HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ZETONNA™Nasal Aerosol safely and effectively. See full prescribing information for ZETONNA™Nasal Aerosol.

ZETONNA™ (ciclesonide) Nasal Aerosol
For Intranasal Use Only
Initial U.S. Approval: 2006

INDICATIONS AND USAGE

ZETONNA Nasal Aerosol is a corticosteroid indicated for treatment of symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 12 years of age and older. (1.1)

DOSAGE AND ADMINISTRATION

For Intranasal use only

- 1 actuation per nostril once daily. (74 mcg per day) (2.1)

DOSAGE FORMS AND STRENGTHS

- Nasal Aerosol: 37 mcg of ciclesonide per actuation. (3)
- Supplied in a 6.1 g canister containing 60 actuations. (16)

CONTRAINDICATIONS

- Patients with a known hypersensitivity to ciclesonide or any of the ingredients of ZETONNA Nasal Aerosol. (4)

WARNINGS AND PRECAUTIONS

- Epistaxis, ulceration, nasal septal perforations, *Candida albicans* infection impaired wound healing. Prior to initiating therapy, examine patients for evidence of septal perforation, erosions, ulceration, nasal surgery, and trauma. Avoid spraying ZETONNA Nasal Aerosol directly onto the nasal septum. Avoid use in patients with recent septal perforation, nasal erosion, nasal ulcers, nasal surgery, or nasal trauma. Monitor patients periodically for signs of adverse effects on the nasal mucosa. Discontinue ZETONNA Nasal Aerosol if erosions, ulcerations or perforations occur. (5.1)

- Development of glaucoma or cataracts. Monitor patients closely with a change in vision or with a history of increased intraocular pressure, glaucoma, or cataracts. (5.2)

- Cases of hypersensitivity reactions following administration of ciclesonide with manifestations such as angioedema, with swelling of the lips, tongue and pharynx have been reported. (5.3)

- Potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. More serious or even fatal course of chicken pox or measles in susceptible individuals. Use caution in patients with the above because of the potential for worsening of these infections. (5.4)

- Hypercorticism and adrenal suppression with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue ZETONNA Nasal Aerosol slowly. (5.5)

- Potential reduction in growth velocity in children. (5.6, 8.4) Monitor growth routinely in pediatric patients receiving ZETONNA Nasal Aerosol.

ADVERSE REACTIONS

The most common adverse reactions (≥2% incidence) included nasal discomfort, headache and epistaxis. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sunovion Pharmaceuticals Inc. at 1-877-737-7226 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch for voluntary reporting of adverse reactions.

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

Revised: 01/2012

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 Treatment of Allergic Rhinitis

ZETONNA™ (ciclesonide) Nasal Aerosol is indicated for the treatment of symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

Administer ZETONNA Nasal Aerosol by the intranasal route only. Prior to initial use, ZETONNA Nasal Aerosol must be primed by actuating three times. If ZETONNA Nasal Aerosol is not used for ten consecutive days, it must be primed by actuating three times. If ZETONNA Nasal Aerosol is dropped, the canister and actuator may become separated. If this happens, reassemble ZETONNA Nasal Aerosol and test spray once into the air before using. Illustrated patient's instructions for proper use accompany each package of ZETONNA Nasal Aerosol.

2.1 Allergic Rhinitis

Adults and Adolescents (12 Years of Age and Older): The recommended dose of ZETONNA Nasal Aerosol is 1 actuation per nostril once daily (37 mcg per actuation). The maximum total daily dosage should not exceed 1 actuation in each nostril (74 mcg per day).

3 DOSAGE FORMS AND STRENGTHS

ZETONNA Nasal Aerosol is provided at strength of 37 mcg per actuation strength containing 60 actuations per canister.

4 CONTRAINDICATIONS

ZETONNA Nasal Aerosol is contraindicated in patients with a known hypersensitivity to ciclesonide or any of the ingredients of ZETONNA Nasal Aerosol [*see Warnings and Precautions (5.3)*].

5 WARNINGS AND PRECAUTIONS

5.1 Local Nasal Effects

Epistaxis and Nasal Ulceration: In clinical trials of 2 to 26 weeks in duration, epistaxis was observed more frequently in patients treated with ZETONNA Nasal Aerosol than those who received placebo. In the 26-week open-label extension of the perennial allergic rhinitis trial, nasal ulceration was identified in 4 of 824 patients administered ZETONNA Nasal Aerosol (148 mcg). [*see Adverse Reactions (6)*]

Nasal Septal Perforation: Nasal septal perforation has been reported in patients following the intranasal application of ZETONNA Nasal Aerosol. Three short-term placebo-controlled trials (2 weeks) and one long-term (26 weeks with placebo control and 26 weeks open-label extension without placebo control) trial were conducted in patients with seasonal and perennial allergic rhinitis. Nasal septal perforations were reported in 2 patients out of 2335 treated with ZETONNA Nasal Aerosol compared with none of 892 treated with placebo.

Before starting ZETONNA Nasal Aerosol conduct a nasal examination to ensure that patients are free of nasal disease other than allergic rhinitis. Periodically monitor patients with nasal examinations during treatment for adverse effects in the nasal cavity. If an adverse reaction (e.g. erosion, ulceration, perforation) is noted, discontinue ZETONNA Nasal Aerosol. Avoid spraying ZETONNA Nasal Aerosol directly onto the nasal septum.

Candida Infection: In clinical trials with another formulation of ciclesonide, the development of localized infections of the nose or pharynx with *Candida albicans* has occurred. If such an infection develops with ZETONNA Nasal Aerosol, it may require treatment with appropriate local therapy and discontinuation of ZETONNA Nasal Aerosol.

Impaired Wound Healing: Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or nasal trauma should not use ZETONNA Nasal Aerosol until healing has occurred.

5.2 Glaucoma and Cataracts

Nasal and inhaled corticosteroids may result in the development of glaucoma and cataracts. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma, or cataracts.

5.3 Hypersensitivity

ZETONNA Nasal Aerosol is contraindicated in patients with a known hypersensitivity to ciclesonide or any of the ingredients of ZETONNA Nasal Aerosol. Cases of hypersensitivity reactions following administration of ciclesonide with manifestations such as angioedema, with swelling of the lips, tongue and pharynx, have been reported.

5.4 Immunosuppression

Patients who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible children or adults using corticosteroids. In children or 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 or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chicken pox, 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; or in patients with untreated local or systemic fungal or bacterial infections; systemic viral or parasitic infections; or ocular herpes simplex because of the potential for worsening of these infections.

5.5 Hypothalamic-Pituitary-Adrenal Axis Effect

Hypercorticism and Adrenal Suppression: When intranasal corticosteroids are used at higher than recommended dosages or in susceptible individuals at recommended dosages, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of ZETONNA Nasal Aerosol should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

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 muscular pain, lassitude, and depression. 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. In those 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.

