Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Rhinaspray 21 micrograms per metered dose, Nasal Spray Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each valve actuation (70 microlitres) delivers 21 micrograms of ipratropium bromide as ipratropium bromide monohydrate.

Excipient(s) with known effect:
Each 70 microlitres of solution contains 17.5 micrograms of benzalkonium chloride (see section 4.4).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal spray, solution (nasal spray)
A clear, colourless or almost colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Rhinaspray is indicated for the symptomatic relief of rhinorrhoea in allergic and non-allergic rhinitis.

4.2 Posology and method of administration

Adults: Two sprays (42 micrograms) in each nostril administered 2 - 3 times a day.

Children: The use of Rhinaspray has not been evaluated in children, and therefore is not recommended for use in patients below the age of 12 years.

Administration

To obtain the best results from your nasal spray follow the simple instructions given below. If you are unclear about how to use the nasal spray ask your doctor or pharmacist to explain.

1. Remove the dust cap.

2. The nasal spray pump must be primed before Rhinaspray is used for the first time. To prime the pump, hold the bottle with your thumb at the base and your index and middle fingers on the white shoulder area. Make sure the bottle points upright and away from your eyes. Press your thumb firmly and quickly against the bottle seven times. The pump is now primed and can be used. Your pump will hold its prime for up to 24 hours. If you have not used your pump for more than 24 hours, you will need to prime it again before use. Reprime the pump as before, but this time only two sprays are required. If you have not used your pump for more than 7 days reprime using 7 sprays.

3. Blow your nose to clear your nostrils if necessary.

4. Close one nostril by gently placing your fingers against the side of your nose. Tilt your head slightly forward and, keeping the bottle upright, insert the nasal tip into the other nostril. Point the tip toward the back and outer side of the nose.

Press firmly and quickly upwards with the thumb at the base while holding the white shoulder portion of the pump between your index and middle fingers. Following each spray, sniff deeply and breathe out through the mouth.

After spraying the nostril and removing the unit, tilt the head backwards for a few seconds to let the spray spread over the back of the nose.

5. Repeat step 4 in the other nostril.

6. Replace the cap.

Avoid spraying Rhinaspray in or around your eye. Should this occur, immediately flush your eye with cold tap water for several minutes. If you accidentally spray Rhinaspray in your eyes, you may experience a temporary blurring of vision and increased sensitivity to light, which may last a few hours. Follow your doctor's instructions about when and how to take your medicine and always read the label.

If the nasal tip becomes clogged, remove the clear plastic dust cap. Hold the nasal tip under warm running water for about a minute. Dry the nasal tip, reprime the nasal spray pump and replace the plastic dust cap.

4.3 Contraindications

Rhinaspray is contraindicated in patients known to be hypersensitive to atropine or its derivatives or to any other component of the product.

4.4 Special warnings and precautions for use

Immediate hypersensitivity reactions following the use of Rhinaspray have been demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal oedema and anaphylaxis.

Caution is advocated in the use of anticholinergic agents in patients predisposed to narrow-angle glaucoma, or with pre-existing urinary outflow tract obstruction (e.g. prostatic hyperplasia or bladder-outflow obstruction).

As patients with cystic fibrosis may be prone to gastro-intestinal motility disturbances, Rhinaspray, as with other anticholinergics, should be used with caution in these patients.

There have been isolated reports of ocular complications (i.e. mydriasis, increased intraocular pressure, angle-closure glaucoma, eye pain) when aerosolised ipratropium bromide, either alone or in combination with an adrenergic beta$_2$-agonist, has come into contact with the eyes. Thus patients must be instructed in the correct administration of Rhinaspray.

Eye pain or discomfort, blurred vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema may be signs of acute narrow-angle glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately.

Benzalkonium chloride

Rhinaspray contains 17.5 micrograms benzalkonium chloride in each valve actuation (70 microlitres), which is equivalent to 0.25 mg/mL.
Long-term use may cause oedema of the nasal mucosa.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of Rhinaspray with other drugs commonly prescribed for perennial rhinitis i.e. antihistamines, decongestants or nasal steroids does not increase the incidence of nasal or non-nasal side effects.

