SUMMARY OF PRODUCT CHARACTERISTICS

1. NAAM VAN HET GENEESMIDDEL

Xylozolin 0,5 mg/ml, neusspray, oplossing
Xylozolin 1 mg/ml, neusspray, oplossing

Xylometazoline hydrochloride 1 / 0.5 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

{(Invented) name 1 mg/ml pharmaceutical form}
One actuation (equivalent to 0.09 ml nasal spray, solution) contains 0.09 mg xylometazoline hydrochloride.

{(Invented) name 0.5 mg/ml pharmaceutical form}
One actuation (equivalent to 0.09 ml nasal spray, solution) contains 0.045 mg xylometazoline hydrochloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, solution (nasal spray)

Clear, almost colourless solution (pH 5.5-6; Osmolality 250-300 mOsm/kg).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For temporary symptomatic treatment of nasal congestion due to rhinitis or sinusitis.

{(Invented) name 1 mg/ml pharmaceutical form} is intended for adults as well as for children 10 years of age and older.
{(Invented) name 0.5 mg/ml pharmaceutical form} is intended for children between 2 and 10 years of age.

4.2 Posology and method of administration

Posology
This medicinal product is intended for nasal use.

{(Invented) name 1 mg/ml pharmaceutical form}:
The dose in adults and children 10 years of age and older is 1-2 sprays of *{(Invented) name 1 mg/ml pharmaceutical form}* into each nostril, according to need, but up to a **maximum** of 3 times daily.
Dosages higher than those recommended must not be used.
{(Invented) name 1 mg/ml pharmaceutical form} is suitable for adults as well as for children over 10 years of age. It must not be used in children below 10 years of age.

{(Invented) name 0.5 mg/ml pharmaceutical form}:
The dose in children between 2 and 10 years of age is one spray of *{(Invented) name 0.5 mg/ml pharmaceutical form}* into each nostril, according to need, but up to a **maximum** of 3 times daily.
Dosages higher than those recommended must not be used.

{(Invented) name 0.5 mg/ml pharmaceutical form} is suitable for children between 2 and 10 years of age. It must not be used in children below 2 years of age.

Paediatric population
{(Invented) name 1 mg/ml pharmaceutical form} is indicated in children aged 10 years and above to be administered as stated above.
{(Invented) name 1 mg/ml pharmaceutical form} should not be used in children less than 10 years old. Other pharmaceutical strengths may be more appropriate for administration to this population

Paediatric population
{(Invented) name 0.5 mg/ml pharmaceutical form} is indicated in children between 2 and 10 years to be administered as stated above.
{(Invented) name 0.5 mg/ml pharmaceutical form} is not recommended to be taken by children under 2 years of age. The safety and efficacy of **{(Invented) name 0.5 mg/ml pharmaceutical form}** in children younger than 2 years have not yet been established.

Duration of use
{(Invented) name 1 mg/ml pharmaceutical form} / {(Invented) name 0.5 mg/ml pharmaceutical form} must not be used for longer than 7 days, unless prescribed by the clinician.
If after 3 days of treatment the patient feel not better or worse, the clinical situation should be reevaluated.
Long and excessive use can cause reactive hyperaemia or rebound congestion respectively (see section 4.4).
The recommended dose should not be exceeded.

An interval of several days should elapse before re-administering the product.

In chronic rhinitis, it may only be administered under medical surveillance, due to the risk of nasal mucosal atrophy.

Method of administration
- Remove the protective cap
- Before the first use - and after interruption of treatment of more than 15 days - activate the pump several times until an even spray mist emerges. For subsequent applications, the metered-dose spray is ready for immediate use.
- Insert the spray aperture into the nostril and activate the pump once. Breathe gently through the nose during the spray procedure.
- After use, carefully wipe the nozzle with a clean paper tissue and replace the protective cap.

Patients are recommended to blow their nose thoroughly before using the preparation. The last dose on each day of treatment should preferably be administered before retiring to bed.