5.6 Effect on Growth

Corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Monitor the growth routinely (e.g., via stadiometry) in pediatric patients receiving ZETONNA Nasal Aerosol. [*see Pediatric Use (8.4)*]

6 ADVERSE REACTIONS

Systemic and local corticosteroid use may result in the following:

- Epistaxis, ulcerations, nasal septal perforations, *Candida albicans* infection, impaired wound healing [*see Warnings and Precautions (5.1)*]
- Glaucoma and cataracts [*see Warnings and Precautions (5.2)*]
- Immunosuppression [*see Warnings and Precautions (5.4)*]
- Hypothalamic-pituitary-adrenal (HPA) axis effects, including growth reduction [*see Warnings and Precautions (5.5, 5.6*), *Use in Specific Populations (8.4)*]

6.1 Clinical Trials Experience

The safety data described below for adults and adolescents 12 years of age and older are based on 4 clinical trials evaluating doses of ciclesonide nasal aerosol from 74 to 282 mcg. Three of the clinical trials were 2 to 6 weeks in duration and one trial was 26 weeks in duration with an additional 26-week open-label extension. Data from the first 6 weeks of the 26-week trial were pooled with data from the three 2-week trials. Short-term data (2 to 6 weeks) included 3001 patients with seasonal and perennial allergic rhinitis, of these, 884 received

ZETONNA Nasal Aerosol 74 mcg once daily and 892 received placebo. The short-term data included 1098 (36.6%) males, 1903 (63.4%) females, 2587 (86.2%) Caucasians, 320 (10.7%) Blacks, 49 (1.6%) Asians, and 45 (1.5%) patients classified as Other. The 26-week trial was conducted in 1110 patients with perennial allergic rhinitis [394 (35.5%) males and 716 (64.5%) females, ages 12 to 78 years old] treated with ZETONNA Nasal Aerosol 74 mcg, 148 mcg or placebo once daily. Of these patients, 298 were treated with 74 mcg ZETONNA Nasal Aerosol, 505 with 148 mcg, and 307 with placebo. The racial distribution in this trial included 922 (83.1%) Caucasians, 146 (13.2%) Blacks, 18 (1.6%) Asians, and 24 (2.2%) patients classified as Other. The 26-week open-label extension included 824 patients [295 (35.8%) males and 529 (64.2%) females, ages 12 to 79 years old] given ZETONNA Nasal Aerosol 148 mcg once daily. The racial distribution in the open-label extension included 690 (83.7%) Caucasians, 104 (12.6%) Blacks, 15 (1.8%) Asians, and 15 (1.8%) patients classified as Other.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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.

***Adults and Adolescents 12 Years of Age and Older in Short-Term (2-6 weeks) Trials*:**

In three short-term trials and the first 6 weeks of one long-term trial, conducted in the US, 884 patients with a history of seasonal or perennial allergic rhinitis were treated with ZETONNA Nasal Aerosol 74 mcg daily. Adverse reactions did not differ appreciably based on age, gender, or race. The table below displays reactions that occurred with an incidence of at least 2.0% and more frequently with ZETONNA Nasal Aerosol 74 mcg than with placebo in seasonal or perennial allergic rhinitis clinical trials of 2 to 6 weeks duration.

Table 1: Adverse Reactions Occurring with a Frequency of at least 2.0% and Greater than Placebo from Controlled Clinical Trials 2 to 6 Weeks in Duration in Patients 12 Years of Age and Older with Seasonal or Perennial Allergic Rhinitis

Adverse Reaction	**ZETONNA Nasal Aerosol 74 mcg Once Daily N = 884 (%)**	**Placebo N = 892 (%)**
Nasal discomfort[a]	28 (3.2)	16 (1.8)
Headache	27 (3.1)	11 (1.2)
Epistaxis	26 (2.9)	24 (2.7)

[a] Nasal discomfort includes both nasal discomfort and instillation site discomfort

When considering the data from higher doses evaluated in the short-term trials, epistaxis demonstrated a dose response. In addition, two patients treated with ZETONNA Nasal Aerosol 74 mcg experienced nasal septal perforations in the short-term trials compared to no patients treated with placebo.

Approximately 1.2% of patients treated with ZETONNA Nasal Aerosol 74 mcg in clinical trials discontinued because of adverse reactions; this rate was similar for patients treated with placebo.

Discontinuations due to local adverse reactions were similar in ZETONNA Nasal Aerosol 74 mcg treated patients (0.8%) compared to placebo treated patients (0.8%). Local adverse reactions leading to discontinuation that occurred only in ZETONNA Nasal Aerosol treated patients included ear infection, nasal discomfort, nasal dryness, nasal mucosal/septum disorders, pharyngitis, streptococcal pharyngitis, sinus headache, and tonsillitis.

***Pediatric Patients Aged 2 to 11 Years*:**

Trials of ZETONNA Nasal Aerosol have not been conducted in pediatric patients aged 2 to 11 years.

Long-Term (26-Week Double-Blind and 26-Week Open-Label) Safety Trial:

In one 26-week double-blind, placebo-controlled safety trial that included 1110 adult and adolescent patients with perennial allergic rhinitis, additional adverse reactions, with an incidence of at least 2%, that occurred more frequently with ZETONNA Nasal Aerosol than with placebo were upper respiratory tract infection, urinary tract infection, oropharyngeal pain, nasal mucosal/septum disorders, viral upper respiratory tract infection, cough, influenza, bronchitis, streptococcal pharyngitis, muscle strain, and nausea. Nasal discomfort (5.7%) and epistaxis (11.4%) were also more frequent in the 26-week safety trial compared to clinical trials 2 to 6 weeks in duration. Nasal mucosal/septum disorders and cough demonstrated a dose response.

Discontinuations due to adverse reactions were higher in ZETONNA Nasal Aerosol treated patients compared to placebo treated patients and demonstrated a dose response. Local adverse reactions leading to discontinuation were also higher in ZETONNA Nasal Aerosol 74 mcg treated patients (1.7%) compared to placebo treated patients (0.7%). The only local adverse reaction leading to discontinuation that occurred in ZETONNA Nasal Aerosol treated patients and was not observed in the 2- to 6-week trials was upper respiratory tract infection.

A total of 824 patients with perennial allergic rhinitis who completed the 26-week double-blind trial enrolled into an open-label extension and received ZETONNA Nasal Aerosol 148 mcg for 26 weeks. Additional adverse reactions, observed with an incidence of at least 2% were sinusitis, nasopharyngitis, and back pain.

A total of 4 nasal septal ulcerations were also reported in the 26-week open-label extension.

There were no reports of nasal septal perforations in the long-term safety trial.

6.2 Post-marketing Experience

Additional adverse reactions have been identified during worldwide post-marketing use with other formulations of ciclesonide, ALVESCO® Inhalation Aerosol and OMNARIS® Nasal Spray. 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.

ALVESCO® Inhalation Aerosol: immediate or delayed hypersensitivity reactions such as angioedema with swelling of the lips, tongue, and pharynx.

OMNARIS® Nasal Spray: nasal congestion, nasal ulcer, and dizziness. Localized infections of the nose or mouth with *Candida albicans* have also occurred with OMNARIS® Nasal Spray.

