Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nasonex 50 micrograms/actuation Nasal Spray Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered actuation contains 50 micrograms mometasone furoate (as the monohydrate)
Excipient: includes benzalkonium chloride

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal Spray Suspension

Product imported from the Greece
White to off white opaque suspension

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Nasonex Nasal Spray is indicated for use in adults and children 12 years of age and older to treat the symptoms of seasonal allergic or perennial rhinitis.

Nasonex Nasal Spray is also indicated for use in children 6 to 11 years of age to treat the symptoms of seasonal allergic or perennial allergic rhinitis.

In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with Nasonex Nasal Spray may be initiated up to four weeks prior to the anticipated start of the pollen season.

Nasonex Nasal Spray is indicated for the treatment of nasal polyps in adults 18 years of age

4.2 Posology and method of administration

After initial priming of the Nasonex Nasal Spray pump (10 actuations, until a uniform spray is observed), each actuation delivers approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms mometasone furoate. If the spray pump has not been used for 14 days or longer, it should be reprimed with 2 actuations, until a uniform spray is observed, before next use.

<u>Seasonal or Perennial Allergic Rhinitis</u>
Adults (including geriatric patients) and children 12 years of age and older: The usual recommended dose is two 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, the dose may be increased to a maximum daily dose of four actuations in each nostril once daily (total dose 400 micrograms). Dose reduction is recommended following control of symptoms.
Children between the ages of 6 and 11 years: The usual recommended dose is one actuation (50 micrograms/actuation) in each nostril once daily (total dose 100 micrograms).
Nasonex Nasal Spray demonstrated a clinically significant onset of action within 12 hours after the first dose in some patients with seasonal allergic rhinitis; however, full benefit of treatment may not be achieved in the first 48 hours. Therefore, the patient should continue regular use to achieve full therapeutic benefit.

Nasal Polyposis
The usual recommended starting dose for polyposis is two actuations (50 micrograms/actuation) in each nostril once daily (total daily dose of 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 twice daily administration, alternative therapies should be considered.

Efficacy and Safety studies of Nasonex Nasal Spray for the treatment of nasal polyposis were four months in duration.

Prior to administration of the first dose, shake container well and actuate pump 10 times (until a uniform spray is obtained). If pump is not used for 14 days or longer, reprime the pump with 2 actuations until a uniform spray is observed. Shake container well before each use. The bottle should be discarded after the labelled number of actuations or within 2 months of first use.

4.3 Contraindications

Hypersensitivity to any ingredients of Nasonex Nasal Spray.
Nasonex Nasal Spray should not be used in the presence of untreated localised infection involving the nasal mucosa.

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

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, systemic viral infections or ocular herpes simplex.

Following 12 months of treatment with Nasonex Nasal Spray there was no evidence of atrophy of the nasal mucosa; also, mometasone furoate tended to reverse the nasal mucosa closer to a normal histologic phenotype. As with any long-term treatment, patients using Nasonex Nasal Spray over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localised fungal infection of the nose or pharynx develops, discontinuance of Nasonex Nasal Spray therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing Nasonex Nasal Spray.

Although Nasonex 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.

There is no evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression following prolonged treatment with Nasonex Nasal Spray. However, 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, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted.

During transfer from systemic corticosteroids to Nasonex Nasal Spray some patients may experience symptoms of withdrawal from systemically active corticosteroids (e.g., joint and/or muscular pain, lassitude, and depression initially) despite relief from nasal symptoms and will require encouragement to continue Nasonex Nasal Spray therapy. Such transfer may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

The safety and efficacy of Nasonex 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.

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.

Following the use of intranasal corticosteroids, instances of nasal septum perforation or increased intraocular pressure have been reported very rarely.

Safety and efficacy of Nasonex Nasal Spray for the treatment of nasal polyposis in children and adolescents under 18 years of age have not been studied.

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 behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses.

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 paediatric specialist.

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.

4.5 Interaction with other medicinal products and other forms of interaction

(See 4.4 Special warnings and special precautions for use with systemic corticosteroids)
A clinical interaction study was conducted with loratadine. No interactions were observed.

4.6 Fertility, pregnancy and lactation

There are no adequate or well-controlled studies in pregnant women. Following intranasal administration of the maximal recommended clinical dose, mometasone plasma concentrations are not measurable; thus foetal exposure is expected to be negligible and the potential for reproductive toxicity, very low. As with other nasal corticosteroid preparations, NASONEX Nasal Spray should not be used in pregnancy or lactation 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.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Treatment-related adverse events reported in clinical studies for allergic rhinitis in adult and adolescent patients are shown below (Table 1).

Table 1: *Allergic Rhinitis*-Treatment Related Undesirable Effects for Nasonex Nasal Spray very common (> 1/10); common (> 1/100, < 1/10); uncommon (> 1/1000, < 1/100); rare (> 1/10,000, < 1/1000); very rare (< 1/10,000)	
Respiratory, thoracic and mediastinal disorders Common:	Epistaxis, pharyngitis, nasal burning, nasal irritation, nasal ulceration
General disorders and administration site conditions Common:	Headache

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%). The incidence of all other effects was comparable with that of placebo.

In the paediatric population, the incidence of adverse effects, e.g., epistaxis (6%), headache (3%), nasal irritation (2%) and sneezing (2%) was comparable to placebo.

