

**Patient leaflet in accordance with the Pharmacists' Regulations
(Preparations) - 1986**

This medicine is dispensed with a doctor's prescription only

Vesoxx
Solution for intravesical use

Active ingredient

oxybutynin hydrochloride

1 ml solution contains 1 mg oxybutynin hydrochloride.
1 pre-filled syringe contains 10 mg oxybutynin hydrochloride.

Inactive ingredients and allergens in this medicine: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Vesoxx is indicated for the suppression of neurogenic detrusor overactivity (NDO) in children from 6 years of age and adults, who are managing bladder emptying by clean intermittent catheterisation (CIC), if they cannot be adequately managed by oral anticholinergic agents due to lack of efficacy and/or intolerable side effects.

Therapeutic group: Medicines for treatment of urinary frequency and urinary incontinence

The medicine works by relaxing the muscles of the bladder, thereby stopping sudden muscle contractions (spasms). This helps control the release of urine.

Vesoxx solution is intended for direct injection into the bladder (intravesical administration) through a tube called a catheter.

Treatment with Vesoxx must be started and supervised by a doctor specialised in the treatment of overactive bladder due to neurological disorders.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to oxybutynin hydrochloride (the active ingredient) or to any of the other ingredients in this medicine (see section 6).
- You have a rare autoimmune disease called myasthenia gravis that makes the muscles of the body to become weak and tire easily.
- You have a severe stomach or bowel disorder such as severe ulcerative colitis or toxic megacolon (an acute widening of the bowel).
- You suffer from glaucoma (increased intraocular pressure, sometimes sudden and painful with blurred vision or loss of vision). If you have a family history of glaucoma, tell your doctor.
- You experience difficulties in urinating or incomplete bladder emptying during urination (urinary retention).

- You experience frequent urination at night caused by heart or kidney disease.
- You receive oxygen therapy.

Special warnings about using this medicine

Before using Vesoxx, tell your doctor if:

- You have an infection of the urinary tract. Your doctor may need to prescribe certain antibiotics for you
- You are above 65 years of age, as you may be more sensitive to Vesoxx
- You take sublingual nitrates (a medicine which is placed under the tongue to treat chest pain)
- You have an obstruction of the digestive system, since Vesoxx might slow down the stomach and bowel movements
- You have a stomach tear (hiatus hernia) or heartburn
- You have a nerve disorder called autonomic neuropathy that affects involuntary body functions including heart rate, blood pressure, perspiration and digestion
- You have problems with memory, language, or thinking abilities
- You have an overactive thyroid gland, which can cause increased appetite, weight loss, or sweating
- You have narrowing of the blood vessels that supply blood and oxygen to the heart
- You have heart problems, which can cause shortness of breath or ankle swelling
- You have irregular and/or rapid heart beat
- You have high blood pressure
- You have an enlarged prostate

Vesoxx may reduce the amount of saliva, resulting in tooth decay (caries), gum disease, or fungal infection of the mouth (oral thrush).

Oxybutynin can cause a certain type of glaucoma. Immediately contact your doctor if you experience blurred vision, loss of vision or any pain in the eye. See also 'Tests and follow-up' section.

Care must be taken when using Vesoxx in hot weather or if you have fever. For example, you should stay out of sun and avoid sports activity in the midday heat. This is because Vesoxx reduces the amount of patient's sweat. This can lead to heat exhaustion and heat stroke.

Children and adolescents

Vesoxx is not recommended for use in children under the age of 6 years. The efficacy and safety of use in children under the age of 6 years have not been examined. See also 'Additional side effects in children and adolescents' in section 4.

Tests and follow-up

You should undergo periodic tests of visual acuity and intraocular pressure during treatment.

Interactions with other medicines

If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

Using Vesoxx at the same time with other medicines that cause similar side effects such as dry mouth, constipation and sleepiness may increase the frequency and severity of these side effects.

The active substance of Vesoxx is oxybutynin hydrochloride, which may slow the digestive tract and thereby influence the absorption of other oral medicines; in

addition, using this medicine together with other medicines may increase the effect of oxybutynin hydrochloride.

