# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Otrivine Extra Dual Relief 0.5mg/ml + 0.6mg/ml nasal spray, solution

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 0.5 mg xylometazoline hydrochloride and 0.6 mg ipratropium bromide.

1 puff (approx. 140 microliters) contains 70 micrograms xylometazoline hydrochloride and 84 micrograms ipratropium bromide.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Nasal spray, solution (Nasal spray)

Clear, colourless solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Symptomatic treatment of nasal congestion and rhinorrhea in connection with common colds.

### 4.2 Posology and method of administration

Posology
*Adults:* 1 puff in each nostril up to 3 times daily. At least 6 hours should elapse between two doses. Do not exceed 3 applications daily into each nostril.

The treatment duration should not exceed 7 days (see section 4.4).

Do not exceed the stated dose. The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

It is recommended to stop treatment, when the symptoms have diminished, even before the maximum duration of treatment of 7 days, in order to minimize the risk of adverse reactions (see section 4.8).

*Paediatric population*
Otrivine Extra Dual Relief is not recommended for use in children and adolescents below 18 years of age due to lack of sufficient documentation.

*Geriatrics*
There is only limited experience of use in patients above 70 years of age.

Method of administration

Two fingers vertically actuated pump:

Before the first application, prime the pump by actuating 4 times. Once primed the pump will normally remain charged throughout regular daily treatment periods.

1. Clear the nose.
2. Hold the bottle upright with thumb under base and nozzle between two fingers.

3. Lean forward slightly and insert the nozzle into a nostril.
4. Spray and breathe in gently through the nose at the same time.
5. Repeat this procedure in the other nostril.
6. Clean and dry the nozzle before replacing back the cap right after use

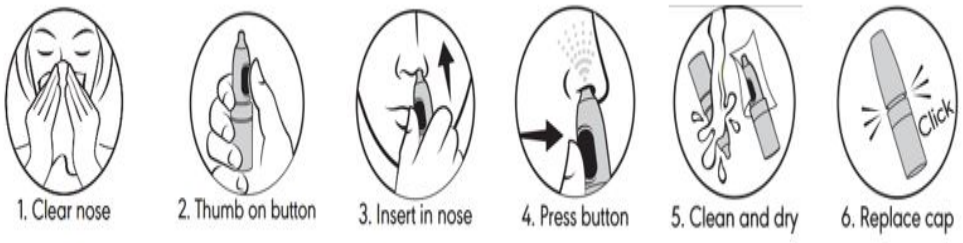
Should the spray not be ejected during the full actuation stroke, or if the product has not been used for longer than 6 days, the pump will need to be re-primed with 4 actuations as initially performed. If the full spray is not administered, the dose should not be repeated.

Thumb laterally actuated pump:

**Before the first use**
Prime the pump by actuating 5 times. Once primed the pump will normally remain charged throughout regular daily treatment periods.

Remove the cap.

1. Clear the nose.
2. Hold the bottle upright with thumb on the actuation button.
3. For a no dripping effect, stay upright and insert the nozzle into a nostril.
4. Press on the button to spray and breath in gently through the nose at the same time.Repeat this procedure (step 2 to 4) in the other nostril.
5. After each use, clean and dry the nozzle.
6. Put the protective cap back on until an audible "click" is heard.




Should the spray not be ejected during the full actuation stroke, or if the product has not been used for longer than 7 days, the pump will need to be re-primed with 2 actuations.

If the full spray is not administered, the dose should not be repeated.
To avoid possible spread of infection, the spray should only be used by one person.
Be careful not to spray in the eyes.

**4.3 Contraindications**

Otrivin Comp should not be given to children under the age of 18 due to lack of sufficient documentation.
Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
Hypersensitivity to atropine or atropine like substances such as hyoscyamine and scopolamine.
After surgical operations where dura mater may have been penetrated, e.g. trans-sphenoidal hypophysectomy or other trans-nasal operations.
Glaucoma.
Rhinitis sicca or atrophic rhinitis.