7 DRUG INTERACTIONS

In vitro studies and clinical pharmacology studies suggested that des-ciclesonide has no potential for metabolic drug interactions or protein binding-based drug interactions [*see Clinical Pharmacology (12.3)*]. In a drug interaction study, co-administration of orally inhaled ciclesonide and oral ketoconazole, a potent inhibitor of cytochrome P450 3A4, increased the exposure (AUC) of des-ciclesonide by approximately 3.6-fold at steady state, while levels of ciclesonide remained unchanged. Erythromycin, a moderate inhibitor of cytochrome P450 3A4, had no effect on the pharmacokinetics of either des-ciclesonide or erythromycin following oral inhalation of ciclesonide [*see Clinical Pharmacology (12.3)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C.

There are no adequate and well-controlled trials in pregnant women. ZETONNA Nasal Aerosol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Experience with oral corticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses suggests that rodents are more prone to teratogenic effects from corticosteroids than humans.

Oral administration of ciclesonide in rats at approximately 120 times the maximum recommended human daily intranasal dose (MRHDID) in adults (on a mcg/m^2 basis at a maternal dose of 900 mcg/kg/day) produced no teratogenicity or other fetal effects. However, subcutaneous administration of ciclesonide in rabbits at similar to MRHDID (on a mcg/m^2 basis at a maternal dose of 5 mcg/kg/day) produced fetal toxicity. This included fetal loss, reduced fetal weight, cleft palate, skeletal abnormalities including incomplete ossifications, and skin effects. No toxicity was observed at ¼ of the MRHDID in adults (on a mcg/m^2 basis at a maternal dose of 1 mcg/kg/day).

Nonteratogenic Effects: Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

8.3 Nursing Mothers

It is not known if ciclesonide is excreted in human milk. However, other corticosteroids are excreted in human milk. In a study with lactating rats, minimal but detectable levels of radiolabeled ciclesonide were recovered in milk. Caution should be used when ZETONNA Nasal Aerosol is administered to nursing women.

8.4 Pediatric Use

The safety and effectiveness for seasonal and perennial allergic rhinitis in children 12 years of age and older have been established. The safety and efficacy of ZETONNA Nasal Aerosol for treatment of the symptoms of seasonal and perennial allergic rhinitis in patients 11 years of age and younger have not been established.

Controlled clinical trials have shown that intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. This effect has been observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA)-axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA-axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch-up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied. The growth of pediatric patients receiving intranasal corticosteroids, including ZETONNA Nasal Aerosol, should be monitored routinely (e.g., via stadiometry). A 52-week, multi-center, double-blind, randomized, placebo-controlled parallel-group trial was conducted to assess the effect of orally inhaled ciclesonide (ALVESCO® Inhalation Aerosol) on growth rate in 609 pediatric patients with mild persistent asthma, aged 5 to 8.5 years. Treatment groups included orally inhaled ciclesonide 40 mcg or 160 mcg or placebo given once daily. Growth was measured by stadiometer height during the baseline, treatment and follow-up periods. The primary comparison was the difference in growth rates between ciclesonide 40 and 160 mcg and placebo groups. Conclusions cannot be drawn from this trial because compliance could not be assured. Ciclesonide blood levels were also not measured during the one-year treatment period. There was no difference in efficacy measures between the placebo and the orally inhaled ciclesonide (ALVESCO® Inhalation Aerosol) groups.

The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of safe and effective noncorticosteroid treatment alternatives. To minimize the systemic effects of intranasal corticosteroids, each patient should be titrated to the lowest dose that effectively controls his/her symptoms.

The potential for ZETONNA Nasal Aerosol to cause growth suppression in susceptible patients or when given at higher than recommended dosages cannot be ruled out.

8.5 Geriatric Use

Clinical trials of ZETONNA Nasal Aerosol did not include sufficient numbers of patients age 65 and over to determine whether they responded differently from younger patients. 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 reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

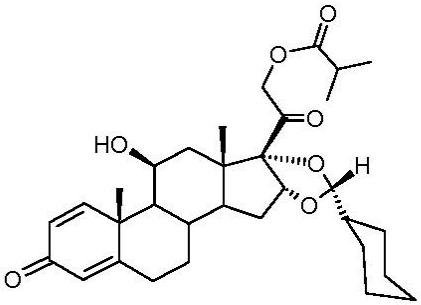
10 OVERDOSAGE

Chronic overdosage may result in signs or symptoms of hypercorticism [*see Warnings and Precautions (5.5)*]. There are no data on the effects of acute or chronic overdosage with ZETONNA Nasal Aerosol.

11 DESCRIPTION

The active component of ZETONNA Nasal Aerosol is ciclesonide, a non-halogenated glucocorticoid having the chemical name pregna -1,4-diene-3,20-dione, 16,17-[[R-

cyclohexylmethylene]bis(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)-,(11ß,16α)-. Ciclesonide is delivered as the R-epimer. The empirical formula is $C_{32}H_{44}O_7$ and its molecular weight is 540.7. Its structural formula is as follows:



Ciclesonide is a white to yellow-white powder. It is soluble in dehydrated alcohol, acetone, dichloromethane, and chloroform. ZETONNA Nasal Aerosol is comprised of a pressurized, metered-dose aerosol canister and actuator, which is fitted with a dose indicator. ZETONNA Nasal Aerosol is intended for intranasal use only. Each canister contains a solution of ciclesonide in propellant HFA-134a (1,1,1,2 tetrafluoroethane) and ethanol. After priming, ZETONNA Nasal Aerosol 37 mcg delivers 50 mcg of ciclesonide from the valve and 37 mcg of ciclesonide from the actuator. This product delivers 50 microliters (59.3 milligrams) of solution as fine particle mist from the valve with each actuation.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ciclesonide is a pro-drug that is enzymatically hydrolyzed to a pharmacologically active metabolite, C21-desisobutyryl-ciclesonide (des-ciclesonide or RM1) following intranasal application. Des-ciclesonide has anti-inflammatory activity with affinity for the glucocorticoid receptor that is 120 times higher than the parent compound.

The precise mechanism through which ciclesonide affects allergic rhinitis symptoms is not known. Corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic inflammation.

12.2 Pharmacodynamics

Adrenal Function: In a 6-week, randomized, double-blind, placebo-controlled, parallel-group trial in adolescents and adults 12-73 years of age with perennial allergic rhinitis, daily doses of 148 mcg and 282 mcg of ZETONNA Nasal Aerosol were compared to placebo nasal aerosol. Dexamethasone 6 mg was used as an active control during the last 4 days of the trial. Adrenal function was assessed by 24-hr serum cortisol AUC before and after the treatment. At the end of 6 weeks of treatment, the mean (SE) change from baseline in serum cortisol $AUC_{(0-24)}$ was -5.0 (4.6) mcg•hour/dL, -2.6 (4.6) mcg•hour/dL, and -4.6 (5.0) mcg•hour/dL for placebo (n=57), 148 mcg ZETONNA Nasal Aerosol (n=60), and 282 mcg ZETONNA Nasal Aerosol (n=50), respectively. The difference from placebo for the change from baseline in serum cortisol

$AUC_{(0-24)}$ was -2.4 mcg•hour/dL (95% CI: -15.1, 10.2) and -0.5 mcg•hour/dL (95% CI: -13.9, 13.0) for 148 mcg/day and 282 mcg/day treatments, respectively. The effects observed with the active control (dexamethasone, n=18) validate the sensitivity of the study to assess the effect of ciclesonide on the HPA axis.

