 DOSAGE AND ADMINISTRATION

2.1 Nasal Polyps

Adults (18 years and older): The recommended dosage of XHANCE nasal spray is 1 spray (93 mcg of fluticasone propionate per spray) in each nostril twice daily (total daily dose, 372 mcg). A dose of 2 sprays (93 mcg of fluticasone propionate per spray) in each nostril twice daily may also be effective in some patients (total daily dose, 744 mcg). The maximum total daily dosage should not exceed 2 sprays in each nostril twice daily (total daily dose, 744 mcg).

Patients should use XHANCE at regular intervals since its effectiveness depends on regular use. Individual patients will experience a variable time to onset and different degrees of symptom relief.

The safety and efficacy of XHANCE when administered in excess of recommended doses have not been established.

2.2 Administration Information

Administer XHANCE by the intranasal route only, avoiding spraying directly on the nasal septum. Shake XHANCE before each use. Before initial use, prime XHANCE by first gently shaking and then pressing the bottle 7 times or until a fine mist appears. Direct the spray into the air, away from the face. When XHANCE has not been used for ≥ 7 days, prime the pump again by shaking and releasing 2 sprays into the air, away from the face.

XHANCE is delivered into the nose by actuating the pump spray into one nostril while simultaneously blowing (exhaling) into the mouthpiece of the device. To administer XHANCE, insert the tapered tip of the cone-shaped nosepiece deep into one nostril and form a tight seal between the nosepiece and the nostril. Next, place the flexible mouthpiece into the mouth, bending it as necessary to maintain a tight seal. Blow into the mouthpiece, and while continuing to blow, push the bottle up to actuate the spray pump. Continuing to blow through the mouth, but not inhaling or exhaling through the nose, at the time of actuation is important to achieve intended drug deposition. Repeat the process in the other nostril for a full dose.

3 DOSAGE FORMS AND STRENGTHS

Nasal spray: Each 106-mg spray delivers 93 mcg of fluticasone propionate. One unit provides 120 metered sprays.

4 CONTRAINDICATIONS

XHANCE is contraindicated in patients with hypersensitivity to any of the ingredients [*see Warnings and Precautions (5.3) and Description (11)*].

5 WARNINGS AND PRECAUTIONS

5.1 Local Nasal Effects

Epistaxis, Nasal Erosions and Ulcerations

In placebo-controlled clinical trials of 16 weeks duration, epistaxis, nasal erosions, and nasal ulcerations were reported more frequently in patients treated with XHANCE than those who received placebo [*see Adverse Reactions (6.1)*].

Nasal Septal Perforation

Nasal septal perforations have been reported in patients following the intranasal application of XHANCE. In placebo-controlled clinical trials of 16 weeks duration, nasal septal perforations were reported in 1 (0.3%) patient treated with XHANCE compared with none treated with placebo. The patient had a prior history of nasal/sinus surgery. Three (0.3%) patients treated with XHANCE in uncontrolled, open-label trials of 3 to 12 months duration developed nasal septal perforations.

As with any long term topical treatment of the nasal cavity, patients using XHANCE over several months or longer should be examined periodically for possible changes in the nasal mucosa. If a septal perforation is noted, discontinue XHANCE. Avoid spraying XHANCE directly on the septum.

Candida Infection

In clinical trials with XHANCE, localized infections with *Candida albicans* have been observed. Eight (0.9%) patients in uncontrolled, open-label trials of 3 to 12 months duration developed *Candida albicans* infections (nasal, pharyngeal, esophageal or intestinal). If such an infection develops, it may require treatment with appropriate local therapy and discontinuation of XHANCE. Patients using XHANCE should be examined periodically for evidence of *Candida* infection in the nasal and oropharyngeal mucosa.

Impaired Wound Healing

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal ulcerations, nasal surgery, or nasal trauma should avoid using XHANCE until healing has occurred.

5.2 Glaucoma and Cataracts

Nasal and inhaled corticosteroids, including fluticasone propionate, may result in the development of glaucoma and/or cataracts. In placebo-controlled clinical trials of 16 weeks duration, cataracts were reported in 4 (1.2%) patients treated with XHANCE, compared with 3 (1.9%) patients treated with placebo. Among these patients, 2 patients treated with XHANCE reported subcapsular cataracts compared with none treated with placebo. Eleven patients (1.2%) in uncontrolled, open-label trials of 3 to 12 months duration developed new or worsening cataracts, of which none were subcapsular. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure (IOP), glaucoma, and/or cataracts.

5.3 Hypersensitivity Reactions Including Anaphylaxis

XHANCE is contraindicated in patients with known hypersensitivity to fluticasone propionate or any of the ingredients of XHANCE. Discontinue XHANCE if such reactions (e.g., anaphylaxis, angioedema, urticaria, contact dermatitis, rash, hypotension, and bronchospasm) occur [*see Contraindications (4) and Adverse Reactions (6.1)*].

