

SUMMARY PRODUCT CHARACTERISTIC

Otrepin-Arpi **Spray nasal, metered-dose 0.1%**

1.1. TRADE NAME – Otrepin-Arpi

1.2. INTERNATIONAL NON-PROPERTY NAME - Xylometazoline

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of Otrepin-Arpi, spray nasal, metered-dose 0.1% contains:

Active ingredient: Xylometazoline hydrochloride – 1 mg;

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spray nasal, metered-dose.

Clear solution, with menthol and eucalyptol (cineole) odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of nasal congestion, perennial and allergic rhinitis (including hay fever), sinusitis.

4.2 Posology and method of administration

Adults and children over 12 years: One application in each nostril up to 3 times daily as needed.

Do not exceed 3 applications daily into each nostril.

Route of administration: Nasal use

The recommended dose should not be exceeded, especially in children and the elderly.

4.3. Contraindications

Hypersensitivity to any ingredient, closed angle glaucoma, atrophic rhinitis, dry rhinitis, trans-sphenoidal hypophysectomy (or transnasal or transoral surgical interventions with exposure of the dura mater).

4.4. Special warnings and precautions for use

Otrepin-Arpi 0.1% Nasal Spray, metered-dose should not be used for more than seven consecutive days, prolonged or excessive use may cause rebound congestion and/or atrophy of the nasal mucosa.

Otrepin-Arpi 0.1% Nasal Spray, metered-dose like other sympathomimetic agents, should be used with caution in patients showing a strong reaction to adrenergic substances, as manifested by signs of insomnia, dizziness, tremor, cardiac arrhythmias or elevated blood pressure.

Caution is recommended in patients with hypertension, cardiovascular disease, hyperthyroidism or diabetes mellitus

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

Keep medicines out of the sight and reach of children.

Information concerning excipients

Otrepin-Arpi 0.1% Nasal Spray, metered-dose with menthol and eucalypt should not be used in children under 12 years of age.

Benzalkonium chloride, which is part of the medicine, can cause irritation and swelling of the nasal mucosa, especially with prolonged use.

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

Monoamine oxidase inhibitors. Xylometazoline can enhance the action of monoamine oxidase inhibitors and cause hypertensive crisis. Xylometazoline is not recommended in patients who are taking or have taken monoamine oxidase inhibitors within the past 14 days.

Tri- or tetracyclic antidepressants. The simultaneous use of tri- or tetracyclic antidepressants with sympathomimetic agents is not recommended, since it can cause an increase in the sympathomimetic action of xylometazoline.

4.6. Fertility, pregnancy and lactation

Pregnancy

In view of its vasoconstrictor effect, as precaution, do not use Otrepin-Arpi during pregnancy.

Lactation

It is not known whether xylometazoline passes into breast milk. The use of the drug Otrepin-Arpi during breastfeeding is possible only as prescribed by a doctor.

Fertility

There are no relevant data on the effect of Otrepin-Arpi on fertility. Controlled animal studies are not available. Since the systemic exposure of xylometazoline is very low, the likelihood of an effect on fertility is extremely small.

4.7. Effects on ability to drive and use machines

Otrepin-Arpi 0.1% Nasal Spray, metered-dose has no or negligible influence on the ability to drive and use machines. With prolonged use and high dosages of xylometazoline, possible systemic effects with cardiovascular effects cannot be ruled out.

4.8. Undesirable effects

The adverse reactions are listed below according to system class and frequency. The frequencies are defined as follows: Very common ($\geq 1/10$), common ($< 1/10$, $\geq 1/100$), uncommon ($< 1/100$, $\geq 1/1,000$), rare ($< 1/1,000$, $\geq 1/10,000$), very rare ($< 1/10,000$).

Within each group, adverse events are presented in decreasing order of severity.

Immune system disorders: very rare - hypersensitivity reactions (rash, itching, angioedema).

Nervous system disorders: common- headache.

Eye disorders: very rare - temporary visual disorder.

Cardiovascular disorders: very rare- irregular or increased heart rate, hypertension, arrhythmia.