12.3 Pharmacokinetics

Absorption: Ciclesonide and des-ciclesonide have negligible oral bioavailability (both less than 1%) due to low gastrointestinal absorption and high first-pass metabolism. The intranasal administration of ciclesonide at recommended doses results in negligible serum concentrations of ciclesonide. However, the known active metabolite (des-ciclesonide) is detected in the serum of some patients after nasal inhalation of ciclesonide. The bioanalytical assay used has a lower limit of quantification of 10 pg/mL, for both ciclesonide and des-ciclesonide, respectively.

The low systemic exposure of des-ciclesonide following ciclesonide nasal aerosol administration was confirmed in a crossover trial in 29 healthy adults. The median C_{max} of des-ciclesonide was 59 pg/mL following a single dose of ciclesonide nasal aerosol (296 mcg) compared to 602 pg/mL following a single dose of orally inhaled ciclesonide (320 mcg) and 12 pg/mL following a single dose of ciclesonide aqueous nasal spray (300 mcg). The pharmacokinetics of intranasally administered ciclesonide have been assessed in perennial allergic rhinitis patients resulting in similar exposure compared to healthy subjects.

Distribution: Following intravenous administration of 800 mcg of ciclesonide, the volumes of distribution of ciclesonide and des-ciclesonide were approximately 2.9 L/kg and 12.1 L/kg, respectively. The percentage of ciclesonide and des-ciclesonide bound to human plasma proteins averaged ≥ 99% each, with ≤ 1% of unbound drug detected in the systemic circulation. Des-ciclesonide is not significantly bound to human transcortin.

Metabolism: Ciclesonide is hydrolyzed to a biologically active metabolite, des-ciclesonide, by esterases. Des-ciclesonide undergoes further metabolism in the liver to additional metabolites mainly by the cytochrome P450 (CYP) 3A4 isozyme and to a lesser extent by CYP 2D6. The full range of potentially active metabolites of ciclesonide has not been characterized. After intravenous administration of ^{14}C-ciclesonide, 19.3% of the resulting radioactivity in the plasma is accounted for by ciclesonide or des-ciclesonide; the remainder may be a result of other, as yet, unidentified multiple metabolites.

Elimination: Following intravenous administration of 800 mcg of ciclesonide, the clearance values of ciclesonide and des-ciclesonide were high (approximately 152 L/hr and 228 L/hr, respectively). ^{14}C-ciclesonide was predominantly excreted via the feces after intravenous administration (66%) indicating that excretion through bile is the major route of elimination. Approximately 20% or less of drug related radioactivity was excreted in the urine.

Special Populations:

Hepatic Impairment: Compared to healthy subjects, the systemic exposure (C_{max} and AUC) in patients with liver impairment increased in the range of 1.4 to 2.7-fold after ex-actuator administration of 1280 mcg ciclesonide via oral inhalation. Dose adjustment in liver impairment is not necessary.

Renal Impairment: Trials in renally-impaired patients were not conducted since renal excretion of des-ciclesonide is a minor route of elimination (≤ 20%).

Drug-Drug Interactions: Ciclesonide inhibited human recombinant cytochrome P450 enzymes at high concentration (3 microM) *in vitro,* but clinically relevant metabolic interactions are not anticipated. Based on *in vitro* studies in human liver microsomes, ciclesonide and des-ciclesonide appear to have no inhibitory or induction potential on the metabolism of other drugs metabolized by cytochrome P450 enzymes. *In vitro* studies demonstrated that the plasma protein binding of des-ciclesonide was not affected by warfarin or salicylic acid, indicating no potential for protein binding-based drug interactions.

In a drug interaction study, co-administration of orally inhaled ciclesonide and oral ketoconazole, a strong inhibitor of cytochrome P450 3A4, increased the exposure (AUC) of the active metabolite of ciclesonide, des-ciclesonide, by approximately 3.6-fold at steady state, while levels of ciclesonide remained unchanged.

In another drug interaction study, co-administration of orally inhaled ciclesonide and oral erythromycin, a moderate inhibitor of cytochrome P450 3A4, had no effect on the pharmacokinetics of either des-ciclesonide or erythromycin.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Ciclesonide demonstrated no carcinogenic potential in mice in a study of oral doses up to 900 mcg/kg (approximately 60 times the maximum recommended human daily intranasal dose (MRHDID) in adults based on mcg/m^2/day) in mice for 104 weeks, nor in a study in rats of inhalation doses up to 193 mcg/kg (approximately 25 times the maximum human daily intranasal dose in adults and adolescents 12 years of age or older based on mcg/m^2/day) for 104 weeks.

Ciclesonide was not mutagenic in an Ames test or in a forward mutation assay and was not clastogenic in a human lymphocyte assay or in an *in vitro* micronucleus test. However, ciclesonide was clastogenic in the *in vivo* mouse micronucleus test. The concurrent reference corticosteroid (dexamethasone) in this study showed similar findings.

No evidence of impairment of fertility was observed in a reproductive study conducted in male and female rats both dosed orally up to 900 mcg/kg/day (approximately 120 times MRHDID in adults based on mcg/m^2/day).

14 CLINICAL STUDIES

14.1 Seasonal and Perennial Allergic Rhinitis

Adults and Adolescent Patients 12 Years of Age and Older:

The efficacy of ZETONNA Nasal Aerosol was evaluated in one randomized, double-blind, parallel-group, multicenter, placebo-controlled dose-ranging trial (74 mcg, 148 mcg, and 282 mcg once daily) and 3 confirmatory trials (74 mcg and 148 mcg once daily) in adolescents and adults with allergic rhinitis. Efficacy endpoints were evaluated at 2 weeks for the two

seasonal allergic rhinitis trials and at 6 weeks for the perennial allergic rhinitis trial. These trials were all conducted in the United States. A total of 3001 patients were included in these 4 trials. The dose-ranging trial included a total of 513 patients [193 males (37.6%) and 320 females (62.4%)], of whom 65 (12.7%) were adolescents. The three confirmatory trials included a total of 2488 patients (905 males and 1583 females) of whom 170 were adolescents, ages 12 to 18 years. Patients enrolled in the trials were 12 to 81 years of age with a history of seasonal or perennial allergic rhinitis, a positive skin test to at least one relevant allergen, and active symptoms of allergic rhinitis at study entry. Assessment of efficacy in these trials was based on patient recording of four nasal symptoms (runny nose, nasal itching, sneezing, and nasal congestion) on a 0-3 categorical severity scale (0 = absent, 1 = mild, 2 = moderate, and 3 = severe) as reflective or instantaneous total nasal symptom scores (rTNSS and iTNSS respectively). Reflective scoring required the patients to record symptom severity over the previous 12 hours; the instantaneous scoring required patients to record symptom severity over the previous 10 minutes.

