

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

This medicine is dispensed with a doctor's prescription only

Timolan-Avenir Eye Drops

Latanoprost 50 mcg/ml

Timolol (as Maleate) 5 mg/ml

Inactive ingredients and allergens: 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 for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

This medicine is intended for treatment of adults over the age of 18 years.

1. What is this medicine intended for?

- Reduction of intraocular pressure in patients with open angle glaucoma and ocular hypertension, who are insufficiently responsive to topical beta-blockers.

Therapeutic group:

Latanoprost – a prostaglandin analog. It works by increasing the outflow of fluid from the eye into the bloodstream.

Timolol – a beta-blocker. It works by slowing the formation of fluid in the eye.

2. Before using this medicine

• Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients or to any of the other ingredients in this medicine (see section 6 of this leaflet).
- You are sensitive (allergic) to medicines from the beta-blocker group.
- You have now or have had in the past respiratory system problems such as asthma, severe chronic obstructive bronchitis (a severe lung disease that may be manifested by wheezing, difficulty breathing, heavy breathing and/or a prolonged cough).
- You have severe heart problems or heart rhythm disturbances.

Special warnings about using this medicine

Before using Timolan-Avenir, tell your doctor if:

- You have now or have previously had coronary heart disease (the symptoms can include chest pain or tightness, breathlessness or choking), heart failure or low blood pressure.
- You have, or have previously had, heart rate disturbances, such as slow heartbeat.
- You have, or have previously had, angina (particularly a type of angina known as Prinzmetal angina).
- You suffer, or have suffered in the past, from respiratory system problems, asthma or chronic obstructive pulmonary disease (COPD).
- You have a disease that affects normal blood circulation, such as Raynaud's disease or Raynaud's syndrome.
- You have, or have previously had, diabetes, as the medicine may mask signs of a low blood sugar level.
- You suffer, or have suffered in the past, from overactivity of the thyroid gland, as the medicine may mask these signs and symptoms.

- You are due to undergo eye surgery (including cataract surgery) or you have had any kind of eye surgery in the past.
- You have eye problems (such as eye pain, eye irritation, eye inflammation or blurred vision).
- You have dry eyes.
- You wear contact lenses. You may still use Timolan-Avenir, however, please follow the instructions for using the drops, in section 3: "How to use this medicine?"
- You suffer from severe allergic reactions that require hospital treatment.
- You have or have previously had a viral infection of the eye caused by the herpes simplex virus (HSV).

Tell the doctor before you undergo surgery that you use Timolan-Avenir, as it may cause a change in the effect of some medicines used during anaesthesia.

Children and adolescents

There is no information about the safety of use and effectiveness of this medicine in children and adolescents under the age of 18.

Drug interactions

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

Timolan-Avenir can affect or be affected when used together with other medicines, including other eye drops for the treatment of glaucoma.

It is particularly important to inform your doctor or pharmacist if you are aware of the use of one of the following types of medicines:

- Prostaglandins, prostaglandin analogues or prostaglandin derivatives.
- Beta-blockers.
- Epinephrine.
- Medicines used to treat hypertension such as oral calcium channel blockers, guanethidine, antiarrhythmics (e.g., amiodarone), digitalis glycosides (e.g., digoxin) or parasympathomimetics.
- Quinidine (used to treat heart diseases and some types of malaria).
- Antidepressants (such as paroxetine and fluoxetine).
- Medicines to treat diabetes.
- Medicines to treat the heart.

Using this medicine and food

A normal diet, food and drink have no effect on when or how Timolan-Avenir is used.

Pregnancy, breast-feeding and fertility

Pregnancy

Do not use this medicine if you are pregnant unless your doctor had decided it is necessary. Tell your doctor immediately if you are pregnant, think you are pregnant or are planning to become pregnant.

Breast-feeding

Do not use this medicine if you are breast-feeding. This medicine may pass into breast milk. Consult your doctor before taking the medicine during breast-feeding.

Fertility

It has been found in animal studies that this medicine does not have an effect on male or female fertility.

