SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Nasadur 0,5 mg/ml neusspray, oplossing

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of nasal spray contains 0.5 mg of xylometazoline hydrochloride.

1 dose (= 90 microlitres) contains 45 micrograms of xylometazoline hydrochloride.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, solution.

Clear, colourless solution.

pH 5.5 – 6.5, osmolality: 0.260 – 0.320 osmol/kg

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of nasal congestion.

Nasadur 0.5 mg/ml nasal spray may be used in children 2-10 years.

4.2 Posology and method of administration

Posology

The dose in children between 2 and 10 years of age is 1 expression into each nostril but no more than once every 10-12 hours. If it should be necessary the medicinal product may be used up to 3 times daily.

Paediatric population
Nasadur 0.5 mg/ml nasal spray is indicated in children between 2 and 10 years to be administered as stated below.
Nasadur 0.5 mg/ml is not recommended to be taken by children under 2 years of age. The safety and efficacy of Nasadur 0.5 mg/ml in children younger than 2 years have not yet been established.

The maximum treatment duration is 5 days, if after 3 days of treatment the patient does not feel better or feels worse, the clinical situation should be evaluated. Long and excessive use can cause rebound congestion. The recommended dose should not be exceeded.

Method of administration

Before the first application it is necessary to spray a few times (4 times) in the air, to achieve a uniformity of dose. The bottle should be in vertical position. If the product is not used for several days at least one test spray in the air should be done in order to achieve a uniform dose.

The products should be used after blowing one's nose.

Nasadur nasal spray is intended for intranasal use only. Nasal spray should be delivered while seated. In addition, small children should be seated on an assistant's lap.

To minimize the risk of spreading infections, the medicinal product should not be used by more than one person, and the pump should be rinsed following use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Must not be taken following transsphenoidal hypophysectomy or transnasal/transoral surgeries exposing dura mater.
- 'Dry' inflammation of the nasal mucosa (rhinitis sicca)

4.4 Special warnings and precautions for use

When taking xylometazoline, caution needs to be exerted in patients with strong reactions to sympathomimetics. Use may cause, for example, insomnia, dizziness, tremors, arrhythmia or hypertension.

Nasadur can only be used after careful evaluation of the risks and benefits of the treatment for patients:

- who are being treated with monoaminooxidase (MAO) inhibitors within the last 2 weeks
- with increased intra-ocular pressure, particularly in patients with narrow angle glaucoma
- with severe cardiovascular disease (e.g. ischemic heart disease, hypertension)
- with phaeochromocytoma
- with metabolic diseases (e.g. hyperthyroidism, diabetes mellitus)
- with porphyria
- in connection with prostatic hyperplasia

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

Mucous swelling may recur in connection with stopping long-term treatment with xylometazoline. In this case, this could also be due to the so-called rebound effect due to the medication itself. In order to prevent this, the treatment period should be kept as short as possible (see Section 4.2). Bacterial infections of the nose and sinuses must be treated appropriately. Infections may spread if the same spray bottle is used by several persons.

4.5 Interaction with other medicinal products and other forms of interaction

Xylometazoline is not recommended to be used concurrently with tricyclic or tetracyclic antidepressants or monoamine oxidase (MAO) inhibitors or within two weeks of having taken MAO inhibitors.

Because of the potential hypertensive effects of xylometazoline, Nasadur should preferably not be used in combination with anti-hypertensive medicaments (e.g. methyldopa). Nasadur and other medicaments with potential hypertensive effect (e.g. doxapram, ergotamine, oxytocin) can potentiate each others hypertensive effects.

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/newborn. No other epidemiological data is available. Animal studies have shown reproductive toxicity of xylometazoline above the recommended 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.
Nasadur can be used during pregnancy according to instructions, for no longer than one week duration.

Breastfeeding
It is unknown 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 Nasadur 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

When used correctly, xylometazoline has no or negligible influence on the ability to drive and use machines, but if the patient feels drowsiness/ sleepiness it would be preferable that he/she does not drive or uses machines.

4.8 Undesirable effects

The most frequently reported undesirable effects of the medication were stinging or burning sensations in the nose and throat as well as dry nasal mucous membranes.

