PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Xalacom® Eye Drops

Latanoprost 50 mcg/ml
Timolol (as Maleate) 5 mg/ml

For a list of inactive and allergenic ingredients in the preparation, please see section 6.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

For reducing intraocular pressure in patients with open-angle glaucoma and intraocular hypertension that are not fully responsive to beta-blockers (intended for external use).

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 THE MEDICINE

Do not use the medicine if:

- x You are sensitive (allergic) to the active ingredients or to any of the other ingredients contained in the medicine (as listed in section 6).
- x You are sensitive (allergic) to preparations from the beta-blocker group.
- x You are suffering, or have suffered in the past, from respiratory system disturbances such as: asthma, severe chronic obstructive bronchitis (a severe lung disease that may be manifested by wheezing, difficulty breathing and/or a prolonged cough).
- x You are suffering from severe heart problems or from heart rhythm disturbances.

Special warnings regarding use of the medicine

Before treatment with Xalacom®, tell the doctor if:

- You are suffering, or have suffered in the past, from coronary heart disease (the symptoms can include chest pain or tightness, breathlessness or choking), heart failure or low blood pressure.
- You are suffering, or have suffered in the past, from heart rate disturbances, such as slow heartbeat.
- You are suffering, or have suffered in the past, from angina (particularly a type known as Prinzmetal angina).
- You are suffering, or have suffered in the past, from respiratory system problems, asthma or chronic obstructive pulmonary disease (COPD).
- You are suffering from a disease that affects normal blood circulation, such as Raynaud's disease or Raynaud's syndrome.
- You are suffering, or have suffered in the past, from diabetes, as the medicine may mask signs of a low blood sugar level.
- You are suffering, 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 are suffering from eye problems (such as eye pain, eye irritation, eye inflammation or blurred vision).
- You are suffering from dry eyes.
- You wear contact lenses. You may still use Xalacom®, however, please follow the instructions for using the drops, in section 3: "How should you use the medicine?".
- You suffer from severe allergic reactions that require hospital treatment.
- You are suffering, or have suffered in the past from a viral infection of the eye caused by the herpes simplex virus (HSV).

Tell the doctor before you undergo surgery that you are using Xalacom®, as it may cause a change in the effect of some medicines used during anesthesia.

Children and adolescents

There is no information regarding the safety and effectiveness of this preparation in children and adolescents under 18 years of age.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist.

Xalacom® 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 the doctor or pharmacist if you are aware of the use of one of the following types of medicines:

- Prostaglandins, prostaglandin analogs 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.

Use of the medicine and food

A normal diet, food and drink have no effect on when or how Xalacom® is used.

Pregnancy, breast-feeding and fertility

Pregnancy

Do not use Xalacom® if you are pregnant unless your doctor considers it necessary. Tell your doctor immediately if you are pregnant, think you are pregnant or are planning to become pregnant.

Breast-feeding

Do not use Xalacom® if you are breast-feeding. This medicine may pass into breast milk. Ask your doctor for advice 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 operating machinery

When using Xalacom® 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 regarding some of the ingredients of the medicine

Xalacom® contains benzalkonium chloride (a preservative) and phosphate buffers.

Benzalkonium chloride may be absorbed by soft contact lenses and cause them to become discolored. 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 corneal problems (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 the course of treatment.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

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

Do not exceed the recommended dose!

Do not use Xalacom® more than once a day as the effectiveness of the treatment is reduced if the drops are instilled more than once a day.

Do not swallow! For external use only.

Use Xalacom® as instructed by your doctor until your doctor tells you to stop.

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

Wearing contact lenses

- If you wear contact lenses, remove them before using Xalacom®. After using Xalacom®, you must wait 15 minutes before putting your contact lenses back in.

Instructions for use:

1. Wash your hands, and sit or stand comfortably.
2. Twist off the outer cap (which can be thrown away).

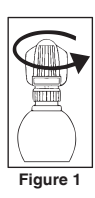

Figure 1

3. Unscrew the protective inner cap. The protective cap should be retained.

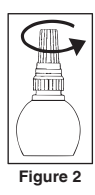

Figure 2

4. Use your finger to gently pull down the lower eyelid of the eye to be treated.
5. Place the tip of the bottle close to, but not touching, your eye.
6. Squeeze the bottle gently so that only one drop goes into your eye, and then release the lower eyelid.