Driving and using machines

When using the medicine, it is possible that you may temporarily suffer from blurred vision. If this happens to you, do not drive or operate dangerous machinery until your vision becomes clear again.

Important information about some of this medicine's ingredients

Timolan-Avenir contains benzalkonium chloride (a preservative) and phosphate buffers.

Benzalkonium chloride may be absorbed by soft contact lenses and cause them to become discoloured. Therefore, you should remove them before using this medicine and put them back in 15 minutes afterwards.

Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel an abnormal eye sensation, stinging or pain in the eye after using the medicine, consult with your doctor. If you suffer from severe damage to the clear layer at the front of the eye (the cornea), in very rare cases phosphates may cause cloudy patches on the cornea due to calcium build-up during treatment.

3. How to use this medicine?

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 take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually: one drop in the treated eye/eyes, once a day.

Do not exceed the recommended dose.

Do not use this medicine more than once a day, as the effectiveness of the treatment is reduced if the drops are used more than once a day.

Do not swallow! For external use only.

Use Timolan-Avenir as instructed by your doctor until your doctor tells you to stop.

Your doctor may ask you to perform additional cardiovascular function tests during treatment with the preparation.

Wearing contact lenses

If you wear contact lenses, remove them before using Timolan-Avenir.

After using Timolan-Avenir, you must wait 15 minutes before putting your contact lenses back in.

Instructions for use:

1. To avoid contaminating the solution, make sure that the tip of the bottle does not come into contact with any surface, including your finger or eye, and keep the bottle well closed.
2. The bottle of drops may not be full; this is to enable better control of the rate of the drops.
3. To avoid further contamination, do not use the same bottle of medicine for more than one person.
4. How to use the drops: First, wash your hands. Tilt your head back. Using your index finger, pull down your eyelid to create a "pocket". Put a drop of the medicine into the "pocket" created. Close your eyes gently. Do not blink.
5. Right after putting the drops into your eye, press your middle finger on the inner corner of your eye. Continue pressing for 1 to 2 minutes after putting the drops in your eye. This helps prevent the absorption of the medicine into the body and thus helps prevent side effects.

6. Repeat the procedure for your other eye, if your doctor has told you to use the medicine in both eyes.
7. Put the protective cap back on the bottle after each use.
8. After using the medicine, wash your hands well to remove residue of the medicine.

If you use this medicine together with other eye drops:

Wait at least 5 minutes between using this medicine and using other eye drops.

If you have accidentally taken a higher dose

If you put more than one drop into your eye, you may experience minor irritation, and your eyes may tear and turn red. These effects should pass, but if you are concerned, consult your doctor.

Contact your doctor as soon as possible if you or your child accidentally swallowed the medicine.

If you forget to take the medicine at the scheduled time, continue the treatment with the next dose as planned, but under no circumstances take a double dose to make up for the forgotten dose.

If you stop taking this medicine

You must consult with your doctor if you want to stop taking Timolan-Avenir.

Adhere to the treatment as recommended by the doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

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

Like with all medicines, using Timolan-Avenir 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 important possible side effect is a gradual and permanent change in eye colour. Likewise, Timolan-Avenir may affect your heart function. If you notice changes in your heart rate or function, inform your doctor that you are using Timolan-Avenir.

The following are known side effects of Timolan-Avenir:

Very common side effects (may occur in more than 1 in 10 users):

- A gradual change in your eye colour by increasing the amount of brown pigment in the coloured part of the eye known as the iris. If you have mixed-colour eyes (blue-brown, grey-brown, yellow-brown or green-brown), you are more likely to see this change than if you have eyes of one colour (blue, grey, green or brown eyes). Any change in your eye colour may take years to develop, although this will normally happen within 8 months of treatment. The colour change may be permanent and may be more noticeable if you use Timolan-Avenir in only one eye. There do not appear to be any functional problems associated with the change in eye colour, and it does not continue after treatment with the medicine is stopped.

Common side effects (may affect 1-10 in 100 users):

- Eye irritation (a feeling of burning, grittiness, itching, stinging or the sensation of a foreign body in the eye) and eye pain.

