SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NASONEX

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

composition: one spray dose contains mometasone furoate monohydrate equivalent to 50 mcg mometasone furoate (anhydrous).
excipients: dispersible cellulose, glycerol, sodium citrate dehydrate, citric acid, polysorbate 80, benzalkonium chloride, purified water.

3. PHARMACEUTICAL FORM

A metered-dose nasal spray.
basic physical and chemical properties: white to off-white powder opaque suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of seasonal allergic or perennial rhinitis in adults and children 2 years of age and older.
- In patients 12 years of age and older who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment may be initiated up to 2-4 weeks prior to the anticipated start of the pollen season.
- Treatment of symptoms associated with acute rhinosinusitis in patients 12 years of age and older without signs of severe bacterial infection.
- Treatment of nasal polyps and associated symptoms including congestion and loss of smell in adult patients 18 years of age and older.

4.2 Posology and method of administration

Treatment of seasonal or perennial allergic rhinitis: for adults (including geriatric patients) and children 12 years of age and older the recommended preventive and therapeutic dose is 2 actuations (50 micrograms/actuation) in each nostril once daily (total dose 200 micrograms). Once symptoms are controlled, dose reduction to one actuation in each nostril (total dose 100 micrograms) may be effective for maintenance.
If symptoms are inadequately controlled at the recommended therapeutic dose, the daily dose may be increased to a maximum daily dose: of 4 actuations in each nostril once daily (total dose 400 micrograms). Dose reduction is recommended following control of symptoms.
This medicinal product demonstrates a clinically significant onset of action within 12 hours after the first dose in some patients with seasonal allergic rhinitis. Therefore, the patient should continue regular use to achieve clinical effect. The full benefit of treatment may not be achieved in the first 48 hours.
Treatment with NASONEX Nasal Spray may need to be initiated some days before the expected start of the pollen season in patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis. For children between the ages of 2 and 11 years the usual recommended dose is one actuation (50 micrograms) in each nostril once daily (total dose 100 micrograms).
Acute rhinosinusitis. For adults (including geriatric patients) and children 12 years of age and older the recommended therapeutic dose is 2 actuations (50 micrograms/actuation) in each nostril twice daily (total dose 400 micrograms).
Nasal polyps. For patients 18 years of age (including geriatric patients) the recommended dose is 2 actuations (50 micrograms/actuation) in each nostril once a day (total dose 200

micrograms). If after 5 to 6 weeks symptoms are inadequately controlled, the dose may be increased to a daily dose of two sprays in each nostril twice daily (total daily dose of 400 micrograms). The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. If no improvement in symptoms is seen after 5 to 6 weeks of administration, the patient should be re-evaluated, and treatment strategy reconsidered.

Preparing your nasal spray for use

Your Nasonex Nasal Spray has a dust cap which protects the nozzle and keeps it clean. Remember to take this off before using the spray and to replace it after use.

If you are using the spray for the first time you need to 'prime' the bottle by pumping the spray 10 times until a fine mist is produced:

1. Gently shake the bottle.
2. Put your forefinger and middle finger either side of the nozzle and your thumb underneath the bottle. **Do Not** pierce the nasal applicator.
3. Point the nozzle away from you and then press down with your fingers to pump the spray 10 times until a fine mist is produced.

If you have not used the spray for 14 days or more, you need to "re-prime" the bottle by pumping the spray 2 times until a fine mist is produced.

How to use your nasal spray

1. Shake the bottle gently and remove the dust cap. (Figure 1)
2. Gently blow your nose.



3. Close one nostril and put the nozzle into the other nostril as shown. (Figure 2) Tilt your head forward slightly, keeping the bottle upright.
4. Start to breathe in gently or slowly through your nose and whilst you are breathing in squirt a spray of fine mist into your nose by pressing down ONCE with your fingers.
5. Breathe out through your mouth. Repeat step 4 to inhale a second spray in the same nostril if applicable.
6. Remove the nozzle from this nostril and breathe out through the mouth.
7. Repeat steps 3 to 6 for the other nostril (Figure 3).



After using the spray, wipe the nozzle carefully with a clean handkerchief or tissue and replace the dust cap.



<u>Cleaning your nasal spray</u>

- It is important to clean your nasal spray regularly, otherwise it may not work properly.
- Remove the dust cap and gently pull off the nozzle.
- Wash the nozzle and dust cap in warm water and then rinse under a running tap.
- **Do not try to unblock the nasal applicator by inserting a pin or other sharp object as this will damage the applicator and cause you not to get the right dose of medicine.**
- Allow the dust cap and nozzle to dry in a warm place.
- Push the nozzle back onto the bottle and replace the dust cap.

- The spray will need to be primed again with 2 sprays when first used after cleaning.

If you use more Nasonex than you should
Tell your doctor if you accidentally use more than you were told.
If you use steroids for a long time or in large amounts they may, rarely, affect some of your hormones. In children this may affect growth and development.