For hygienic reasons and to avoid infections, each spray bottle should only be used by the same person.

4.3 Contraindications

This medicinal product must not be used in the following cases:
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- status post transsphenoidal hypophysectomy or other surgery exposing the dura mater
- dry, inflamed nasal mucosa (rhinitis sicca) - except in the diagnostic workup to identify rhinitis sicca or atrophic rhinitis.

{(Invented) name 1 mg/ml pharmaceutical form} must not be used in children below 10 years of age.

{(Invented) name 0.5 mg/ml pharmaceutical form} must not be used in children below 2 years of age.

4.4 Special warnings and precautions for use

This medicinal product may only be used after careful consideration of the risks and benefits in the following cases:

- patients treated with monoamine oxidase inhibitors (MAO inhibitors) or other medicinal products with a potentially hypertensive effect
- severe cardiovascular disorders (e.g. coronary heart disease [CHD], hypertension)
- phaeochromocytoma (adrenal tumour)
- metabolic disorders (e.g. hyperthyroidism, diabetes mellitus)
- porphyria
- prostatic hyperplasia
- increased intraocular pressure, particularly narrow-angle glaucoma

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

Direct contact with the eyes should be avoided.

Particularly during prolonged use and in the event of an overdose with nasal decongestants, their effect may be attenuated. The following may occur as a result of misusing nasal decongestants:

- reactive hyperaemia of the nasal mucosa (rhinitis medicamentosa)
- atrophy of the nasal mucosa.

In order to maintain at least partial nasal respiration, the sympathomimetic should not be used on the second nostril until symptoms have resolved in the first.

4.5 Interaction with other medicinal products and other forms of interaction

Combined use of xylometazoline and:

- tricyclic antidepressants
- monoamine oxidase inhibitors of the tranylcypromine type
- hypertensive medications

can lead to a rise in blood pressure. For this reason, such combined use should preferably be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy
Data from a limited number of exposures during the first trimester of pregnancy did not reveal any adverse effects to the pregnancy or the foetus/new-born child. To date, no other epidemiological data is available. Animal studies have shown reproductive toxicity of xylometazoline above the therapeutic dose (see section 5.3). Caution should be exercised in the case of hypertension or signs of decreased uterine blood flow. With high doses and longer duration of use, a decrease in uterine blood flow cannot be excluded.
{(Invented) name 1 mg/ml pharmaceutical form} / {(Invented) name 0.5 mg/ml pharmaceutical form} can be used during pregnancy according to instructions, for not longer than one week duration.

Breastfeeding
It is not known whether xylometazoline is excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from **{(Invented) name 1 mg/ml pharmaceutical form} / {(Invented) name 0.5 mg/ml pharmaceutical form}** therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

As overdosing may lead to a reduction of milk production, the recommended dose of xylometazoline may not be exceeded during lactation.

Fertility
There are no known effects on fertility from xylometazoline treatment.

4.7 Effects on ability to drive and use machines

No impairment is expected when used as directed.

4.8 Undesirable effects

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Immune system disorders:
Uncommon: systemic allergic reactions (angioedema, skin rash, pruritus)

Psychiatric disorders:
Very rare: nervousness, insomnia, sleepiness/drowsiness (mainly in children)

Nervous system disorders:
Very rare: hallucinations (mainly in children), headache, dizziness.

Cardiac disorders:
Rare: palpitations, tachycardia
Very rare: arrhythmia

Vascular disorders
Rare: hypertension

Respiratory, thoracic and mediastinal disorders:
Common: stinging or burning sensation in the nose and throat; sneezing, dry nasal mucous membranes
Uncommon: increased swelling of mucous membranes after discontinuation of treatment, epistaxis.
Very rare: apnoea in infants and neonates.