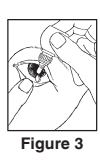

Figure 3

7. Press your finger on the corner of your eye, close to your nose (Figure 4) for about 2 minutes. This helps prevent the absorption of active ingredients into the rest of your body.

Figure 4

8. Repeat the procedure for your other eye if your doctor has told you to do this.
9. Put the protective inner cap back on the bottle.

If you are using Xalacom® together with other eye drops

Wait at least 5 minutes between using Xalacom® and instilling other eye drops.

If you accidentally take a higher dosage

If you instilled more than one drop into the eye, you may experience minor irritation in the eye, and your eyes may tear and become 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 this medicine at the required time, continue the treatment with the next dose as planned, but under no circumstances take a double dose to make up the forgotten dose.

If you stop taking the medicine

You must consult with your doctor if you wish to stop taking Xalacom®.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your condition, do not discontinue treatment with the medicine without consulting the doctor.

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

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of the medicine may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

The most important possible side effect is a gradual and permanent change in eye color. Likewise, Xalacom® may affect your heart function. If you notice changes in your heart rate or function, inform the doctor immediately that you are using Xalacom®.

The following side effects are known side effects of Xalacom®:

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

- A gradual change in your eye color by increasing the amount of brown pigment in the colored part of the eye known as the iris. If you have mixed-color 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 color (blue, grey, green or brown eyes). Any change in your eye color may take years to develop, although this will normally happen within 8 months of treatment. The color change may be permanent and may be more noticeable if you use Xalacom® in only one eye. There appears to be no problems associated with the change in eye color. The eye color change does not continue after Xalacom® treatment is stopped.

Common side effects (may occur in up to 1 in 10 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 occur in up to 1 in 100 users):

- Headache.
- Eye redness, conjunctivitis, blurred vision, watery eyes, inflammation of the eyelids, irritation or damage to the surface of the eye.
- Skin rash or itching.

Additional side effects

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

- 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 and a localized or generalized itchy rash and a generalized or localized itchy rash, itchiness, severe sudden life-threatening allergic reaction.
- Low blood sugar levels.
- Dizziness.
- Difficulty sleeping (insomnia), depression, nightmares, memory loss, hallucinations.
- Fainting, stroke, reduced blood supply to the brain, worsening of symptoms of myasthenia gravis (muscle disorder), unusual sensation of pins or needles, and headache.
- Swelling at the back of the eye (macular edema), 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., a feeling of burning, stinging, itching, tearing, redness), inflammation of the eyelid, inflammation in the cornea, blurred vision and detachment of the vascular layer below the retina as a result of 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 (causing the eye to remain half closed), double vision.
- Darkening of the skin around the eyes, changes to the eyelashes and fine hairs around the eye (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), edema (fluid retention), changes in heart rhythm or rate, congestive heart failure (heart disease characterized by shortness of breath and swelling of the legs and feet due to fluid retention), a type of heart rhythm disorder, heart attack, heart failure.
- Low blood pressure, poor blood circulation in the body which makes the fingers and toes numb.
- Shortness of breath, constriction of the airways in the lungs (predominantly in patients with pre-existing disease), breathing difficulties, cough, asthma, worsening of asthma.
- Taste disturbances, nausea, indigestion, diarrhoea, dry mouth, abdominal pain, vomiting.
- Hair loss, white-silver colored skin rash (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, during treatment, in some patients with severe damage to the clear area at the front of the eye (the cornea), cloudy patches developed on the cornea due to calcium build-up.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Before opening:** Store in the refrigerator, at a temperature of 2°-8°C.
- **After opening:** Store below 25°C. Do not use for more than 4 weeks after first opening the bottle.
- Keep the bottle in the original outer package to protect from light.
- Do not use this medicine if the color of the solution has changed or if it becomes cloudy.

6. FURTHER INFORMATION

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

Sodium dihydrogen phosphate monohydrate, sodium chloride, disodium phosphate anhydrous, benzalkonium chloride, water for injections.

This medicine contains 0.2 mg of benzalkonium chloride in each milliliter.

This medicine contains 6.3 mg phosphates in each milliliter which is equivalent to 0.2 mg per drop.

What the medicine looks like and the contents of the pack:

A bottle containing 2.5 ml transparent liquid.

Manufacturer and address: Pfizer Manufacturing Belgium NV/SA, Puurs, Belgium.

License holder and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 124-62-30356.

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