**4.4 Special warnings and precautions for use**

The medicinal product must be administered with caution to patients with:
- hypertension, cardiovascular diseases
- hyperthyroidism, diabetes mellitus
- hypertrophy of the prostate, stenosis of the bladder bar
- pheochromocytoma

Caution is recommended in patients predisposed to:
- angle closure glaucoma
- epistaxis (e.g. elderly)
- paralytic ileus
- cystic fibrosis

Immediate hypersensitivity including urticaria, angioedema, rash, bronchospasm, pharyngeal oedema and anaphylaxis may occur.

The medicinal product must be used with caution in patients who are sensitive to adrenergic substances, which may give symptoms such as sleeping disturbances, dizziness, tremor, cardiac arrythmias or elevated blood pressure.

The treatment duration should not exceed 7 days, as chronic treatment with xylometazoline hydrochloride may cause swelling of the nasal mucosa and hypersecretion because of increased sensibility in the cells, "rebound effect" (rhinitis medicamentosa).

Patients should be instructed to avoid spraying Otrivine Extra Dual Relief in or around the eye. If Otrivine Extra Dual Relief gets in contact with the eyes, the following may occur: temporary blurred vision, irritation, pain, red eyes. Aggravation of angle closure glaucoma may also develop. The patient should be instructed to rinse their eyes with cold water if Otrivine Extra Dual Relief gets in direct contact with the eyes and to contact a doctor if they experience pain in the eyes or blurred vision.

**4.5 Interaction with other medicinal products and other forms of interaction**

| | |
|---|---|
| Monoamine oxidase (MAO) inhibitors or tri- and tetra-cyclic antidepressants | Concomitant use or use within the last 2 weeks of sympathomimetic preparations may induce severely elevated blood pressure and is therefore not recommended. Sympathomimetic preparations release catecholamine, which results in a major release of noradrenaline which in turn has a vasoconstrictive effect resulting in elevated blood pressure. In critical cases of elevated blood pressure, treatment with Otrivine Extra Dual Relief should be discontinued and the elevated blood pressure treated (*see section 4.4 Warnings and Precautions)*. |
| Beta 2-agonists | Concomitant use with ipratropium may cause an increased risk of acute glaucoma in patients with a history of angle closure glaucoma.<br>There have been isolated reports of ocular complications (i.e. mydriasis, increased intraocular pressure, narrow-angle glaucoma and eye pain) when aerosolised ipratropium bromide either alone or in combination with an adrenergic beta 2-agonist, has come into contact with the eyes (*see section 4.4 Warnings and Precautions)*. |

Concomitant administration of other *anticholinergic drugs* may enhance the anticholinergic effect.

The above interactions have been studied individually for both of the active substances of Otrivine Extra Dual Relief, not in combination.

No formal interaction studies with other substances have been performed.

**4.6 Fertility, pregnancy and lactation**

Pregnancy
There are insufficient data on the use of this product in pregnant women.. Animal studies are insufficient with respect to reproductive toxicity (see *Non-clinical* information). It is advisable not to take this product during pregnancy.

**Xylometazoline**
The available data indicate the potential for xylometazoline to exert a systemic vasoconstrictor effect. In view of its systemic vasoconstrictor effect, it is advisable not to take xylometazoline during pregnancy.

**Ipratropium**
The clinical safety ipratropium bromide during human pregnancy has not been established. Non-clinic data have demonstrated embryotoxicity following administration of ipratropium bromide to rabbits via inhalation at doses greater than the clinical dose (see Non-clinical information).

Breast-feeding
There are insufficient data to determine if this product is excreted in human breast milk. This product should only be used while breast feeding under medical advice. If the expected benefit to the mother is greater than possible risk to the infant, the lowest effective dose and the duration of treatment should be considered.

**Xylometazoline**
There is no evidence of any adverse effect on the breast-fed infant. It is unknown if xylometazoline is excreted in breast milk.

**Ipratropium**
It is not known whether ipratropium bromide is excreted in breast milk.

Fertility
There are insufficient data on the impact of this product on fertility.

**Xylometazoline**
There are no adequate data for the effects of xylometazoline hydrochloride on fertility and no animal studies are available.