In particular, tell your doctor if you are taking any of the following medicines:

- bisphosphonates (used to treat osteoporosis) and other medicines that can cause or worsen inflammation of the oesophagus
- ketoconazole, itraconazole or fluconazole (used to treat fungal infections)
- erythromycin, a macrolide antibiotic (used to treat bacterial infections)
- biperiden, levodopa, or amantadine (used to treat Parkinson's disease)
- antihistamines (used to treat allergies such as hay fever)
- phenothiazine, butyrophenones or clozapine (used to treat mental illness)
- tricyclic antidepressants (used to treat depression)
- dipyridamole (used to treat blood clotting problems)
- quinidine (used to treat heart rhythm disorders)
- atropine and other anticholinergic medicines (used to treat gastrointestinal disorders such as irritable bowel syndrome)
- cholinesterase inhibitors (against dementia or certain muscle diseases)

Medicines for treatment of angina pectoris (chest tightness due to reduced blood flow to the heart) that should melt under the tongue may dissolve to a lesser extent under the tongue due to mouth dryness. It is therefore recommended to moisten (wet) the mouth before taking these medicines.

Using this medicine and alcohol consumption

Vesoxx may cause sleepiness or blurred vision. Sleepiness may be increased by alcohol consumption.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or plan to become pregnant, ask your doctor for advice before using this medicine.

Pregnancy

Do not use Vesoxx if you are pregnant unless your doctor has told you to.

Breastfeeding

It is not known whether Vesoxx is secreted in breast milk, therefore using Vesoxx during breastfeeding is not recommended.

Driving and using machines

Vesoxx may cause sleepiness or blurred vision. Special care is required while driving or using machines.

Important information about some of this medicine's ingredients

Vesoxx contains sodium

This medicine contains 3.56 mg sodium (main component of cooking/table salt) in each ml. This quantity is equivalent to 0.18% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Vesoxx?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to use this medicine.

Dosage

Your doctor will calculate the correct amount of Vesoxx needed to treat the overactive bladder. Do not change the dosage on your own mind.

During the start of treatment, your doctor will regularly check your bladder function and adjust the dosage as necessary.

Adolescents (aged 12 years and above), adults and elderly (over 65 years)

The recommended starting dosage is normally 10 ml per day.

Children (aged 6 - 12 years)

The recommended starting dosage is normally 0.1 mg/kg body weight in the morning and evening.

Do not exceed the recommended dose.

If you have liver or kidney problems

Please tell your doctor if you have a liver or kidney problem.

Method of administration

Your doctor will prescribe Vesoxx for you only if you or your relatives/caregiver are familiar with the procedure called 'clean intermittent catheterisation (CIC)'. This is a procedure which is performed at least 6 times a day to help empty urine from the bladder using a catheter.

CIC means clean intermittent catheterisation:

Clean: as germ-free as possible

Intermittent: performed on a regular schedule many times during the day

Catheterisation: using a catheter, a kind of thin tube, to drain urine out of the bladder

Your doctor will instruct you and/or your relatives/caregiver on the procedure of clean intermittent catheterisation (CIC) and the procedure of Vesoxx administration.

The procedure is as follows:

Polypropylene pre-filled syringe (for direct connection with standard catheter systems)

1. Disinfect your hands as indicated on the disinfectant package. Open the pre-filled syringe package at the spot marked for this purpose.
2. Take the pre-filled syringe out of the package. Remove the cap by turning it slightly.
3. Advice: If you were prescribed a dose lower than the amount in the syringe, remove the unnecessary amount from the syringe before instillation (Unused medicinal product or waste material should be disposed of in accordance with instructions of the medical team. For the sake of the environment, do not dispose of medicines in wastewater).
4. Now put the syringe back into its package without touching the tip of the syringe.
5. Disinfect your hands and begin catheterisation.
6. Empty your bladder completely through the catheter and make sure that the catheter is still in the bladder before you start instillation.
7. Take the pre-filled syringe out of the package again and connect it to the catheter.

8. Instil the contents of the pre-filled syringe into the bladder by pressing the syringe plunger. Remove the pre-filled syringe together with the catheter for disposal.
9. Unused medicinal product or waste material should be disposed of in accordance with instructions of the medical team. For the sake of the environment, do not dispose of medicines in wastewater.

The injected solution remains in the bladder until the next catheterisation. Each syringe is intended for single use only. The urethral catheter and any unused medicinal product should be discarded.

If you use more Vesoxx than you should

If you have accidentally instilled more than your prescribed dose, empty the bladder immediately via the catheter.

Overdose can cause symptoms such as restlessness, dizziness, disorders in speech and vision, muscle weakness or faster heartbeat.

If you experience one or more of these symptoms, contact your doctor or the nearest hospital as soon as possible.

If you forget to use Vesoxx

If you forget to use a dose at the usual time, use the usual dose in combination with the next catheterisation procedure. However, if it is nearly time for the next dose, skip the missed dose.

Do not use a double dose to make up for a forgotten dose.