Additional secondary efficacy variables were assessed, including the total ocular symptom score (TOSS) in the seasonal allergic rhinitis trials and the Rhinoconjunctivitis Quality of Life Questionnaire with Standardised Activities [RQLQ(S)] in both seasonal and perennial allergic rhinitis trials. TOSS is calculated as the sum of the patients' scoring of the three individual ocular symptoms (itching, tearing, and redness) on a 0 to 3 categorical severity scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe) as reflective (rTOSS) or instantaneous (iTOSS) scores. To assess efficacy, rTOSS and iTOSS were evaluated as described above for the TNSS. Patients perceptions of disease specific quality of life were evaluated through the use of the RQLQ(S), which assesses the impact of allergic rhinitis symptoms and treatment through 28 items in 7 domains (activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional) on a 7-point scale where 0 = not troubled and 6 = extremely troubled. An overall RQLQ(S) score is calculated from the average of the domain scores. An absolute difference of ≥ 0.5 in mean change from baseline over placebo is considered the minimally clinically important difference (MCID) for the RQLQ(S).

Dose-Ranging Trial: There was a 2-week placebo-controlled, double-blind, dose-ranging trial that evaluated efficacy of three doses of ZETONNA Nasal Aerosol (74 mcg, 148 mcg, and 282 mcg once daily) in patients with seasonal allergic rhinitis. The primary efficacy endpoint was the difference from placebo in the change from baseline of the average of morning and evening reflective total nasal symptom score (rTNSS) averaged over the 2-week treatment period. The rTNSS showed a statistically significant estimated treatment difference from placebo of 0.81 (95% CI: 0.32, 1.29); 0.90 (95% CI: 0.40, 1.39); and 0.66 (95% CI: 0.16, 1.16) for 282 mcg, 148 mcg and 74 mcg, respectively.

Confirmatory Seasonal Allergic Rhinitis Trials: There were two 2-week placebo-controlled, double-blind confirmatory trials that evaluated efficacy of two doses of ZETONNA Nasal Aerosol (74 mcg and 148 mcg once daily) in patients with seasonal allergic rhinitis. The primary efficacy endpoint was the difference from placebo in the change from baseline of the average of morning and evening rTNSS averaged over the 2-week treatment period. Table 2 displays the efficacy results from one of these trials in patients with seasonal allergic rhinitis. The other trial showed similar results. In these trials, ZETONNA Nasal Aerosol 74 mcg once daily was statistically significantly different from placebo. Statistically significant differences in the morning pre-dose iTNSS indicate that the effect was maintained over the full 24-hour dosing interval. ZETONNA Nasal Aerosol 74 mcg demonstrated a statistically significant decrease from

baseline in the rTOSS compared to placebo. Similarly, a clinically significant decrease (≥ 0.5) from baseline compared to placebo for the RQLQ(S) was also shown. ZETONNA Nasal Aerosol 148 mcg once daily did not provide an efficacy benefit over the 74 mcg once daily dose.

Confirmatory Perennial Allergic Rhinitis Trial: There was one 26-week placebo-controlled, double-blind trial that evaluated efficacy of two doses of ZETONNA Nasal Aerosol (74 mcg and 148 mcg once daily) in patients with perennial allergic rhinitis. The primary efficacy endpoint was the difference from placebo in the change from baseline of the average of morning and evening rTNSS averaged over the first 6 weeks of treatment. In this trial, ZETONNA Nasal Aerosol 74 mcg once daily was statistically significantly different from placebo (Table 2) in decreasing nasal symptom scores. Statistically significant differences in the morning pre-dose instantaneous total nasal symptom score indicate that the effect was maintained over the full 24-hour dosing interval. ZETONNA Nasal Aerosol 74 mcg did not demonstrate a clinically significant change from baseline in the overall RQLQ(S) compared to placebo. TOSS was not evaluated in this trial. ZETONNA Nasal Aerosol 148 mcg once daily did not provide an efficacy benefit over the 74 mcg once daily dose.

Table 2: Mean Changes in Efficacy Variables in Adult and Adolescent Patients With Seasonal or Perennial Allergic Rhinitis

Treatment	N	Mean Baseline[a]	LS Mean Change from Baseline	Difference from Placebo[b]		
				Estimate (LS Mean)	95% CI	p-value[c]
Seasonal Allergic Rhinitis						
Reflective Total Nasal Symptom Score						
Ciclesonide 74 mcg	237	9.3	-1.5	0.9	0.6, 1.3	<0.001
Placebo	235	9.1	-0.5			
Instantaneous Total Nasal Symptom Score						
Ciclesonide 74 mcg	237	8.7	-1.3	0.9	0.5, 1.3	<0.001
Placebo	235	8.6	-0.5			
Reflective Total Ocular Symptom Score						
Ciclesonide 74 mcg	237	5.8	-0.8	0.5	0.3, 0.8	0.001
Placebo	235	5.7	-0.2			
Rhinoconjunctivitis Quality of Life Questionnaire with Standardised Activities						
Ciclesonide 74 mcg	237	4.0	-0.8	0.6	0.4, 0.8	<0.001
Placebo	234	4.0	-0.2			
Perennial Allergic Rhinitis						
Reflective Total Nasal Symptom Score						
Ciclesonide 74 mcg	298	8.5	-2.0	0.7	0.4, 1.0	<0.001

Treatment	N	Mean Baseline[a]	LS Mean Change from Baseline	Difference from Placebo[b]		
				Estimate (LS Mean)	95% CI	p-value[c]
Placebo	307	8.6	-1.3			
Instantaneous Total Nasal Symptom Score						
Ciclesonide 74 mcg	298	7.7	-1.8	0.6	0.3, 0.9	<0.001
Placebo	307	7.7	-1.2			

a Baseline for rTNSS, iTNSS, and rTOSS are averages of the AM and PM responses obtained during the Run-in Period up to 6 days prior to randomization and includes AM score prior to randomization. Baseline for morning iTNSS is the average of the AM responses obtained during the Run-in Period up to 6 days prior to randomization and includes the AM score prior to randomization. Baseline RQLQ(S) is from the randomization visit assessment.

[b] Estimates (LS Mean), 95% Confidence Intervals, and p-values were obtained from ANCOVA analyses with treatment and center as fixed effects and baseline as covariate in the model.

[c] P-values are significant at the 0.025 level based on Bonferroni correction.

Onset of Action: Onset of action was evaluated in both 2-week seasonal and one 6-week perennial allergic rhinitis trials by frequent recording of instantaneous symptom score. In these trials, onset of effect was seen after 36 hours following the first dose. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing.

Pediatric Patients Aged 11 Years and Younger: Efficacy of ZETONNA Nasal Aerosol in patients 11 years of age and younger has not been established [*see Use in Specific Populations (8.4)*].

16 HOW SUPPLIED/STORAGE AND HANDLING

ZETONNA Nasal Aerosol is supplied as a pressurized aluminum canister with a purple and white plastic actuator integrated with a dose indicator and a cap. The contents of one 6.1 gram canister provide 60 actuations, after initial priming. Each actuation delivers 37 mcg of ciclesonide from the nasal actuator. Prior to initial use, or when not used for ten consecutive days, ZETONNA Nasal Aerosol must be primed by actuating three times. If ZETONNA Nasal Aerosol is dropped, the canister and actuator may become separated. If this happens, ZETONNA Nasal Aerosol should be reassembled and actuated once into the air to test before using. The actuator and canister should be discarded after reaching zero in the indicator window since the amount of ciclesonide delivered per spray thereafter may be substantially less than the labeled dose.