If you forget to use Nasonex
If you forget to use your nasal spray at the right time, use it as soon as you remember, then carry on as before. Do not take a double dose to make up for a forgotten dose.

4.3 Contraindications

Hypersensitivity to the active substance, mometasone furoate, or to any of the excipients.

NASONEX Nasal Spray should not be used in the presence of untreated localized infection involving the nasal mucosa, such as herpes simplex.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred.

4.4 Special warnings and precautions for use

Immunosuppression
NASONEX Nasal Spray should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, or systemic viral infections.
Patients receiving corticosteroids who are potentially immunosuppressed should be warned of the risk of exposure to certain infections (e.g., chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs.
Local Nasal Effects
Following 12 months of treatment with NASONEX Nasal Spray in a study of patients with perennial rhinitis, there was no evidence of atrophy of the nasal mucosa; also, mometasone furoate tended to reverse the nasal mucosa closer to a normal histological phenotype. Nevertheless, patients using NASONEX Nasal Spray over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localized fungal infection of the nose or pharynx develops, discontinuation of NASONEX Nasal Spray therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuation of NASONEX Nasal Spray.
Nasonex is not recommended in case of nasal septum perforation.
In clinical studies, epistaxis occurred at a higher incidence compared to placebo. Epistaxis was generally self-limiting and mild in severity.
NASONEX Nasal Spray contains benzalkonium chloride which may cause nasal irritation.
Systemic Effects of Corticosteroids
Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioral effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).
Following the use of intranasal corticosteroids, instances of increased intraocular pressure have

been reported.
Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.
Patients who are transferred from long-term administration of systemically active corticosteroids to NASONEX Nasal Spray require careful attention. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of HPA axis function. If these patients exhibit signs and symptoms of adrenal insufficiency or symptoms of withdrawal (e.g., joint and/or muscular pain, lassitude, and depression initially) despite relief from nasal symptoms, systemic corticosteroid administration should be resumed, and other modes of therapy and appropriate measures instituted. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.
Treatment with higher than recommended doses may result in clinically significant adrenal suppression.
If there is evidence for higher than recommended doses being used, then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.
Nasal Polyps
The safety and efficacy of NASONEX Nasal Spray has not been studied for use in the treatment of unilateral polyps, polyps associated with cystic fibrosis, or polyps that completely obstruct the nasal cavities.
Unilateral polyps that are unusual or irregular in appearance, especially if ulcerating or bleeding, should be further evaluated.
Effect on Growth in Pediatric Population
It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a pediatric specialist.
Non-nasal Symptoms
Although NASONEX Nasal Spray will control the nasal symptoms in most patients, the concomitant use of appropriate additional therapy may provide additional relief of other symptoms, particularly ocular symptoms.
Pediatric patients. In placebo-controlled clinical trials in which pediatric patients were administered NASONEX 100 micrograms daily for one year, no reduction in growth velocity was observed. However, long-term effects of intranasal/inhalation steroids were not well-established. Children treated with corticosteroids for a long time should be under careful medical supervision for growth and development.
Safety and efficacy of NASONEX for the treatment of nasal polyposis in children and adolescents under 18 years of age, rhinosinusitis symptoms in children under 12 years of age, seasonal and perennial allergic rhinitis in children under 2 years of age have not been studied.
High doses or prolong treatment with corticosteroids can result in systemic adverse effects, including growth retardation in children. Long-term effects of intranasal/inhalation steroids in children were not fully established. Children treated with corticosteroids for a long time should be under careful medical supervision for growth and development. In a clinical trial in which 49 pediatric patients were administered Nasonex 100 micrograms daily for one year, no reduction in growth velocity was observed.

4.5 Interactions with other medicaments and other forms of interaction

A clinical interaction study was conducted with loratadine. No interactions were observed.
Mometasone furoate is metabolized by CYP3A4. Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, ritonavir, cobicistat-containing products) may lead to increased plasma concentrations of corticosteroids and potentially increase the risk for systemic corticosteroid side-effects. Consider the benefit of coadministration versus the potential risk of systemic corticosteroid effects, in which case patients should be monitored for systemic corticosteroid side-effects.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of mometasone furoate in pregnant women. Studies in animals have shown reproductive toxicity. As with other nasal corticosteroid preparations, NASONEX Nasal Spray should not be used in pregnancy unless the potential benefit to the mother justifies any potential risk to the mother, foetus or infant. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.
Lactation
It is unknown whether mometasone furoate is excreted in human milk. As with other nasal corticosteroid preparations, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from NASONEX Nasal Spray therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Summary of the safety profile
Epistaxis was generally self-limiting and mild in severity and occurred at a higher incidence compared to placebo (5%), but at a comparable or lower incidence when compared to the active control nasal corticosteroids studied (up to 15%) as reported in clinical studies for allergic rhinitis. The incidence of all other adverse events was comparable with that of placebo. In patients treated for nasal polyposis, the overall incidence of adverse events was similar to that observed for patients with allergic rhinitis.
Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Tabulated list of adverse reactions
Treatment related adverse reactions (≥1%) reported in clinical trials in patients with allergic rhinitis or nasal polyposis and post-marketing regardless of indication are presented in Table 1. Adverse reactions are listed according to MedDRA primary system organ class. Within each system organ class, adverse reactions are ranked by frequency. Frequencies were defined as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100). The frequency of post-marketing adverse events are considered as "not known (cannot be estimated from the available data)".