If you are in doubt, always consult your doctor.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

If you stop using Vesoxx

If you stop using Vesoxx, your symptoms and condition of overactive bladder may return or worsen. Always consult your doctor, if you consider stopping the treatment.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, using Vesoxx may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

The most common side effects are typical of this kind of medicine and include dry mouth, sleepiness and constipation.

The following side effects have been reported with respect to the use of oxybutynin hydrochloride, although not all of them have been reported for intravesical administration. The frequency of these side effects is not known (the frequency cannot be estimated from the available data):

Stop using Vesoxx and/or contact a doctor immediately if:

- You experience a (severe) allergic reaction which causes swelling of the face or throat (angioedema)*
- You feel reduced sweating, leading to overheating in hot environment (heat stroke)*
- You experience sudden eye pain with blurred vision or loss of vision (glaucoma)*
- You experience mental clouding or confusion
- You experience loss of consciousness
- You experience a feeling of dizziness or 'spinning'
- You experience irregular heart rhythm (arrhythmia)*
- You experience seizures (fits)

Tell your doctor or pharmacist if any of the following side effects worsens.

Kidneys

- urinary tract infection
- occurrence of bacteria in the urine without causing symptoms
- urgent need to urinate (urinary urgency)
- protein in urine
- blood in urine
- pain when the solution is injected (instilled) into the bladder
- disorder in passing urine or difficulty to start urinating

Mental illnesses

- seeing or hearing things that are not there (hallucinations)
- cognitive disorders
- restlessness and excessive movement (hyperactivity)
- agitation*
- difficulty in sleeping
- agoraphobia (e.g. fear of leaving the house, entering shops, being in crowds and in public places)
- inability to concentrate
- anxiety*
- nightmares*
- feeling excessively suspicious and distrustful of others (paranoia)*
- symptoms of depression*
- becoming dependent on oxybutynin (in patients with history of drug or substance abuse)*

Consciousness

- disorientation
- fatigue
- feeling tired
- sleepiness

Eyes

- dry eyes
- abnormal sensation in the eyes
- inability of the eye to automatically change focus from distance to near objects, which can cause blurred vision, double vision, tired eyes
- blurred vision*

- increased intraocular pressure*

Heart and blood vessel diseases

- regular but abnormally fast heart rate (supraventricular tachycardia)
- low blood pressure

Skin

- facial flushing
- rash
- decreased sweating
- night sweats
- itchy lumpy rash (urticaria)*
- dry skin*
- skin that is more sensitive to the sun (photosensitivity)*

Digestive problems

- constipation
- dry mouth
- abdominal discomfort
- lower or upper abdominal pain
- nausea
- indigestion
- diarrhoea
- vomiting*
- loss of appetite (anorexia)*
- decreased appetite*
- difficulty in swallowing (dysphagia)*
- heartburn*
- abnormal swelling together with pain and nausea or vomiting (pseudo-obstruction)*
- change in the sense of taste
- thirst

General disorders

- chest discomfort
- feeling cold
- headache
- disease of the nervous system (anticholinergic syndrome)
- high level of a hormone called prolactin in the blood. Women might experience disruptions in the normal menstrual period or spontaneous flow of breast milk. Men might experience libido or erection disorders, as well as enlargement of the breast tissue.

* These side effects have been reported for this kind of medicines. However, it is not known whether these side effects will also occur during use of Vesoxx that you have been prescribed.

One patient experienced oxygen deficiency during home oxygen therapy (see section 2 under 'Do not use Vesoxx').

Additional side effects in children and adolescents

Children may be more sensitive to the effects of this medicine, particularly to central nervous system and psychiatric side effects.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage: Store below 30°C.

For single dose use only.

Any unused solution must be discarded immediately. If not used immediately, the storage time and storage conditions before administration are in responsibility of the user.

Do not throw away the medicine via wastewater or household waste. Ask the pharmacist how to dispose of this medicine (medicines you no longer use). These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

sodium chloride, hydrochloric acid, water for injections

What the medicine looks like and contents of the pack:

A clear and colourless solution in a polypropylene pre-filled syringe containing 10 ml solution with a synthetic bromobutyl rubber plunger and a tip cap.

A pack containing 12 or 100 pre-filled syringes for direct connection to standard catheter systems.

Not all pack sizes may be marketed.

Registration holder's name and address: Propharm Ltd., P.O.Box 4046, 23 Ben Gurion St., Zichron Yaacov.

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Registration number of the medicine in the Ministry of Health National Drug Registry:
174-61-37610-99