Rhinaspray is minimally absorbed into the systemic circulation; nonetheless, there is some potential for additive interaction with other concomitantly administered anticholinergic medications, including ipratropium bromide-containing aerosols for oral inhalation.

4.6 Fertility, pregnancy and lactation

The safety of Rhinaspray during human pregnancy has not been established. The benefits of using Rhinaspray during a confirmed or suspected pregnancy must be weighed against the possible hazards to the unborn child. Preclinical studies have shown no embryotoxic or teratogenic effects following inhalation or intranasal application at doses considerably higher than those recommended in man.

It is not known whether ipratropium bromide is excreted into breast milk. It is unlikely that ipratropium bromide would reach the infant to an important extent, however caution should be exercised when Rhinaspray is administered to nursing mothers.

Preclinical studies performed with ipratropium bromide showed no adverse effect on fertility. Clinical data on fertility are not available for ipratropium bromide.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness, accommodation disorder, mydriasis and blurred vision during treatment with Rhinaspray. Therefore, caution should be recommended when driving a car or operating machinery. If patients experience the above mentioned side effects they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

Many of the listed undesirable effects can be assigned to the anticholinergic properties of Rhinaspray. As with all topical therapy Rhinaspray may show symptoms of local irritation. Adverse drug reactions were identified from data obtained in clinical trials and pharmacovigilance during post approval use of the drug.

The most frequent side effects reported in clinical trials were epistaxis, nasal dryness, headache, nasal discomfort and throat irritation

Frequencies
Very common ≥ 1/10
Common ≥ 1/100 < 1/10
Uncommon ≥ 1/1,000< 1/100
Rare ≥ 1/10,000 < 1/1,000
Very rare < 1/10,000

Immune system disorders

Hypersensitivity	Uncommon
Anaphylactic reaction	Uncommon

Nervous system disorders

Headache	Common
Dizziness	Uncommon

Eye disorders

Vision blurred	Uncommon
Mydriasis [(1)]	Uncommon
Intraocular pressure increased [(1)]	Uncommon
Glaucoma [(1)]	Uncommon
Eye pain [(1)]	Uncommon
Halo vision	Uncommon
Conjunctival hyperaemia	Uncommon
Corneal oedema	Uncommon
Accommodation disorder	Uncommon

Cardiac Disorders

Supraventricular tachycardia	Uncommon
Atrial fibrillation	Uncommon
Heart rate increased	Uncommon
Palpitations	Rare

Respiratory, Thoracic and Mediastinal Disorders

Epistaxis	Common

Nasal dryness	Common
Throat irritation	Common
Nasal discomfort	Common
Dry Throat	Uncommon
Bronchospasm	Uncommon
Laryngospasm	Uncommon
Pharyngeal Oedema	Uncommon

Gastro-intestinal Disorders

Dry mouth	Uncommon
Nausea	Uncommon
Gastrointestinal motility disorder	Uncommon
Stomatitis	Uncommon
Oedema mouth	Uncommon

Skin and subcutaneous tissue disorders

Rash	Uncommon
Angioedema	Uncommon
Urticaria	Rare
Pruritus	Rare

Renal and Urinary Disorders

Urinary retention[(2)]	Uncommon

[(1)] ocular complications have been reported when aerolised ipratropium bromide, either alone or in combination with an adrenergic beta$_2$-agonist, has come into contact with the eyes– see section 4.4.
[(2)]the risk of urinary retention may be increased in patients with pre-existing urinary outflow tract obstruction.

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, Website: www.hpra.ie.

4.9 Overdose

No symptoms specific to overdosage have been encountered. In view of the wide therapeutic window and topical administration of Rhinaspray, no serious anticholinergic symptoms are to be expected. As with other anticholinergics, dry mouth, visual accommodation disorder and tachycardia would be the expected symptoms and signs of overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ipratropium bromide, a quaternary ammonium derivative of atropine is an anticholinergic drug.

Ipratropium bromide administered intranasally has a localised parasympathetic blocking action, which reduces watery hypersecretion from mucosal glands in the nose.

