NOVARTIS

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
The medicine is dispensed with a doctor's prescription only

AZARGA
Ophthalmic Drops (Suspension)

Active ingredients: Each 1 ml contains:
Timolol (as timolol maleate) 5 mg
Brinzolamide 10 mg

The inactive ingredients appear in section 6 - "Further information".
Also see "Important information about some of the ingredients of the medicine" in section 2.

Read this 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 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.
The medicine is intended for adult patients from age 18 and above.

1. WHAT IS THE MEDICINE INTENDED FOR?

Azarga is intended for reduction of high intraocular pressure in adults, in cases of open-angle glaucoma and intraocular hypertension that do not fully respond to treatment for intraocular hypertension with a single medicine.

Therapeutic group: Brinzolamide - inhibitors of the enzyme carbonic anhydrase, for decreasing intraocular pressure.
Timolol– beta-blockers, for decreasing intraocular pressure.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine if:
- You have a known sensitivity to brinzolamide, sulfonamides (e.g., medicines to treat diabetes, infections, diuretics), timolol, beta-blockers (medicines to lower blood pressure or to treat heart disease), or to any of the additional ingredients contained in the medicine (see section 6 "Further information").
- You suffer, or have suffered in the past, from a respiratory problem such as: asthma, severe long-lasting obstructive bronchitis (a severe lung problem that may cause wheezing, breathing difficulties and/or persistent cough) or other respiratory problems.
- You suffer from severe hay fever.
- You suffer from slow heart rate, heart failure or heart rhythm disturbances (irregular heartbeat).
- You suffer from excessive acidity of the blood (hyperchloremic acidosis).
- You suffer from severe kidney problems.

Special warnings regarding use of this medicine
- **Azarga** should only be used for instilling into the eyes.
- If serious signs of allergic reactions or hypersensitivity occur, discontinue use of this medicine and refer to the attending doctor.

! Before treatment with Azarga, tell the doctor if you are suffering, or have suffered in the past, from:
- coronary heart disease (symptoms such as: chest pain or pressure in the chest, shortness of breath or choking), heart failure, low blood pressure.
- heart rate disturbances such as: slow heart rate.
- respiratory problems, asthma or chronic obstructive pulmonary disease.
- poor blood circulation (such as: Raynaud's disease or syndrome).
- diabetes, as timolol may mask signs and symptoms of low blood sugar levels.
- hyperactivity of the thyroid gland, as timolol may mask signs and symptoms of thyroid disease.
- muscle weakness (myasthenia gravis).
- Tell the doctor that you are using **Azarga** before you undergo surgery, as timolol may alter the effect of certain medicines given for anesthesia.
- if you have suffered in the past from atopy (a tendency to develop an allergic reaction) and from severe allergic reactions, you may be more susceptible to developing an allergic reaction during the use of **Azarga**, and adrenaline may be less effective in treating an allergic reaction. Before you undergo any other/additional treatment, inform the doctor or nurse that you are receiving **Azarga**.
- liver problems.
- dry eyes or corneal problems.
- kidney problems.

! Children and adolescents:
Azarga is not intended for use in children and adolescents under the age of 18.

! Drug interactions:
If you are taking, or have recently taken, or intend to take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular, if you are taking or intend to take:
- Other eye drops to treat glaucoma.
- Medicines for lowering blood pressure such as: parasympathomimetic medicines and guanethidine.
- Heart medicines such as: quinidine (for treatment of heart disease and some types of malaria), amiodarone or other medicines to treat heart rhythm disorders, glycosides for treatment of heart insufficiency.
- Medicines to treat diabetes.
- Medicines for the treatment of gastric ulcers.
- Antifungal preparations, antiviral medicines or antibiotics.
- Antidepressants such as: fluoxetine, paroxetine.
- Another carbonic anhydrase inhibitor such as: acetazolamide and dorzolamide.

Occasionally, pupil dilation has been reported when **Azarga** and adrenaline (epinephrine) were used concomitantly.

! Pregnancy and breast-feeding:
Pregnancy: Do not use **Azarga** if you are pregnant or might get pregnant, unless the doctor considers its use necessary. Consult with the doctor before using **Azarga**.
Breast-feeding: Do not use **Azarga** if you are breast-feeding. Timolol may pass into the mother's milk.
Consult the doctor before taking any medicine while breast-feeding.

