# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Otrivin Comp 0.5 mg/ml + 0.6 mg/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.

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).

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*
Otrivin Comp 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

Before the first application, prime the pump by actuating 4 times. Once primed the pump will normally remain charged throughout regular daily treatment periods. 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 reprimed with 4 actuations as initially performed.

**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.

Known hypersensitivity to atropine or similar substances, e.g. hyoscyamine and scopolamine.

After surgical operations where dura mater may have been penetrated, e.g. transsphenoidal hypophysectomy or other transnasal operations.

In patients with glaucoma.

In patients with rhinitis sicca.

**4.4 Special warnings and precautions for use**

The medicinal product must be administered with caution to patients with:

- hypertension, cardiovascular diseases. Patients with long QT syndrome treated with xylometazoline may be at increased risk of serious ventricular arrhythmias.
- 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 Otrivin Comp in or around the eye. If Otrivin Comp 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 Otrivin Comp 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

*Monoaminoxidase inhibitors (MAO inhibitors)*: 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 Otricomb should be discontinued and the elevated blood pressure treated.

*Tri- and tetra-cyclic antidepressants*: Concomitant use or use within the last 2 weeks of tri-cyclic antidepressants and sympathomimetic preparations may result in an increased sympathomimetic effect of xylometazoline and is therefore not recommended.

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 Otrivin Comp, not in combination.

No formal interaction studies with other substances have been performed.

## 4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of Otrivin Comp in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development. The potential risk for humans is unknown. Otrivin Comp should not be used in pregnancy unless clearly necessary.

Breast-feeding
It is not known whether ipratropium bromide and xylometazoline hydrochloride are excreted in the mother’s milk. The systemic exposure to ipratropium bromide and xylometazoline hydrochloride is low. Effects on the breast-fed infant are therefore unlikely. The mother’s need for treatment with Otrivin Comp and the advantages of breast-feeding must be weighed against the potential risks to the infant.

## 4.7 Effects on ability to drive and use machines

Visual disturbances (including blurred vision and mydriasis), dizziness and fatigue have been reported with Otrivin Comp. 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 following adverse reactions were reported in two randomised clinical studies and one non-interventional post-marketing study with the product as well as from post-marketing surveillance.

The adverse reactions are listed below 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)

| **Frequency** / **Organ class** | **Very Common** | **Common** | **Uncommon** | **Rare** | **Not known** |
|---|---|---|---|---|---|
| Immune system disorders | | | | | Hypersensitivity |
| Psychiatric disorders | | | Insomnia | | |
| Nervous system disorders | | Dysgeusia, headache | Parosmia, dizziness, tremor | | |
| Eye disorders | | | Eye irritation, dry eye | | Accommodation disorder, aggravation of angle closure glaucoma, eye pain, photopsia, intraocular pressure increased, blurred vision, mydriasis, halo vision |
| Cardiac disorder | | | Palpitations, tachycardia | | Atrial fibrillation |
| Respiratory, thoracic and mediastinal disorders | Epistaxis, nasal dryness | Nasal discomfort, nasal congestion, dry throat, throat irritation, rhinalgia | Nasal ulcer, sneezing, oropharyngeal pain, cough, dysphonia | Rhinorrhoea | Paranasal sinus discomfort, laryngospasm, pharyngeal oedema |
| Gastrointestinal disorders | | Dry mouth | Dyspepsia, nausea | | Dysphagia |

| Frequency / Organ class | Very Common | Common | Uncommon | Rare | Not known |
|---|---|---|---|---|---|
| Skin and subcutaneous disorders | | | | | Pruritus, rash, urticaria |
| Renal and urinary disorders | | | | | Urine retention |
| General disorders and administration site conditions | | | Discomfort, fatigue | | Chest discomfort, thirst |

*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 treatedwith Otrivin Comp can not 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 the national reporting system listed in Appendix V.

**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.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

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

Xylometazoline hydrochloride is a sympathomimetic which acts on α-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

Both ipratropium bromide and xylometazoline were tested in preclinical studies, which revealed no relevant clinical safety problems with the actual doses of Otrivin Comp. Intranasal daily dose of Otrivin Comp in dogs for 28 days in doses up to four times the intended clinical dosing regimen has shown no local or systemic effects.

## 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.

**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

[To be completed nationally]
{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

## 8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]
<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

## 10. DATE OF REVISION OF THE TEXT

**2019-04-02**