Gastrointestinal disorders
Rare: nausea

Musculoskeletal and connective tissue disorders
Very rare: convulsions (mainly in children)

Paediatric population
Xylometazolin has been shown to be safe in children in several clinical trials. Data from clinical trials and case reports indicates that frequency, type and severity of adverse reactions in children are expected to be similar as in adults. The majority of adverse events reported in children occurred after overdosing of xylometazolin. These include nervousness, insomnia, sleepiness/drowsiness, hallucinations and convulsions. Cases of irregular breathing have been recorded in infants and neonates.

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 can occur due to both nasal and oral administration.

Overdose in infants can cause serious depression of the central nervous system. The clinical picture after intoxication with imidazoline derivatives can be confusing due to the occurrence of alternating periods of

hyperactivity with periods of depression of the central nervous system and the cardiovascular and pulmonary system.

Stimulation of the central nervous system manifests itself in fear, agitation, hallucinations and convulsions. Depression of the central nervous system manifests itself in: drop in body temperature, lethargy, drowsiness and coma. Other symptoms may include miosis, mydriasis, sweating, pallor, cyanosis, apnea, and palpitations. When central effects dominate, especially in children, bradycardia and hypertension followed by hypotension may be observed.

Administration of activated charcoal (adsorbent) and sodium sulphate (laxative), or possibly gastric lavage in case of large quantities, should be done immediately, because rapid xylometazoline absorption can take place. In severe overdosage hospitalization in an intensive care department is indicated. A non-selective alpha-adrenergic antagonist, e.g. phentolamine, could be given as antidote.

Naloxone may influence the depression of the central nervous system in patients with severe intoxication. However, this has not yet been established. Further treatment is supportive and symptomatic..

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: nasal preparations, alpha-sympathomimetics
Decongestants and other nasal preparations for topical use, sympathomimetics, plain, ATC code: R01AA07

Xylometazoline, an imidazoline derivative, is an alpha-adrenergic sympathomimetic agent. It has a vasoconstrictive effect, thereby reducing swelling of the mucous membranes. In the literature, an onset of action at 15 min post dose (i.e. time of first measurement) has been described, manifested by improved nasal breathing as a result of reduced mucosal swelling and improved mucus drainage.

5.2 Pharmacokinetic properties

The effect of **{(Invented) name 1 mg/ml pharmaceutical form} / {(Invented) name 0.5 mg/ml pharmaceutical form}** starts within 15 min post dose (i.e. time of first measurement) and lasts for several hours (6-8 hours on average).

With intranasal administration, the absorbed amount can occasionally be sufficient to induce systemic effects, e.g. on the central nervous system and cardiovascular system.

There are no available data from pharmacokinetic studies in humans.

5.3 Preclinical safety data

Preclinical data from conventional studies on acute toxicity, repeated dose toxicity, carcinogenicity, genotoxicity and reproductive toxicity reveal no special hazard for humans in addition to those already included elsewhere in other sections of this SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate,
sodium citrate dihydrate,
glycerol 85%,
water for injections.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

Shelf life after opening: 1 year.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

{(Invented) name **1 mg/ml** pharmaceutical form}
Brown glass bottle containing 10 ml (not less than 81 actuations), 15 ml (not less than 126 actuations) or 2x10 ml (not less than 2x81 actuations) nasal spray, solution, sealed with a PP/PE/Steel spray pump with a nose adapter and a protecting cap.

{(Invented) name **0.5 mg/ml** pharmaceutical form}
Brown glass bottle containing 10 ml (not less than 90 actuations) or 2x10 ml (not less than 2x90 actuations), nasal spray solution, sealed with a PP/PE/Steel spray pump with a nose adapter and a protecting cap.

< Not all pack sizes may be marketed >

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Pharmachemie B.V.
Swensweg 5
2031 GA Haarlem
Nederland

8. NUMMER(S) VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

RVG 109042 - Xylozolin 0,5 mg/ml, neusspray, oplossing
RVG 109043 - Xylozolin 1 mg/ml, neusspray, oplossing

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENGING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 18 september 2012
Datum van laatste verlenging: 31 januari 2015

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft rubriek 6.5: 7 juni 2023