Table 1: Treatment-related adverse reactions reported by system organ class and frequency			
	Very common	Common	Not known
Infections and infestations		Pharyngitis Upper respiratory tract infection†	
Immune system disorders			Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm, and dyspnoea
Nervous system disorders		Headache	
Eye disorders			Glaucoma Increased intraocular pressure Cataracts Vision blurred
Respiratory, thoracic and mediastinal disorders	Epistaxis*	Epistaxis Nasal burning Nasal irritation Nasal ulceration	Nasal septum perforation
Gastrointestinal disorders		Throat irritation*	Disturbances of taste and smell

*recorded for twice daily dosing for nasal polyposis

†recorded at uncommon frequency for twice daily dosing for nasal polyposis

Pediatric population
In the pediatric population, the incidence of recorded adverse events in clinical studies, e.g., epistaxis (6%), headache (3%), nasal irritation (2%) and sneezing (2%) was comparable to placebo.

4.9 Overdose

Symptoms
Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA axis function.

Management
Because the systemic bioavailability of NASONEX Nasal Spray is <1%, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacodynamics.
Mechanism of action
Mometasone furoate is a topical glucocorticosteroid with local anti-inflammatory properties at doses that are not systemically active.
It is likely that much of the mechanism for the anti-allergic and anti-inflammatory effects of mometasone furoate lies in its ability to inhibit release of mediators of allergic reactions. Mometasone furoate significantly inhibits the release of leukotrienes from leucocytes of allergic patients. In cell culture, mometasone furoate demonstrated high potency in inhibition of synthesis and release of IL-1, IL-5, IL-6 and TNFα; it is also a potent inhibitor of leukotriene production. In addition, it is an extremely potent inhibitor of production of the Th_2 cytokines, IL-4 and IL-5, from human $CD4^+$ T-cells.
Pharmacodynamic effects.
In studies utilizing nasal mucosal antigen challenge, NASONEX Nasal Spray has shown anti-inflammatory activity in both the early- and late- phases allergic responses. This has been demonstrated by decrease (vs placebo) in histamine and eosinophil activity and reductions (vs baseline) in eosinophils, neutrophils, and epithelial cell adhesion proteins.
In 28% of the patients with seasonal allergic rhinitis, NASONEX Nasal Spray demonstrated a clinically significant onset of action within 12 hours after the first dose. The median (50%) onset time of relief was 35.9 hours.
Pediatric population
In a placebo-controlled clinical trial in which pediatric patients (n=49/group) were administered NASONEX Nasal Spray 100 micrograms daily for one year, no reduction in growth velocity was observed.
There are limited data available on the safety and efficacy of NASONEX Nasal Spray in the pediatric population aged 3 to 5 years, and an appropriate dosage range cannot be established. In a study involving 48 children aged 3 to 5 years treated with intranasal mometasone furoate 50, 100 or 200 mkg/day for 14 days, there was no significant differences from placebo in the mean change in plasma cortisol level in response to the tetracosactrin stimulation test.

5.2 Pharmacokinetic properties

Mometasone furoate, administered as an aqueous nasal spray, has a systemic bioavailability of <1% in plasma, using a sensitive assay with a lower quantitation limit of 0.25 pg/ml.
Distribution
Not applicable as mometasone is poorly absorbed via the nasal route.
Biotransformation
The small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism.
Elimination
Absorbed mometasone furoate is extensively metabolized and the metabolites are excreted in urine and bile.

6. PHARMACEUTICAL PARTICULARS

6.1 Incompatibilities

Not applicable

6.2 Shelf life

3 years

6.3 Special precautions for storage

Do not store above 25°C, keep out of reach of children. Do not freeze.
Do not use after expiry date.

6.4 Nature and contents of container

For 18 g of the suspension is placed in an oval, opaque white colored polyethylene bottle, on the neck of which the measuring spray dose is fixed, the pump-sprayer closing with a protective cap. The amount of the drug contained in the vial ensures the spraying of 140 doses of 50 μg each. Vial with instructions for use in a cardboard box.

6.5 Special precautions for disposal and other handling

N/A

7. MARKETING AUTHORISATION HOLDER IN ARMENIA

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