5.4 Immunosuppression

Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals and may experience a worsening of existing infections. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible adults using corticosteroids. In such adults who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If a patient is exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

Corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex [*see Adverse Reactions (6.1)*].

5.5 Hypothalamic-Pituitary-Adrenal Axis Effects

Hypercorticism and adrenal suppression may occur when intranasal corticosteroids, such as XHANCE, are used at higher than recommended dosages or in susceptible individuals at recommended dosages. Since fluticasone propionate is absorbed into the circulation and can be systemically active at higher doses, recommended dosages of XHANCE should not be exceeded to avoid hypothalamic-pituitary-adrenal (HPA) dysfunction. A relationship between plasma levels of fluticasone propionate and inhibitory effects on stimulated cortisol production has been shown after 4 weeks of pulmonary treatment with fluticasone propionate inhalation aerosol. Since individual sensitivity to effects on cortisol production exists, physicians should consider this information when prescribing XHANCE.

Patients treated with XHANCE should be observed carefully for any evidence of systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis). If such effects occur, the dosage of XHANCE should be reduced slowly, consistent with accepted procedures for reducing systemic corticosteroids, and other treatments for management of nasal symptoms should be considered. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response.

The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency. In addition, some patients may experience symptoms of corticosteroid withdrawal (e.g., joint and/or muscular pain, lassitude, depression). After withdrawal from systemic corticosteroids, a number of months are required for recovery of HPA function. Patients previously treated for prolonged periods with systemic corticosteroids and transferred to topical corticosteroids should be carefully monitored for acute adrenal insufficiency in response to stress such as trauma, surgery, infection (particularly gastroenteritis), or other conditions associated with severe electrolyte loss. In patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, rapid decreases in systemic corticosteroid dosages may cause a severe exacerbation of their symptoms *[see Adverse Reactions (6.1) and Clinical Pharmacology (12.2)]*.

5.6 Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors

The use of strong cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin, conivaptan, lopinavir, voriconazole) with XHANCE is not recommended because increased systemic corticosteroid adverse effects may occur [*see Drug Interactions (7.1) and Clinical Pharmacology (12.3)*].

5.7 Reduction in Bone Mineral Density

Decreases in bone mineral density (BMD) have been observed with long-term oral inhalation of products containing corticosteroids into the lungs. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids), should be monitored and treated with established standards of care.

A 2-year trial in 160 subjects (females aged 18 to 40 years, males aged 18 to 50 years) with asthma receiving chlorofluorocarbon (CFC)-propelled fluticasone propionate inhalation aerosol 88 or 440 mcg twice daily demonstrated no statistically significant changes in BMD at any time point (24, 52, 76, and 104 weeks of double-blind treatment) as assessed by dual-energy x-ray absorptiometry at lumbar regions L1 through L4.

5.8 Effect on Growth

Intranasal corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. The safety and efficacy of XHANCE has not been established in pediatric patients [*see Use in Specific Populations (8.4)*].

6 ADVERSE REACTIONS

Systemic and local corticosteroid use may result in the following:

- Local nasal effects: epistaxis, erosion, ulceration, septal perforation, *Candida albicans* infection, and impaired wound healing [*see Warnings and Precautions (5.1)*]
- Cataracts and glaucoma [*see Warnings and Precautions (5.2)*]
- Hypersensitivity reactions including anaphylaxis [*see Contraindications (4) and Warnings and Precautions (5.3)*]
- Immunosuppression [*see Warnings and Precautions (5.4)*]
- HPA axis effects, including growth reduction [*see Warnings and Precautions (5.5* and *5.8)*]
- Reduction in bone mineral density [*see Warnings and Precautions (5.7)*]
- Effect on Growth [*see Warnings and Precautions (5.8)*]

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 with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below are based on two placebo-controlled clinical trials evaluating doses of a fluticasone propionate nasal spray with an exhalation delivery system from 93 mcg twice daily to 372 mcg twice daily. Both trials were 16-weeks in duration with an additional 8-week open-label extension. The trials included a total of 643 adult subjects with bilateral nasal polyps and associated moderate or severe nasal congestion of which 161 received 93 mcg twice daily, 160 received 186 mcg twice daily, 161 received 372 mcg twice daily and 161 received placebo. The overall pooled safety data included 296 (46.0%) Female, 347 (54.0%) Male, 584 (90.8%) White, 39 (6.1%) Black, 9 (1.4%) Asian, and 11 (1.7%) subjects classified as Other. Of these patients, 45 (7%) were 65 years of age or older.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.