**Ipratropium**
Non-clinical data have demonstrated no evidence of impaired fertility following oral administration of ipratropium bromide to rats at doses greater than the clinical dose (see Preclinical safety data).

**4.7 Effects on ability to drive and use machines**

Visual disturbances (including blurred vision and mydriasis), dizziness and fatigue have been reported with Otrivine Extra Dual Relief. Patients should be advised that if affected they should not drive, operate machinery or take part in activities where these symptoms may put themselves or others at risk.

**4.8 Undesirable effects**

*Summary of the safety profile*
The most commonly reported adverse reactions are epistaxis occurring in 14.8 % and nasal dryness occurring in 11.3 % of patients.
Many of the adverse events reported are also symptoms of common cold.

*Tabulated list of adverse reactions*
The adverse reactions are presented by system organ class and frequency. Frequencies are defined as:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 and <1/100); rare (≥1/10000 and <1/1000); very rare (< 1/10,000); not known (can not be estimated from the available data).

**Xylometazoline and Ipratropium**
The following adverse reactions for the combination of xylometazoline and ipratropium were reported in two randomised clinical studies and one non-interventional post-marketing study with the product as well as from post-marketing surveillance.

| MeDRA SOC | Adverse Reactions | Frequency |
|---|---|---|
| Immune system disorders | Hypersensitivity reaction (angioedema, rash, pruritis) | Very rare |
| Psychiatric disorders | Insomnia | Uncommon |
| Nervous system disorders | Dysgeusia | Common |
| | Parosmia, Tremor | Uncommon |
| Eye disorders | Eye irritation, dry eye | Uncommon |
| | Photopsia | Not known |

| | | |
|---|---|---|
| Cardiac disorders | Palpitations, tachycardia | Uncommon |
| Respiratory, thoracic and mediastinal disorders | Epistaxis | Very common |
| | Nasal congestion, rhinalgia | Common |
| | Nasal ulcer, dysphonia, oropharyngeal pain, sneezing | Uncommon |
| | Rhinorrhea | Rare |
| | Paranasal sinus discomfort | Not known |
| Gastrointestinal disorder | Dyspepsia | Uncommon |
| | Dysphagia | Not known |
| General disorders and administration site conditions | Fatigue, discomfort | Uncommon |
| | Chest discomfort, thirst | Not Known |

**Xylometazoline**
The following adverse reactions have been reported in clinical trials and post-marketing surveillance with xylometazoline.

| **MeDRA SOC** | **Adverse Reactions** | **Frequency** |
|---|---|---|
| Nervous system disorders | Headache | Common |
| Eye disorders | Visual impairment | Very rare |
| Respiratory, thoracic and mediastinal disorders | Nasal dryness, nasal discomfort | Common |
| | Epistaxis | Uncommon |
| Gastrointestinal disorders | Nausea | Common |
| General disorders and administration site conditions | Application site burn | Common |

**Ipratropium bromide**
The following adverse reactions were identified from data obtained in clinical trials and pharmacovigilance during post approval use of the drug.

| **MeDRA SOC** | **Adverse Reactions** | **Frequency** |
|---|---|---|
| Immune system disorders | Anaphylactic reaction, hypersensitivity | Not known |
| Nervous system disorders | Dizziness, headache | Common |
| Eye disorders | Corneal oedema, conjunctival hyperaemia | Uncommon |
| | Glaucoma, intraocular pressure increased, accommodation disorder, blurred vision, halo vision, mydriasis, eye pain | Not known |
| Cardiac disorders | Supraventricular tachycardia, palpitations | Uncommon |
| | Atrial fibrillation | Not known |
| Respiratory, thoracic and mediastinal disorders | Throat irritation, dry throat | Common |
| | Cough | Uncommon |
| | Laryngospasm, pharyngeal oedema | Not known |
| Gastrointestinal disorders | Dry mouth | Common |
| | Nausea | Uncommon |
| Skin and subcutaneous tissue disorders | Rash, urticaria,, pruritis | Not known |
| Renal and urinary disorders | Urinary retention | Not Known |

*Description of selected adverse reactions*
Several of the adverse reactions listed under "Not known" have only been reported once for the product in clinical trials or are reported from postmarketing surveillance only, thus an estimate of the frequency based on the present number of patient treated with Otrivine Extra Dual Relief cannot be given.