The ZETONNA Nasal Aerosol canister should only be used with the ZETONNA Nasal Aerosol actuator. The actuator is fitted with a dose indicator and should not be used with other inhalation aerosol medications. The correct amount of medication in each inhalation cannot be ensured after the labeled number of actuations from the canister has been used, even though the inhaler may not feel completely empty and may continue to operate. Illustrated patient's instructions for proper use accompany each package of ZETONNA Nasal Aerosol.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [See USP Controlled Room Temp]. For optimal results, canister should be at room temperature when used.

CONTENTS UNDER PRESSURE

Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 49°C (120°F) may cause bursting. Never throw canister into fire or incinerator.

Keep out of reach of children. Avoid spraying in eyes or directly onto the nasal septum.

ZETONNA Nasal Aerosol 37 mcg, 60 metered actuations; net fill weight 6.1 g.

NDC Number 63402-737-60

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling accompanying the product.

17.1 Local Nasal Effects

Patients should be informed that treatment with ZETONNA Nasal Aerosol may lead to adverse reactions, which include nasal septal perforation, epistaxis, and nasal ulceration. In addition, ciclesonide is associated with candidal infection, and nasal corticosteroids are associated with impaired wound healing. Do not spray ZETONNA Nasal Aerosol directly onto the nasal septum. Patients who have experienced recent nasal septal perforation, nasal erosion, nasal ulcers, nasal surgery, or nasal trauma should not use ZETONNA Nasal Aerosol until healing has occurred [*see Warnings and Precautions (5.1)*].

17.2 Glaucoma and Cataracts

Patients should be informed that glaucoma and cataracts are associated with nasal and inhaled corticosteroid use. Patients should inform his/her health care provider if a change in vision is noted while using ZETONNA Nasal Aerosol [*see Warnings and Precautions (5.2)*].

17.3 Immunosuppression

Patients who are on immunosuppressive doses of corticosteroids should be warned to avoid exposure to chickenpox or measles, and if exposed, to consult their physician without delay. Patients should be informed of potential worsening of existing tuberculosis, fungal, bacterial, viral or parasitic infections, or ocular herpes simplex [*see Warnings and Precautions (5.4)*].

17.4 Use Daily

Patients should use ZETONNA Nasal Aerosol on a regular, once daily basis since its effectiveness depends on its regular use. In clinical trials, the onset of effect was seen after 36 hours following the first dose. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing. Initial assessment of response should be made during this timeframe and periodically until the patient's symptoms are stabilized. The patient should take the medication as directed and should not exceed the prescribed dosage. The patient should contact the physician if symptoms do not improve by a reasonable time or if the condition worsens.

17.5 Keep Spray Out of Eyes and Off Nasal Septum

Patients should be informed to avoid spraying ZETONNA Nasal Aerosol in their eyes or directly on the nasal septum.

17.6 Storage and Handling

Patients should use the ZETONNA Nasal Aerosol canister only with the ZETONNA Nasal Aerosol actuator supplied with the product. The dose indicator display window will show a red zone when it is about time to replace the ZETONNA Nasal Aerosol. Replace ZETONNA Nasal Aerosol when the indicator shows zero.

Manufactured for:

Sunovion Pharmaceuticals Inc.

Marlborough, MA 01752 USA

Made in the United Kingdom

For customer service, call 1-888-394-7377

To report adverse events, call 1-877-737-7226

For medical information, call 1-800-739-0565

901641R00

January 2012

620392213

Patient Information

ZETONNA™ <<Ze toe' nah>>
(ciclesonide) Nasal Aerosol

Note: For Use in the Nose Only.

- **Do not** spray ZETONNA Nasal Aerosol in your eyes or directly onto your nasal septum (the wall between the 2 nostrils).
- **Do not** use your ZETONNA Nasal Aerosol near heat or an open flame.

Read this Patient Information leaflet before you start using ZETONNA Nasal Aerosol and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment. If you have any questions about ZETONNA Nasal Aerosol, ask your healthcare provider or pharmacist.

What is ZETONNA Nasal Aerosol?

ZETONNA Nasal Aerosol is a prescription medicine that treats seasonal and year-round allergy symptoms in adults and children 12 years of age and older.
ZETONNA Nasal Aerosol contains ciclesonide, which is a man-made (synthetic) corticosteroid. Corticosteroids are natural substances found in the body and reduce inflammation. When you spray ZETONNA Nasal Aerosol into your nose, it may help reduce nasal symptoms of allergic rhinitis (inflammation of the lining of the nose) such as stuffy nose, runny nose, itching and sneezing. ZETONNA Nasal Aerosol may also help you if you have red, itchy, and watery eyes.

It is not known if ZETONNA Nasal Aerosol is safe and effective in children 11 years of age and younger.

Who should not use ZETONNA Nasal Aerosol?

Do not use ZETONNA Nasal Aerosol if you are allergic to ciclesonide or any of the ingredients in ZETONNA Nasal Aerosol. See the end of this Patient Information leaflet for a complete list of ingredients in ZETONNA Nasal Aerosol.

What should I tell my healthcare provider before using ZETONNA Nasal Aerosol?

Before you use ZETONNA Nasal Aerosol tell your healthcare provider if you:

- have had recent nose problems such as a hole in the cartilage of your nose, nasal ulcers, nasal surgery, or nasal injury.

- have or have had eye problems such as increased intraocular pressure, glaucoma, or cataracts.
- have any infections including tuberculosis or ocular herpes simplex.
- have not had or been vaccinated for chicken pox or measles.
- are pregnant or plan to become pregnant. It is not known if ZETONNA Nasal Aerosol will harm your unborn baby. Talk to your healthcare provider about the best way to feed your baby if you are using ZETONNA Nasal Aerosol.
- are breastfeeding or plan to breastfeed. It is not known if ZETONNA Nasal Aerosol passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you are using ZETONNA Nasal Aerosol.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctors and pharmacist when you get a new medicine.

How should I use ZETONNA Nasal Aerosol?

- Read the Instructions for Use at the end of this leaflet for specific information about the right way to use ZETONNA Nasal Aerosol.
- Use ZETONNA Nasal Aerosol exactly as your healthcare provider tells you to use it. Do not take more of your medicine or take it more often than your healthcare provider tells you.
- ZETONNA Nasal Aerosol is used 1 time each day, 1 spray in each nostril. Do not use more than a total of 1 spray in each nostril per day.
- ZETONNA Nasal Aerosol may begin to work within 36 hours after you take your first dose. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing.
- If your symptoms do not improve or get worse, call your healthcare provider.

What are the possible side effects of ZETONNA Nasal Aerosol?