! Driving and operating machinery:
You may notice that your vision is blurred for some time after using **Azarga**. Do not drive or operate machinery until your vision clears up.
One of the active ingredients may impair your ability to perform tasks requiring mental alertness and/or coordination. If you notice this effect, exercise caution with regards to driving or operating machinery.

! Important information about some of the ingredients in this medicine:
The medicine contains 3.34 microgram benzalkonium chloride in each drop (=1 dose), which is equivalent to 0.01% or 0.1 mg/ml.
Azarga contains a preservative (benzalkonium chloride), which may be absorbed by soft contact lenses and discolor them. Remove contact lenses before using the medicine and reinsert them into the eyes after 15 minutes. Benzalkonium chloride may also cause eye irritation, especially if you suffer from dry eyes or disturbances of the cornea (the clear layer in the front of the eyes). If you have an unusual sensation in your eyes, stinging or pain in the eye after using the medicine, refer to the doctor.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
If you are switching to **Azarga** from other eye drops used to treat glaucoma, stop using the other medicine and start using **Azarga** the following day. Check with the doctor or pharmacist if you are uncertain.
To avoid contamination of the tip of the bottle and the suspension, do not allow the tip of the bottle to touch the eyelids, surrounding areas or any other surfaces. Keep the bottle tightly closed when not in use.

The following step is important to limit the amount of medicine that passes to the blood after using the eye drops:
Keep the eyelid closed while simultaneously pressing gently on the corner of the eye near the nose with a finger, for at least 2 minutes.

The bottle of drops may not be full; this is to allow for better control of the drip rate.
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally 1 drop in the treated eye(s), twice a day. Only use in both eyes if the doctor has instructed you to do so. Use the medicine for as long as the doctor has told you to.
Do not exceed the recommended dose.
Do not swallow. This medicine is intended for use in the eyes only.

How to use the drops: Shake the bottle well before use. If the tamper evident snap collar is loose, remove it before use.
Wash your hands. Tilt your head back. Bring the tip of the bottle close to the eye. Use a mirror if it helps. Using the index finger, pull down the lower eyelid to create a sort of "pocket" (Figure 1). Instill the medicine into the "pocket" that has been formed. Close your eyes gently. Do not blink. Keep your eyes closed for at least 2 minutes.
Do not squeeze the bottle; a gentle press on the base of the bottle is sufficient to release a drop (Figure 2).
In addition to the instructions provided above - immediately after instilling the drop into the eye, put pressure on the inner corner of the eye using your middle finger. Continue applying pressure for at least 2 minutes after instilling into the eye. This action helps prevent absorption of the medicine into the body and thereby helps prevent side effects (Figure 3).

1 2 3

Repeat the above-mentioned steps in the other eye, if the doctor has instructed to treat both eyes.
Close the bottle tightly.
After using the medicine, wash your hands thoroughly in order to clean them of any remnants of the medicine.

To prevent the infection from spreading, do not use the same medicine bottle for more than one person.

If a drop misses the eye, try again.

Wait at least 5 minutes between administration of this medicine and administration of other ophthalmic drops or ointments. Eye ointments should be applied last.

If you used a larger dose than required, rinse your eye with lukewarm water. Do not instill any additional drops until it is time for your next dose.

You may experience a decreased heart rate, reduced blood pressure, heart failure, breathing difficulties. Likewise, there may also be an effect on the nervous system.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

Use this medicine at the scheduled times, as determined by the attending doctor.

If you forgot to take the medicine at the required time, take the next dose as planned. Do not take a double dose in order to compensate for a forgotten dose. Do not exceed the dosage of one drop, twice a day, in the treated eye(s).
Adhere to the treatment regimen recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist. This may lead to an uncontrolled increase in intraocular pressure, which may cause loss of vision.
Do not take medicines in the dark! Check the label and the 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 **Azarga** may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Discontinue use and refer to a doctor immediately if you develop skin rash, severe skin reaction or severe eye redness and itching. These could be signs of an allergic reaction (frequency not known).
You can usually continue using the drops, unless the side effects are serious. If you are worried, refer to the doctor or pharmacist. Do not stop using **Azarga** without consulting the doctor.

Common side effects - effects that occur in 1-10 in 100 users
- **Eyes:** inflammation on the surface of the eye, blurred vision, signs and symptoms of eye irritation (such as: burning, stinging, itching, tearing, redness), eye pain.
- **General side effects:** reduced heart rate, taste disturbances.