Uncommon side effects (may affect 1-10 in 1,000 users):

- Headache
- Redness of the eye, eye infection (conjunctivitis), blurred vision, watery eyes, inflammation of the eyelids, irritation or disruption of the surface of the eye.
- Skin rash or itching (pruritus).

Additional side effects:

Side effects that occur during use of medicines that contain one of the ingredients in this medicine and that can also occur when using this medicine:

- Nausea and vomiting (uncommon)
- Development of a viral infection of the eye caused by the herpes simplex virus (HSV).
- Generalized allergic reactions, including swelling beneath the skin that can occur in areas such as the face and limbs and can obstruct the airway, which may cause difficulty swallowing or breathing, hives or generalized or localized itchy rash, itchiness, severe sudden life-threatening allergic reaction.
- Low blood glucose levels.
- Dizziness.
- Difficulty sleeping (insomnia), depression, nightmares, memory loss, hallucinations.
- Fainting, stroke, reduced blood supply to the brain, worsening of signs and symptoms of myasthenia gravis (muscle disorder), unusual sensations like pins and needles, and headache.
- Swelling at the back of the eye (macular oedema), fluid filled cyst within the iris, light sensitivity (photophobia), sunken eye appearance (deepening of the eye sulcus).
- Signs and symptoms of eye irritation (e.g. burning, stinging, itching, tearing, redness), inflammation of the eyelid, inflammation in the cornea, blurred vision and detachment of the layer below the retina that contains blood vessels following a surgical procedure which may cause visual disturbances, decreased corneal sensitivity, dry eyes, corneal erosion (damage to the front layer of the eyeball), drooping of the upper eyelid (making the eye stay half closed), double vision.
- Darkening of the skin around the eye.
- Changes to the eyelashes and fine hairs around the eyes (such as increased number, length, thickness and darkening), changes to the direction of eyelash growth, swelling around the eye, scarring of the surface of the eye.
- Whistling/ringing in the ears (tinnitus).
- Angina, worsening of angina in patients with heart disease.
- Slow heart rate, chest pain, palpitations (awareness of heart rhythm), oedema (fluid build up), changes in the rhythm or speed of the heartbeat, congestive heart failure (heart disease with shortness of breath and swelling of the legs and feet due to fluid build up), a type of heart rhythm disorder, heart attack, heart failure.
- Low blood pressure, poor blood circulation which makes the fingers and toes numb.
- Shortness of breath, constriction of the airways in the lungs (predominantly in patients with pre-existing disease), difficulty breathing, cough, asthma, worsening of asthma.
- Taste disturbances, indigestion, diarrhoea, dry mouth, abdominal pain.
- Hair loss, skin rash with white silvery coloured appearance (psoriasiform rash) or worsening of psoriasis, skin rash.
- Joint pain, muscle pain not caused by exercise, muscle weakness, tiredness.
- Sexual dysfunction, decreased libido.

In very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.

Reporting 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 link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. 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 a 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 conditions:**
Before opening: Store in the refrigerator, at a temperature of 2°-8°C.
After opening: Do not store above 25°C.
Do not use for more than 4 weeks after first opening the bottle.

6. Additional information

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

Water for injections, Sodium dihydrogen phosphate monohydrate, Sodium chloride, Disodium phosphate anhydrous, Benzalkonium chloride, Hydrochloric Acid 0.1N or Sodium Hydroxide 1N (for pH adjustment).

This medicine contains 0.2 mg benzalkonium chloride per millilitre.

This medicine contains 6.3 mg phosphate per millilitre, which are equivalent to 0.2 mg in each drop.

What the medicine looks like and contents of the pack: 2.5 ml of clear eye drop solution.

Manufacturer: Vianex S.A. Tatoiou St., 18°Km National Road, 146 71 Nea Erithrea Attiki, Greece

Registration holder: BioAvenir Ltd., 1 David Hamelech St., Herzelia Pituach 4666101, Israel.

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Registration number of the medicine in the Ministry of Health's National Drug Registry:
159 54 34958 00