1. NAME OF THE MEDICINAL PRODUCT

Zymelin 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

Zymelin Comp is indicated in adults for the symptomatic treatment of nasal congestion and rhinorrhoea 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.

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

Elderly
There is only limited experience of use in patients above 70 years of age,

Paediatric population

Zymelin Comp is contraindicated in children and adolescents below 18 years of age due to lack of sufficient documentation (see section 4.3).

Method of administration
For nasal use.

Before using the pump for the first time or when the product has not been used in 9 days: the spray should be pumped a number of times until a uniform spray is obtained.

4.3 Contraindications

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.
Zymelin Comp should not be given to children and adolescents under the age of 18 due to lack of sufficient documentation.
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

Zymelin Comp must be administered with caution to patients predisposed to narrow-angle glaucoma or patients with hypertrophy of the prostate and stenosis of the bladder bar.

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

Caution is recommended in patients predisposed to epistaxis (e.g. elderly), paralytic ileus or cystic fibrosis.

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

Caution is recommended in patients with hyperthyroidism, diabetes mellitus, hypertension, cardiovascular diseases or pheochromocytoma.

Patients with long QT syndrome treated with xylometazoline may be at increased risk of serious ventricular arrhythmias.

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 Zymelin Comp 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.

Anticholinergic drugs: 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 Zymelin 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 Zymelin 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. Zymelin Comp should not be used in pregnancy unless clearly necessary.

Breastfeeding
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 Zymelin 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

Zymelin Comp has no or negligible influence on the ability to drive and use machines.

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 Zymelin Comp.

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 to <1/100)
Rare (≥1/10000 to <1/1000)
Not known (cannot be estimated from the available data).

Frequency **System Organ Class**	**Very common**	**Common**	**Uncommon**	**Rare**	**Not known**
Psychiatric disorders			Insomnia		
Nervous system disorders		Dysgeusia, headache	Parosmia, dizziness, tremor		
Eye disorders			Eye irritation, dry eye		Accomodation disorder, aggravation of narrow-angle glaucoma, eye pain, photopsia
Cardiac disorders			Palpitations, tachycardia		
Respiratory, thoracic and mediastinal disorders	Epistaxis nasal dryness	Nasal discomfort, nasal congestion, dry and irritated throat, rhinalgia	Nasal ulcer, sneezing, pharyngolaryngeal pain, cough, dysphonia	Rhinorrhoea	Paranasal sinus discomfort
Gastrointestinal diorders		Dry mouth	Dyspepsia, nausea		Dysphagia
Skin and subcutaneous disorders					Pruritus
Renal and urinary disorders					Urine retention
General disorders and administration site conditions			Discomfort, fatigue		Chest discomfort, thirst; systemic allergic reactions

Description of selected adverse reactions
Several of the adverse reactions listed under “Not known” have only been reported once for Zymelin Comp, thus an estimate of the frequency based on the present number of patient treated with Zymelin 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 [to be completed nationally].

4.9 Overdose

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

The absorption being very small after nasal or oral administration, an acute overdose after intranasal ipratropium bromide is hardly possible, but if an overdosing should occur the clinical picture is dry mouth, accommodation difficulties and tachycardia.

Management
The treatment is symptomatic.

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

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 Zymelin Comp there are low contents of ipratropium bromide and xylometazoline in plasma.

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 Zymelin Comp.

Intranasal daily dose of Zymelin Comp in dogs for 28 days with doses up to four times the intended clinical exposure has shown no local or systemic effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Glycerol (85 per cent)
Hydrochloric acid (to adjust pH)
Sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and contents of container

10 ml multidose (approx. 70 puffs) HDPE bottle with pump spray.

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

8. MARKETING AUTHORISATION NUMBER(S)

To be completed Nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2006-04-07/2011-04-07

10. DATE OF REVISION OF THE TEXT

2026-05-18