Uncommon side effects - effects that occur in 1-10 in 1,000 users
- **Eyes:** Corneal erosion (damage of the front layer of the eyeball), inflammation with damage to the surface of the eye, inflammation inside the eye, corneal staining, abnormal sensation in the eyes, eye discharge, dry eyes, tired eyes, itchy eye, eye redness, eyelid redness.
- **General side effects:** reduced white blood cell count, low blood pressure, cough, blood in the urine, body weakness.

Rare side effects - effects that occur in 1-10 in 10,000 users
- **Eyes:** corneal disorder, sensitivity to light, increased tear production, eyelid crusting.
- **General side effects:** sleeping difficulties (insomnia), sore throat, runny nose.

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- **Eyes:** Eye allergy, vision disturbances, damage to the optic nerve, increased pressure in eye, deposits on the eye surface, decreased eye sensation, inflammation or infection of the conjunctiva (the white of the eye), abnormal vision, double vision or reduced vision, increased pigmentation of the eye, growth on the surface of the eye, eye swelling, sensitivity to light, decreased growth or number of eyelashes, drooping of the upper eyelids (such that the eyes are half-closed), inflammation of the eyelids and eyelid glands, inflammation of the cornea and detachment of the layer below the retina, that contain blood vessels, due to filtration surgery, which may cause visual disturbances, decreased corneal sensitivity.
- **Heart and blood circulation:** Changes in heart rhythm, slow heart rate, palpitations, a type of heart rhythm disorder, an abnormal increase in heart rate, chest pain, reduced heart function, heart attack, increased blood pressure, reduced blood supply to the brain, stroke, edema (fluid retention), heart failure (a heart disease accompanied by shortness of breath and swelling of the feet and legs due to fluid retention), swelling of the extremities, low blood pressure, discoloration of the fingers, toes, and occasionally other areas of the body (Raynaud's phenomenon), cold hands and feet.
- **Respiration:** Constriction of the airways in the lungs (predominantly in patients with pre-existing diseases), shortness of breath or difficulty breathing, cold symptoms, chest congestion, sinusitis, sneezing, stuffy nose, dry nose, nosebleed, asthma, throat irritation.
- **Nervous system and general disorders:** Hallucinations, depression, nightmares, memory loss, headaches, nervousness, restlessness, fatigue, tremor, general abnormal feeling, fainting, dizziness, drowsiness, general or severe weakness, unusual sensations such as 'pins and needles'.
- **Digestive system:** Nausea, vomiting, diarrhea, intestinal gas or abdominal discomfort, inflammation of the throat, dry or abnormal sensation in the mouth, indigestion, stomach aches.
- **Blood:** Abnormal liver function values, increased blood chloride levels or decreased red blood cell counts seen in blood tests.
- **Allergy:** Increased allergy symptoms, general allergic reactions including swelling beneath the skin that can occur in areas such as: the face and limbs and may cause obstruction of the airways. This may cause difficulty swallowing or breathing, hives (skin disease), localized and generalized rash, itching, severe, sudden, life-threatening allergic reaction.
- **Ears:** Ringing in the ears, sensation of lightheadedness or dizziness.
- **Skin:** Rash, skin redness or inflammation, decreased or abnormal skin sensation, hair loss, rash with a white-silvery colored appearance (psoriasiform rash) or worsening of psoriasis.
- **Muscles:** Widespread back, joint or muscular pain not caused by physical activity, muscle spasms, pain in the extremities, muscle weakness/fatigue, increased symptoms and signs of the muscle disease myasthenia gravis (muscle weakness).
- **Kidneys:** Kidney pain such as lower back pain, frequent urination.
- **Reproduction:** Sexual function problems, decreased libido, sexual dysfunction among men.
- **Metabolism:** Low blood sugar levels.

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.

Reporting side effects

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 in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the carton/label. The expiry date refers to the last day of that month.
- **Storage conditions:** Do not store above 30°C.
- To prevent contamination, can be used for 4 weeks after first opening. After 4 weeks, throw out the old bottle and use a new bottle. Record the opening date on the carton.

6. FURTHER INFORMATION

In addition to the active ingredients, the medicine also contains: Mannitol, carbomer (974P), sodium chloride, tyloxapol, benzalkonium chloride, disodium edetate, sodium hydroxide and/or hydrochloric acid (to adjust pH), purified water.

What the medicine looks like and the contents of the package: A plastic bottle containing 5 ml of white/cream colored uniform liquid (suspension).

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 145 12 32030

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