<u>เอกสารกำกับยาภาษาอังกฤษ</u>

(เหมือนกันทุกขนาดบรรจุ)

DENOX 0.05% SPRAY

DENOX 0.1% SPRAY

Metered-dose Nasal Spray

Relieves Nasal Congestion, Fast acting

1. Name of the medicinal product

DENOX 0.05% SPRAY, Nasal spray, solution: Xylometazoline hydrochloride 0.5 mg/mL

DENOX 0.1% SPRAY, Nasal spray, solution: Xylometazoline hydrochloride 1 mg/mL

2. Qualitative and quantitative composition

DENOX 0.05% SPRAY: Each 1 mL contains xylometazoline hydrochloride 0.5 mg

DENOX 0.1% SPRAY: Each 1 mL contains xylometazoline hydrochloride 1 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Nasal spray, solution

Clear, colorless solution for spray

4. Clinical Particulars

4.1 Therapeutic indications

- For the relief of nasal congestion due to the colds, hay fever or other allergic rhinitis, sinusitis.
- To aid drainage of secretions in affections of the paranasal sinuses.
- As an adjuvant in otitis media, to decongest the nasopharyngeal mucosa.
- To facilitate rhinoscopy.

4.2 Posology and method of administration

(1) Posology

<u>DENOX 0.1% SPRAY</u> should not be used in children aged less than 12 years old.

Adults and children over 12 years, apply one application in each nostril up to 3 times daily as needed. Do not exceed 3 applications daily into each nostril.

<u>DENOX 0.05% SPRAY</u> should not be used in children aged less than 1 year old. It is recommended for use in children aged 1 to 11 years old only under adult supervision.

Children 1-5 years of age: 1 spray into each nostril once or twice daily (every 8 to 10 hours).
Children 6-11 years of age: 1 to 2 sprays into each nostril, 2 to 3 times daily.
Do not exceed 3 applications daily into each nostril.

DENOX SPRAY should not be used for more than seven consecutive days. The recommended dose should not be exceeded, especially in children and older people.

It is recommended to make the last application shorty before retiring to bed.

The metered-dose spray permits accuracy of dosage and ensures that the solution is well distributed over the surface of the nasal mucosa. It precludes the possibility of unintentional overdose. Before the first application, prime the pump by actuating 4 times. Once primed, the pump will normally remain charged throughout regular daily treatment periods. If the spray is not ejected during the full actuation stroke, or if the product has not been used for longer than 7 days, the pump will need to be reprimed with 4 actuations.

(2) Method of administration

Nasal use. Do not exceed the stated dose.
Keep out of the reach and sight of children.

Instructions for use/handling

1. Do not cut the nozzle. The metered dose spray is ready to prime before use.
2. Gently clear nose.
3. Remove protective cap.
4. Before using for the first time, prime the pump by actuating 4 times. Once primed, the pump will normally remain charged throughout regular daily treatment periods. If the spray is not ejected during the full actuation stroke, or if the product has not been used for longer than 7 days, the pump will need to be reprimed with 4 actuations. Be very careful not to spray in the eyes or mouth.
5. Hold the bottle upright with thumb under base and nozzle between two fingers.
6. Lean your head forward slightly and insert the nozzle into a nostril. Spray and breath in gently through the nose at the same time.
7. Repeat with the other nostril.
8. Clean and dry the nozzle before replacing back the cap right after use.
9. To avoid possible spread of infection, the spray should only be used by one person.

4.3 Contraindication

- Hypersensitivity to xylometazoline or to any of the excipients.
- Like other vasoconstrictors, DENOX SPRAY should not be used in patients with trans-sphenoidal hypophysectomy or surgery exposing the dura mater, narrow-angle glaucoma, rhinitis sicca or atrophic rhinitis.
- Use in people with phaeochromocytoma, prostatic hypertrophy or those receiving monoamine oxidase inhibitors (MAOI) treatment or who have used them in the last two weeks.

4.4 Special warning and precautions for use

DENOX SPRAY 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.

DENOX SPRAY, like other sympathomimetic agents, should be used only 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.

Use with caution in occlusive vascular disease

If any of the following occur, DENOX SPRAY should be stopped

- Hallucinations
- Restlessness
- Sleep disturbances

Keep medicines out of the sight and reach of children.