ZETONNA Nasal Aerosol may cause serious side effects, including:

- **nose bleeds and nasal ulcers.** Call your healthcare provider right away if you start to have more nose bleeds or nasal ulcers.
- **hole in the cartilage in the nose (nasal septal perforation).** Stop using ZETONNA Nasal Aerosol and call your doctor right away if you have symptoms of a nasal perforation. Symptoms of nasal perforation may include:

- crusting in the nose
- nosebleeds
- runny nose
- whistling sound when you breathe

- **thrush (*Candida*), a fungal infection in your nose, mouth, or throat.** Tell your healthcare provider if you have any redness or white colored patches in your mouth or throat.
- **slow wound healing.** You should not use ZETONNA Nasal Aerosol until your nose has healed, if you have a sore in your nose, if you have had surgery in your nose, or if your nose has been injured.
- **eye problems such as glaucoma and cataracts.** If you have a history of glaucoma or cataracts or have a family history of eye problems, you should have regular eye exams while you use ZETONNA Nasal Aerosol.
- **immune system problems that may increase your risk of infections.** You are more likely to get infections if you take medicines that may weaken your body's ability to fight infections. Avoid contact with people who have contagious diseases such as chicken pox or measles while you use ZETONNA Nasal Aerosol. Symptoms of an infection may include:
    - fever
    - pain
    - aches
    - chills
    - feeling tired
    - nausea
    - vomiting
- **adrenal insufficiency.** Adrenal insufficiency is a condition in which the adrenal glands do not make enough steroid hormones. Call your healthcare provider right away if you experience the following symptoms of adrenal insufficiency:
    - tiredness
    - weakness
    - dizziness
    - nausea
    - vomiting
- **slowed or delayed growth in children.** A child's growth should be checked regularly while using ZETONNA Nasal Aerosol.
- **allergic reactions.** Call your healthcare provider right away if you experience swelling of the lips, tongue, or throat.

The most common side effects with ZETONNA Nasal Aerosol include:

- Nasal discomfort

- Headache
- Nose bleeds

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ZETONNA Nasal Aerosol.

For more information, ask your doctor or pharmacist.

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

How should I store ZETONNA Nasal Aerosol?

- Store ZETONNA Nasal Aerosol at room temperature between 59°F and 86°F (15°C to 30°C).
- **Do not** puncture the ZETONNA Nasal Aerosol canister.
- **Do not** store the ZETONNA Nasal Aerosol canister near heat or a flame. Temperatures above 120°F (49°C) may cause the canister to burst.
- **Do not** throw the ZETONNA Nasal Aerosol canister into a fire or an incinerator.
- Safely throw away medicine that is out of date or no longer needed.
- Keep ZETONNA Nasal Aerosol clean and dry at all times.

Keep ZETONNA Nasal Aerosol and all medicines out of the reach of children.

General Information About the Safe and Effective Use of ZETONNA Nasal Aerosol

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ZETONNA Nasal Aerosol for a condition for which it was not prescribed. Do not give ZETONNA Nasal Aerosol to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information summarizes the most important information about ZETONNA Nasal Aerosol. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about ZETONNA Nasal Aerosol that is written for health professionals. You may want to read this leaflet again. Please DO NOT THROW IT AWAY until you have finished your medicine.

For more information, go to www.ZETONNA.com or call 1-888-394-7377.

What are the ingredients in ZETONNA Nasal Aerosol?

Active ingredient: ciclesonide
Inactive ingredients: HFA propellant and ethanol

Instructions for Use

ZETONNA™ <<Ze toe' nah>>
(ciclesonide)
Nasal Aerosol

Read these Instructions for Use for ZETONNA Nasal Aerosol before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your doctor about your medical condition or treatment.

Note: For Use in the Nose Only.

- **Do not** spray ZETONNA Nasal Aerosol in your eyes or directly onto your nasal septum (the wall between your 2 nostrils).
- **Do not** use your ZETONNA Nasal Aerosol near heat or an open flame.

The Parts of Your ZETONNA Nasal Aerosol

ZETONNA Nasal Aerosol comes as a canister fitted into a nasal actuator with a dose indicator. Do not use the actuator with a canister of medicine from any other inhaler. Do not use the ZETONNA Nasal Aerosol canister with an actuator from any other inhaler. (See **Figure A**)

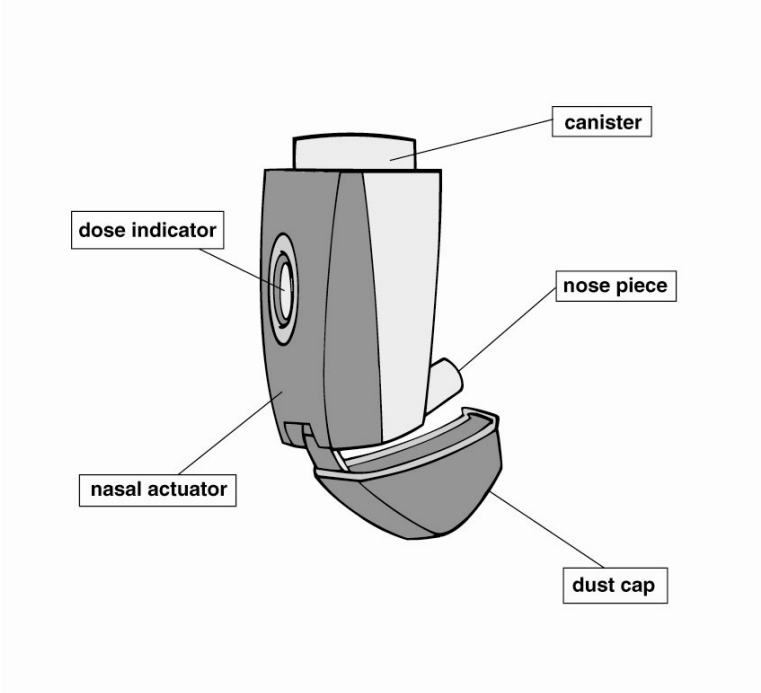


Figure A

Priming Your ZETONNA Nasal Aerosol For Use

- Remove ZETONNA Nasal Aerosol from its package.
- **Before you use ZETONNA Nasal Aerosol for the first time** or if you have not used your medicine for 10 days in a row, you will need to prime your ZETONNA Nasal Aerosol.
- Open the purple plastic dust cap by gently squeezing both sides and pulling the cap away from the nasal actuator. Hold the nasal actuator upright. (See **Figure B**)

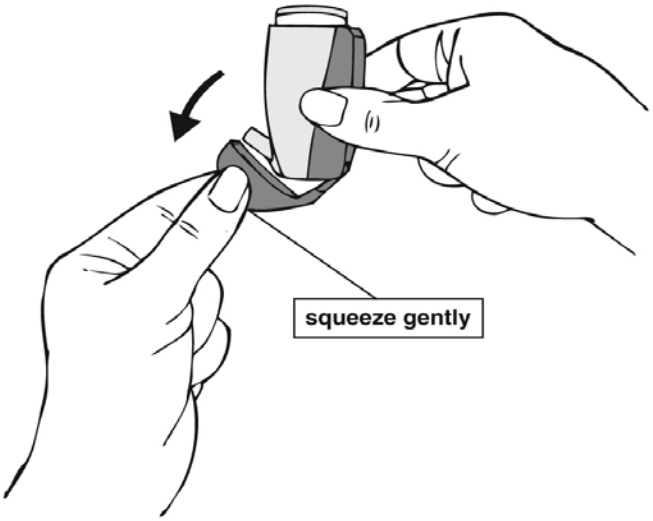


Figure B

- Spray 3 times into the air away from the face, by pressing down fully on the top of the canister three times (See **Figure C**). Make sure the canister returns to its original position after each spray.