Nasal provocation trials in perennial rhinitis patients (n=44) using Rhinaspray showed a dose-dependent increase in inhibition of methacholine-induced nasal secretion with an onset of action within 15 minutes. The duration of action of Rhinaspray was also dose-dependent.

Controlled clinical trials showed that intranasal ipratropium bromide is effective for controlling the severity and duration of rhinorrhoea in patients with allergic and non-allergic perennial rhinitis.

Two placebo controlled studies of Rhinaspray administered twice a day in adults and children, allergic and non allergic perennial rhinitis patients showed that Rhinaspray 42 micrograms per nostril was more effective in non-allergic than in allergic perennial rhinitis patients.

Ipratropium bromide administration via nasal aerosol had no marked effect on sense of smell, nasal mucociliary transport, ciliary beat frequency, or the air-conditioning capacity of the nose.

5.2 Pharmacokinetic properties

Ipratropium is a quaternary amine that is rapidly absorbed from the nasal mucosa, however to a low extent. In healthy volunteers approximately 10% of a nasally given dose was excreted unchanged in the urine over 24 hours.
The systemic absorption of ipratropium across inflamed nasal mucosa was not altered due to experimentally induced cold, as estimated from the renal excretion of ipratropium over 24 hours. After a single dose or 4 times daily dosing 6-8% of ipratropium was excreted unchanged in healthy as well as in infected volunteers. Following chronic dosing in rhinitis patients the amount of unchanged ipratropium excreted in the urine over a 24-hour period at steady state was 4-6% of the dose. Assuming the literature value of 50% of the dose excreted into the urine following intravenous administration, the estimated bioavailability of ipratropium following nasal administration is less than 20%.

Kinetic parameters describing the disposition of ipratropium were calculated from plasma concentrations after i.v. administration.

A rapid biphasic decline in plasma concentrations is observed. The apparent volume of distribution at steady-state (Vdss) is approximately 176L (2.4L/kg). The drug is minimally (less than 20%) bound to plasma proteins. The quarternary amine of the ipratropium ion does not cross the blood-brain barrier.

The half-life of the terminal elimination phase is approximately 1.6 hours.

Ipratropium has a total clearance of 2.3 L/min and a renal clearance of 0.9 L/min. After intravenous administration approximately 60% of a dose is metabolised; probably the major portion in the liver by oxidation.

In an excretion balance study cumulative renal excretion (6 days) of drug-related radioactivity (including parent compound and all metabolites) accounted for 72.1% after intravenous administration, 9.3% after oral administration and 3.2% after inhalation. Total radioactivity excreted via the faeces was 6.3% following intravenous application, 88.5% following oral dosing and 69.4% after inhalation. Therefore the dominant excretion of drug-related radioactivity occured via the kidneys. The main urinary metabolites bind poorly to the muscarinic receptor and have to be regarded as ineffective.

5.3 Preclinical safety data

The toxicity of ipratropium bromide has been investigated extensively in the following types of studies: acute, subchronic and chronic toxicity, carcinogenicity, reproductive toxicity and mutagenicity via oral, intravenous, subcutaneous, intranasal and/or inhalation routes. Based on these toxicity studies, the probability of systemic anticholinergic side effects decreases in the following order: intravenous > subcutaneous > oral > inhalation > intranasal.

Pre-clinically, ipratropium bromide was found to be well-tolerated. Two-year carcinogenicity studies in rats and mice have revealed no carcinogenic activity at doses up to approximately 1200 times the maximum recommended human daily dose for Rhinaspray. Results of various mutagenicity tests were negative.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Benzalkonium Chloride
Disodium Edetate
Purified Water
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: 2 years
Once opened: Discard twelve months after first priming the nasal spray pump.

6.4 Special precautions for storage

No special storage condition is necessary.

6.5 Nature and contents of container

The solution is filled into either 15 ml (180 metered doses) or 30 ml (300 metered doses) amber glass bottles (Type I glass) fitted with 70 microlitre manually activated nasal pump with white polypropylene nasal adapter and LDPE cap.

Not all pack sizes may be marketed.

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 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd
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8 MARKETING AUTHORISATION NUMBER

PA0126/418/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 March 1997

Date of last renewal: 21 May 2005

10 DATE OF REVISION OF THE TEXT

January 2026