In patients treated for nasal polyposis, the overall incidence of adverse events was comparable to placebo and similar to that observed for patients with allergic rhinitis. Treatment-related adverse events reported in ≥1% of patients in clinical studies for polyposis are shown below (Table 2)

Table 2: *Polyposis* – treatment Related Undesirable Effects ≥1% for Nasonex Nasal Spray very common (> 1/10); common (> 1/100, < 1/10); uncommon (> 1/1000, < 1/100); rare (> 1/10,000, < 1/1000); very rare (< 1/10,000)		
	(200 mcg once a day)	(200 mcg twice a day)
Respiratory, thoracic and mediastinal disorders Upper respiratory tract infection	common	uncommon
Epistaxis	common	very common
Gastrointestinal disorders Throat irritation	---	common
General disorders and administration site conditions Headache	common	common

In patients treated for acute rhinosinusitis, the incidence of epistaxis for NASONEX was 3.3% vs. 2.6% for placebo and similar to that observed for patients treated with allergic rhinitis.
Rarely, immediate hypersensitivity reactions, including bronchospasm and dyspnoea, may occur after intranasal administration of mometasone furoate monohydrate. Very rarely, anaphylaxis and angiodema have been reported.

Disturbances of taste and smell have been reported very rarely.

Systematic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

4.9 Overdose

Because of the negligible (≤0.1%) systemic bioavailability of Nasonex, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage. Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of HPA axis function.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and Other Nasal Preparations for Topical Use-Corticosteroids,
ATC code: R01A D09

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 the 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 the production of the Th2 cytokines, IL-4 and IL−5, from human CD4+ T-cells.

In studies utilising nasal antigen challenge, NASONEX Nasal Spray has shown anti-inflammatory activity in both the early- and late- phase allergic responses. This has been demonstrated by decreases (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.

In two trials with 1954 patients, Nasonex Nasal Spray 200 mcg administered twice daily-demonstrated significant improvement in symptoms associated with acute rhinosinusitis compared to placebo as evaluated by the Major Symptom Score (MSS) composite of symptoms (facial pain/pressure/tenderness, sinus headache, rhinorrhea, post nasal drip, and nasal congestion/stuffiness) during the 15 day treatment period (P02683 $p < 0.001$; P02692 $p = 0.038$). A 500 mg three times a day amoxicillin arm was not significantly different from placebo in reducing these symptoms of acute rhinosinusitis as evaluated by the MSS.

The SNOT-20 HRQL showed a significant level of benefit at the 200 mcg twice daily dose of mometasone furoate vs. placebo ($p=0.047$). Treatment duration beyond 15 days was not evaluated in acute rhinosinusitis.

In a placebo-controlled clinical trial in which paediatric patients (n=49/group) were administered NASONEX 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 in the paediatric 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 μg/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 negligible (≤0.1%) systemic bioavailability and is generally undetectable in plasma, despite the use of a sensitive assay with a lower quantitation limit of 50 pg/ml; thus, there are no relevant pharmacokinetic data for this dosage form.

Mometasone furoate suspension is very poorly absorbed from the gastrointestinal tract, and the small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism prior to excretion in urine and bile.

5.3 Preclinical safety data

No toxicological effects unique to mometasone furoate exposure were demonstrated. All observed effects are typical of this class of compounds and are related to exaggerated pharmacologic effects of glucocorticoids.

Preclinical studies demonstrate that mometasone furoate is devoid of androgenic, antiandrogenic, estrogenic or antiestrogenic activity but, like other glucocorticoids, it exhibits some antiuterotrophic activity and delays vaginal opening in animal models at high oral doses of 56 mg/kg/day and 280 mg/kg/day.

Like other glucocorticoids, mometasone furoate showed a clastogenic potential in-vitro at high concentrations. However, no mutagenic effects can be expected at therapeutically relevant doses.

In studies of reproductive function, subcutaneous mometasone furoate, at 15 micrograms/kg prolonged gestation and prolonged and difficult labour occurred with a reduction in offspring survival and body weight or body weight gain. There was no effect on fertility.
Like other glucocorticoids, mometasone furoate is a teratogen in rodents and rabbits. Effects noted were umbilical hernia in rats, cleft palate in mice and gallbladder agenesis, umbilical hernia, and flexed front paws in rabbits. There were also reductions in maternal body weight gains, effects on foetal growth (lower foetal body weight and/or delayed ossification) in rats, rabbits and mice, and reduced offspring survival in mice.

The carcinogenicity potential of inhaled mometasone furoate (aerosol with CFC propellant and surfactant) at concentrations of 0.25 to 2.0 micrograms/l was investigated in 24−month studies in mice and rats. Typical glucocorticoid-related effects, including several non-neoplastic lesions, were observed. No statistically significant dose-response relationship was detected for any of the tumour types.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dispersible cellulose BP 65 cps (microcrystalline cellulose and carmellose sodium)
Glycerol
Sodium citrate
Citric acid monohydrate
Polysorbate 80
Benzalkonium chloride
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date of this product shall be the date shown on the container and outer package of the product as marketed in the country of origin.

Use within 2 months of first use.

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze

6.5 Nature and contents of container

Nasal spray which contains 18g (140 metered actuations) of product formulation in a white bottle, in an overlabelled cardboard carton.
Each package contains 1 nasal spray.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

G & A Licensing Ltd
Ballymurray
Co. Roscommon
Ireland

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1447/42/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th August 2010

10 DATE OF REVISION OF THE TEXT

January 2012