Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Rhinex Relief 50 micrograms/actuation Nasal spray, suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each actuation of the pump delivers a metered dose of 50 micrograms of mometasone furoate (as mometasone furoate monohydrate).

The total weight of one actuation is 100 mg

Excipient(s) with known effect
This medicinal product contains 0.02 mg of benzalkonium chloride per actuation.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal spray, suspension

White, homogenous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Rhinex Relief is indicated for use in adults to treat the symptoms of seasonal allergic rhinitis, after a seasonal allergic rhinitis has been diagnosed by a physician.

4.2 Posology and method of administration

Posology

Adults (including the elderly)
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.

Rhinex Relief 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.

Treatment with Rhinex Relief 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.

If there is no/insufficient improvement of the symptoms after a maximum of 14 days of use, medical advice is required. Rhinex Relief should not be used continuously for longer than three months without medical advice.

Paediatric population

Rhinex Relief should not be used in children and adolescents below the age of 18.

Method of administration

For nasal use.

Prior to administration of the first dose patients should be advised to shake the bottle well and to actuate the pump 10 times (until a uniform spray is obtained). If the pump is not used for 14 days or longer, the pump should be reprimed with 2 actuations until a uniform spray is observed, before next use.

The bottle should be shaken well before each use. The medicinal product should be discarded after the labelled number of actuations or within 2 months of first use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Rhinex Relief must not be used in the presence of untreated localised 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 must not use a nasal corticosteroid until healing has occurred.

4.4 Special warnings and precautions for use

Immunosuppression
Rhinex Relief 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
Rhinex Relief is not recommended in case of nasal septum perforation (see section 4.8).

In clinical studies, epistaxis occurred at a higher incidence compared to placebo. Epistaxis was generally self-limiting and mild in severity (see section 4.8).

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, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression.

Following the use of intranasal corticosteroids, instances of increased intraocular pressure have been reported (see section 4.8).

Patients who are transferred from long-term administration of systemically active corticosteroids to Rhinex Relief 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.

Non-nasal symptoms
Although Rhinex Relief 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.

Visual disturbance

Visual disturbance may be reported with systemic and topical 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 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.

Rhinex Relief nasal spray contains benzalkonium chloride which may cause irritation or swelling inside the nose, especially if used for a long time.

4.5 Interaction with other medicinal products and other forms of interaction

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

A clinical interaction study was conducted with loratadine. No interactions were observed.

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 (see section 5.3). As with other nasal corticosteroid preparations, Rhinex Relief 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.

Breast-feeding
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 Rhinex Relief therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
There are no clinical data concerning the effect of mometasone furoate on fertility. Animal studies have shown reproductive toxicity, but no effects on fertility (see section 5.3)**.**

4.7 Effects on ability to drive and use machines

Rhinex Relief has no known influence on the ability to drive and use machines.

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.

Systemic effects of nasal corticosteroids may occur, particularly when used 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 Blurred vision (see also section 4.4)
Respiratory, thoracic and mediastinal disorders		Epistaxis Nasal burning Nasal irritation Nasal ulceration	Nasal septum perforation
Gastrointestinal disorders			Disturbances of taste and smell

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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 Rhinex Relief 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

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use-corticosteroids
ATC Code: R01A D09

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 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.

Pharmacodynamic effects
In studies utilising nasal antigen challenge, mometasone furoate 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, mometasone furoate 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.

5.2 Pharmacokinetic properties

Absorption
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.

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

Microcrystalline cellulose
Carmellose sodium
Glycerol
Citric acid monohydrate
Sodium citrate dihydrate
Polysorbate 80
Benzalkonium chloride
Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

After first opening of the bottle:
2 months

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and contents of container

White high density polyethylene (HDPE) bottle fitted with LDPE/PP nasal spray pump with a blue protective cap.
Do not unscrew the nasal spray pump system.

Pack sizes:
1 bottle containing 10 g nasal spray, suspension, corresponding to 60 actuations
1 bottle containing 17 g nasal spray, suspension, corresponding to 120 actuations
1 bottle containing 18 g nasal spray, suspension, corresponding to 140 actuations
2 bottles containing 18 g nasal spray, suspension, corresponding to 140 actuations each
3 bottles containing 18 g nasal spray, suspension, corresponding to 140 actuations each

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/279/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th July 2018
Date of last renewal: 8th May 2023

10 DATE OF REVISION OF THE TEXT

April 2023