Figure C

Using Your ZETONNA Nasal Aerosol

Step 1. Open the purple plastic dust cap.

Step 2. Hold the nasal actuator upright, with the nose piece pointing upwards, between your thumb and forefinger (and middle finger) (See **Figure D**).

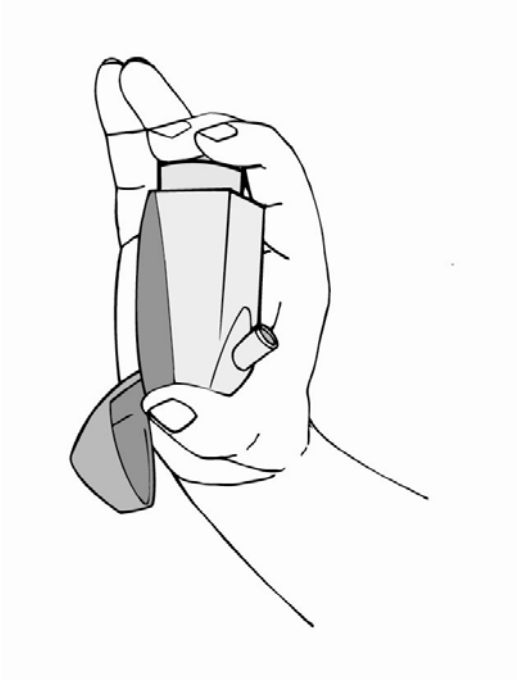


Figure D

Step 3. Tilt your head back slightly and insert the end of the nose piece into 1 nostril, pointing it slightly toward the outside nostril wall away from the nasal septum (the wall between the 2 nostrils), while holding your other nostril closed with 1 finger (See **Figure E**). **Do not get any spray in your eyes or directly on your nasal septum.**

Figure E

Step 4. Press down on the canister to release 1 spray and at the same time breathe in gently through the nostril. Hold your breath for a few seconds then breathe out slowly through your mouth.

Step 5. Remove the nose piece from your nostril. Make sure the canister has returned to its original position and repeat steps 2-4 for the second spray in your other nostril.

Step 6. Replace the protective purple dust cap on the nasal actuator.

Step 7. Avoid blowing your nose for the next 15 minutes.

Cleaning Your Nasal Actuator

The outside of the nose piece should be cleaned weekly, by wiping with a clean, dry tissue or cloth (see **Figure F**).

Do not wash or put any part of the ZETONNA Nasal Aerosol canister or actuator in water.

Figure F

How to Tell if Your ZETONNA Nasal Aerosol Is Empty

- Each canister of ZETONNA Nasal Aerosol contains enough medicine for you to spray medicine 60 times (or 30 times for sample size product). This does not count the first 3 priming sprays.
- The actuator of your ZETONNA Nasal Aerosol is fitted with a dose indicator which shows you how much medicine is left after each use. The dose indicator will display the number of sprays remaining in groups of 5 or 10 actuations.
- The display window will begin showing a green color. As you continue to use the medicine, the window will show a yellow color. A yellow color in the window means that you need to replace your medicine soon. When the medicine is almost empty, the window will show a red color.
- When the window shows red and you see the dose indicator read zero, “0” (see **Figure G**), you should throw away the canister and nasal actuator.

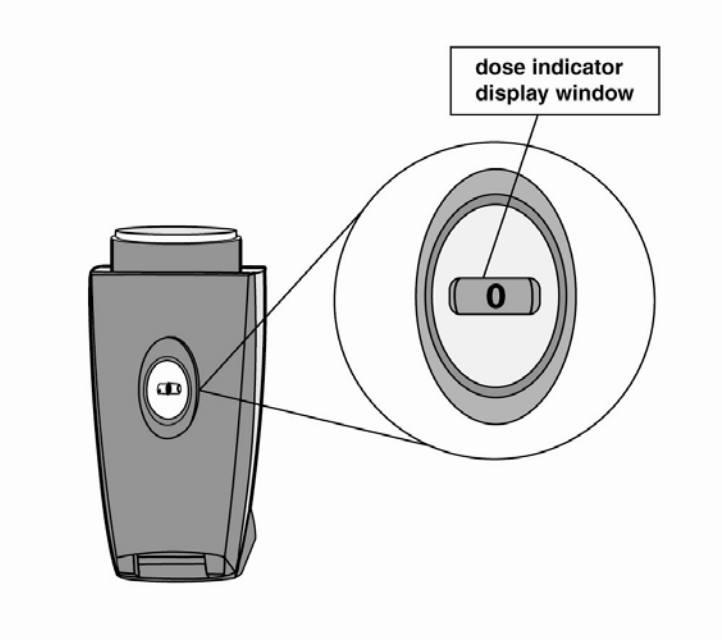


Figure G

- **Do not** throw your ZETONNA Nasal Aerosol canister in the fire or an incinerator.
- **Do not** use your ZETONNA Nasal Aerosol after zero is shown in the window of the dose indicator even though it may look like there is medicine left in the canister. You may not get the right amount of medicine.
- Talk with your healthcare provider before your supply of ZETONNA Nasal Aerosol runs out to see if you should get a refill of your medicine.

What to Do if You Drop Your ZETONNA Nasal Aerosol

- If you drop your ZETONNA Nasal Aerosol, the canister may become separated from the actuator. If this happens, insert the canister into the actuator as shown in **Figure H**, test spray once into the air away from your face, then use as described above.

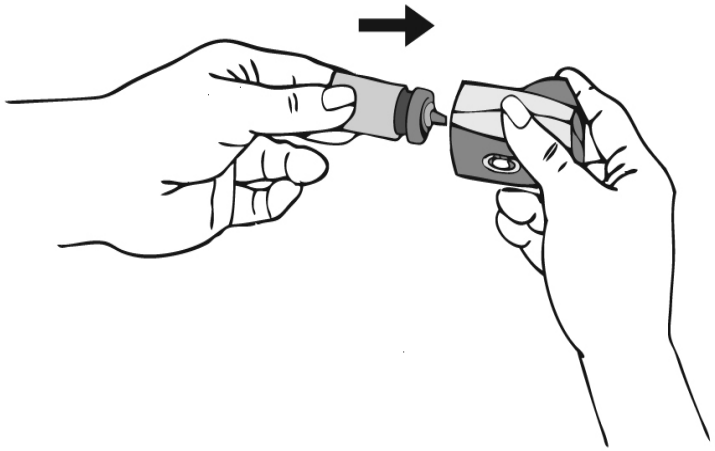


Figure H

- If the ZETONNA Nasal Aerosol is dropped, the dose counter may not work. It is recommended to keep track of the number of sprays taken from your ZETONNA Nasal Aerosol based on your records.

This Patient Information and Instructions for Use have been approved by the U.S. Food and Drug Administration.

SUNOVION

Manufactured for:
Sunovion Pharmaceuticals Inc.
Marlborough, MA 01752 USA
Made in the United Kingdom

.

For customer service, call 1-888-394-7377

Revised: January 2012
901641R00

620392213