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**

Overdose of oral or excessive administration of topical xylometazoline hydrochloride may cause severe dizziness, perspiration, severely lowered body temperature, headache, bradycardia, hypertension, respiratory depression, coma and convulsions. Hypertension may be followed by hypotension. Small children are more sensitive to toxicity than adults.

The absorption being very small after nasal or oral administration, an acute overdose after intranasal ipratropium bromide is unlikely but if an overdose occurs the symptoms are dry mouth, accommodation difficulties and tachycardia. The treatment is symptomatic.

A considerable overdose may cause anticholinergic CNS symptoms such as hallucinations, which must be treated with cholinesterase inhibitors.

Appropriate supportive measures should be initiated in all individuals suspected of an overdose, and urgent symptomatic treatment under medical supervision is indicated when warranted. This would include observation of the individual for at least 6 hours. In the event of a severe overdose with cardiac arrest, resuscitation should be continued for at least 1 hour. Further management should be as clinically indicated or as recommended by the national poison centres where available.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sympathomimetics, combinations excluding corticosteroids.
ATC code: R 01 AB 06

Xylometazoline hydrochloride is a s ympathomimetic which acts on a-adrenergic receptors. Xylometazoline has a vasoconstrictive effect. An effect is obtained after 5-10 minutes and lasts for 6-8 hours.

Ipratropium bromide is a quaternary ammonium combination with anticholinergic effect. Nasal administration reduces the nasal secretion through competitive inhibition of cholinergic receptors situated around the nasal epithelium. An effect is usually obtained within 15 minutes and lasts for 6 hours on an average.

### 5.2 Pharmacokinetic properties

After administration of one puff/nostril of 140 µg Xylometazoline and 84 µg Ipratropium bromide in 24 healthy subjects, mean maximum concentrations of 0.085 ng/ml and 0.13 ng/ml were reached 1 hour and 2 hours post administration for Ipratropium bromide and Xylometazoline, respectively. The blood levels are very low. However, based on data available, it is expected that Ipratropium bromide and especially Xylometazoline will accumulate at the proposed 3 times per day dosing.

### 5.3 Preclinical safety data

Non-clinical data safety data for xylometazoline hydrochloride and ipratropium bromide have not revealed findings which are of relevance to the recommended dosage and use of the product.

**Carcinogenesis and Mutagenesis**
There are no carcinogenicity data available for xylometazoline hydrochloride. However, the available in-vitro and in-vivo genotoxicity data or this active ingredient do not indicate a genotoxic potential. Non-clinical studies with ipratropium bromide demonstrated this compound was not mutagenic, genotoxic, or carcinogenic.

**Reproductive toxicology**
Non-clinical data are not available on the reproductive and developmental toxicology of xylometazoline. Non-clinical data for ipratropium bromide demonstrated embryotoxicity following inhalation administration to rabbits at a dose that was approximately 14-fold greater than the clinical dose based on human equivalent dose.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Disodium edetate
Glycerol (85 per cent)
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Purified water

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.
After first opening, the nasal spray can be used until the end of the shelf-life.

**6.4 Special precautions for storage**

Do not store above 25°C.

**6.5 Nature and contents of container**

10 ml multidose (approx. 70 puffs) HDPE bottle mounted with metered-dose spray pump (materials in contact with the solution: LDPE, HDPE, PE / butyl, stainless steel) and PP nozzle with protective cap.
2 different spray pumps are available: a two fingers vertically actuated pump and a thumb laterally actuated pump (with protective cap).

**6.6 Special precautions for disposal**

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

**7 MARKETING AUTHORISATION HOLDER**

Haleon Ireland Limited
Clocherane
Youghal Road
Dungarvan
X35 Y983
Co. Waterford
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**8 MARKETING AUTHORISATION NUMBER**

PA0678/131/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 18th December 2012
Date of last renewal: 9th October 2017

**10 DATE OF REVISION OF THE TEXT**

September 2026