4.5 Interactions with other medicinal products and other forms of interactions

The concomitant use of xylometazoline with monoamine oxidase (MAO) inhibitors or tri- and tetra-cyclic antidepressants, may cause an increase in blood pressure due to the cardiovascular effects of these substances.

Moclobemide: risk of hypertensive crisis.

Antihypertensives (including adrenergic neurone blockers & beta-blockers): DENOX SPRAY may block the hypotensive effects.

Cardiac glycosides: increased risk of dysrhythmias

Ergot alkaloids (ergotamine & methylsergide): increased risk of ergotism

Appetite suppressants and amphetamine-like psychostimulants: risk of hypertension

Oxytocin – risk of hypertension

4.6 Pregnancy and lactation

Pregnancy:

No fetal toxicity or fertility studies have been carried out in animals. In view of its potential systemic vasoconstrictor effect, it is advisable to take the precaution of not using xylometazoline during pregnancy.

Lactation:

No evidence of any adverse effect on the breast-fed infant. However, it is not known if xylometazoline is excreted in breast milk, therefore caution should be exercised and xylometazoline should be used only on the advice of a doctor whilst breastfeeding.

Fertility:

There are no adequate data for the effects of DENOX SPRAY on fertility and no animal studies are available. As the systemic exposure to xylometazoline hydrochloride is very low, effects on fertility are therefore very unlikely.

4.7 Effects on ability to drive and use machine

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

4.8 Undesirable effects

The adverse effects listed below are classified by system organ class and frequency 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) or very rare (<1/10,000).

MeDRA SOC	Adverse reaction	Frequency
Immune System Disorders	Hypersensitivity reaction (angioedema, rash, pruritus)	Very rare
Nervous System Disorders	Headache	Common
	Irritability, Anxiety, Restlessness, Excitability, Insomnia, Hallucinations and Paranoid Delusions – particularly with prolonged and/or excessive use	Unknown
Eye Disorders	Transient visual impairment	Very rare
Cardiac Disorders	Heart rate irregular, Heart rate increased – particularly with prolonged and/or excessive use	Very rare
	Other cardiac dysrhythmias and hypertension particularly with prolonged and/or excessive use	Unknown
Respiratory, thoracic and mediastinal disorders	Nasal Dryness Nasal Discomfort Epistaxis	Common Common Uncommon
Gastrointestinal disorders	Nausea	Common
General disorders and administration site	Application site burning	Common
	Tolerance with diminished effect – especially with prolonged and/or heavy use	Unknown
	Rebound congestion (rhinitis medicamentosa) – especially with prolonged and/or heavy use	Unknown
	Irritation & dryness	Unknown

4.9 Overdose

Symptoms and Signs

Excessive administration of topical xylometazoline hydrochloride or accidental ingestion 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.

Treatment

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 several 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: decongestants for topical use, sympathomimetics, plain.

ATC Code: R01A A07

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 neighboring regions of the pharynx. This decongests nasal passages and enables patients suffering from blocked nose to breathe more easily through the nose. The effect of xylometazoline 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 0.1% 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.

DENOX SPRAY has a balanced pH within the range found in the nasal cavity. The moisturizing formula contains soothing ingredients that help prevent dryness and irritation of the nasal mucosa. DENOX SPRAY may also be used in case of ear infections, by helping to decongest the nasopharyngeal mucosa.

5.2 Pharmacokinetic properties

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

Xylometazoline has no mutagenic effect. 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 phosphate dibasic anhydrous
Sodium phosphate monobasic monohydrate
Disodium EDTA
Sodium chloride
70% Sorbitol solution
Hypromellose
Benzalkonium chloride
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30 ^{O}C.
Protect from heat.

6.5 Nature and contents of container

DENOX 0.05% SPRAY are filled in plastic bottle with spray nozzle cap of 10 and 15 mL packed in paper box of 1, 10, 50 and 100 bottles.

DENOX 0.1% SPRAY are filled in plastic bottle with spray nozzle cap of 10 and 15 mL packed in paper box of 1, 10, 50 and 100 bottles.

7. Manufacturer

MILLIMED CO., LTD.

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8. Marketing authorization number(s)

1A 81/67, 1A 82/67

9. Date of first authorization/renewal of the authorization

31 July 2024

10. Date of revision of the text

06 April 2024