The frequency of undesirable effects has been defined according to the following convention: 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).
The adverse events recorded in the table below derive from clinical trials on the efficacy and/or safety of xylometazoline as well as from case reports.

Immune system disorders	Uncommon: hypersensitivity reactions (angioedema, skin eruptions, pruritus)
Psychiatric disorders	Very rare: nervousness, insomnia, sleepiness/drowsiness (mainly in children)
Nervous system disorders	Very rare: hallucinations (mainly in children), headache. Very rare: convulsions (mainly in children)
Cardiac disorders	Rare: palpitations, tachycardia Very rare: arrhythmia
Vascular disorders	Rare: hypertension
Respiratory, thoracic and mediastinal disorders	Uncommon: increased swelling of mucous membranes after discontinuation of treatment, epistaxis Very rare: apnoea in infants and neonates
Gastrointestinal disorders	Rare: nausea

General disorders and administration site conditions	Common: Stinging or burning sensation on the nose and throat; dry nasal mucous membranes. Very rare: fatigue

Paediatric population
Xylometazoline 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 xylometazoline. 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 Nederlands Bijwerkingen Centrum Lareb, website: www.lareb.nl

4.9 Overdose

Reported cases of overdosing have occurred mainly in children. The observed toxic effects were suppression of the central nervous system, including serious cases, sedation, oral dryness, perspiration and symptoms caused by stimulation of the sympathetic nervous system (tachycardia, irregular heartbeat and hypertension). Intranasal administration of drops (a single dose) for adults (1 mg/ml) containing xylometazoline caused a 4-hour coma in a 15-day-old child. The child fully recovered after subsequent treatment.
Intoxication treatment is symptomatic.
Administration of activated charcoal (adsorbens) and natriumsulfate (laxans), or where necessary gastric lavage is only useful in case of severe overdose and immediately after intake since xylometazoline can be absorbed rapidly. In case of severe overdose admission on the intensive care is indicated. As an antidotum a non- selective alfa-sympathicolyticum can be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other preparations for topical use, sympathomimetics, plain,
ATC Code: R01AA07.

Xylometazoline is an imidazoline derivative with sympathomimetic effects. When used topically, vasoconstriction is usually achieved within minutes of administration. The nasal anti-congestive effect usually lasts 6 to 8 hours.

Patients with sinusitis or tubular catarrh could be treated with this medicinal product if any other complications (e.g. bacterial sinusitis) can be excluded.

Symptoms of a rebound effect which sometimes occur with long-term use (mucous membrane swelling and congestion) are probably caused by the stimulating effects of the constituents on pre-synaptic alpha2 receptors and the suppressing effects on noradrenaline release. With vasoconstrictors, rebound-effect symptoms usually occur after 2 to 3 weeks of continuous treatment. However, xylometazoline has been administered in tests to healthy individuals for a period of 6 weeks without occurrence of mucous membrane swelling or tachyphylaxis.
A reduction of cilia function caused by xylometazoline has been observed i*n vitro;* this effect, however, is not permanent.

5.2 Pharmacokinetic properties

With correct use and dosage, absorption of xylometazoline into systemic circulation is minimal. However, absorption and subsequent systemic effects may occur with higher doses or when swallowed. There are no sufficient data on breakdown, metabolism or secretion of xylometazoline in humans.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.
No teratogenic effects could be observed in rats and mice. Doses above the therapeutic levels led to a reduced growth of the foetus. Milk production was reduced in rats. There is no evidence of effects on fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Purified sea water
- Potassium dihydrogen phosphate
- Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened bottle: 36 months.
Opened bottle: 3 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions. Do not freeze.

6.5 Nature and contents of container

Each package of Nasadur contains one multidose HDPE bottle with a PP/PE/Steel spray pump attached to the bottle neck and a plastic cover. The bottle is filled with 10 ml of nasal spray solution.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

JADRAN-GALENSKI LABORATORIJ d.d.
Svilno 20
51000 Rijeka
Croatia

8. MARKETING AUTHORISATION NUMBER(S)

RVG 107408

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 4 september 2012
Datum van laatste verlenging: 20 september 2016

10. DATE OF REVISION OF THE TEXT

Laatste gedeeltelijke wijziging betreft rubriek 4.4: 19 februari 2019