Respiratory disorders: common- dryness, discomfort, burning of the nasal mucosa, drug rhinitis. uncommon: epistaxis (nosebleeds)

Gastrointestinal disorders: common- nausea.

General disorders: common- burning sensation at the place of application.

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 Arpimed “LLC” by going to www.arpimed.com and fill out the appropriate form **“Report an adverse reaction or inefficiency of drug”**. Hotline number: (+374 55) 05 79 86. And by using Scientific Centre of Drug and Medical Technology Expertise after academician E. Gabrielyan “CJSC”, going to the site: www.pharm.am in “Report about adverse effect of medicine” section and fill out the “Report of adverse reaction or manufacturing problem of medicinal product”.

Hotline numbers: +37410200505; +37496220505.

4.9. Overdose

Excessive topical use of xylometazoline or accidental ingestion can cause sympatholytic effects, including central nervous system depression (e.g., drowsiness, coma), hypertension or hypotension, tachycardia, and bradycardia. Gastrointestinal symptoms may also occur, such as nausea and vomiting. Other symptoms are pallor, excessive diaphoresis, hypothermia, myosis, respiratory depression, ataxia, and anxiety.

Severe symptoms after accidental overdose were not observed.

In one newborn (age 2 weeks), the use of 1 drop of a 0.1% solution into each nasal passage led to a coma.

In small children, the use of the drug up to 0.5 mg / kg body weight did not cause clinically relevant symptoms. Due to the lack of data on the use of more than 0.5 mg / kg of body weight, severe symptoms cannot be excluded. In such cases, medical supervision after consultation with an experienced clinician or toxicological information center and taking a single dose of activated charcoal are indicated. There is no specific antidote.

Symptomatic treatment; with bradycardia use atropine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action and pharmacodynamic effects

Xylometazoline is a sympathomimetic agent acting on alpha-adrenergic receptors in the nasal mucosa. Administered in the nose, it constricts the nasal blood vessels, thereby decongesting the mucosa of the nose and pharyngonasal cavity. This decongests nasal passages and enables patients suffering from blocked nose to breathe more easily through the nose, it means relieves nasal breathing. The effect of Otrepin-Arpi begins within a few minutes and lasts for up to 10 hours.

In a double-blind, saline solution controlled study in patients with common cold, the decongestant effect of xylometazoline was significantly superior ($p < 0.0001$) to saline solution based on rhinomanometry measurement. Relief of blocked nose developed twice as fast in the xylometazoline group compared to saline solution as of 5 minutes post treatment ($p = 0.047$).

Xylometazoline is well tolerated, even by patients with a sensitive mucosa, and does not impair the mucociliary function.

Contains sorbitol, which can reduce the symptoms of dryness of the nasal mucosa.

Pharmacotherapeutic group: decongestants for topical use, sympathomimetics, plain, ATC code: R01A A07.

5.2 Pharmacokinetic properties

Plasma concentrations of xylometazoline after local application of the product are near to the limit of detection.

Plasma concentrations of xylometazoline in man after local nasal application of the product are very low and close to the limit of detection.

5.3 Preclinical safety data

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

Carcinogenesis and mutagenesis

There are no carcinogenicity data available for xylometazoline hydrochloride, however, available *in-vitro* and *in-vivo* genotoxicity data for this active ingredient do not indicate a genotoxic potential.

Reproductive Toxicology

No teratogenic effects were shown in a study where xylometazoline was given subcutaneously in mice and rats.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

sodium dihydrogen phosphate dihydrate,
disodium hydrogen phosphate dodecahydrate,
benzalkonium chloride as 50% water solution,
macrogol glycerol hydroxystearate,
sodium chloride,
disodium edetate,
cineol (eucalyptol),
levomenthol,
sorbitol,
purified water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2.5 years.

Do not use the medicine for more than 28 days after opening.

6.4 Special precautions for storage

Store at a temperature not higher than 25⁰C, in the original package, out of the reach of children.

6.5 Nature and contents of container

15 ml solution in plastic bottle with a metered-dose pump, plastic nozzle with cap. 1 bottle with insert-leaflet in cardboard box.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MANUFACTURER

“ARPIMED” LLC

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8. MARKETING AUTHORIZATION HOLDER

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