NOVARTIS

PATIENT PACKAGE INSERT IN ACCORDANC WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

SIMBRINZA®

Eye drops, suspension

Active ingredients:
Brimonidine tartrate 2 mg/ml
Brinzolamide 10 mg/ml

Inactive and allergenic ingredients in the preparation appear in section 6 "Further Information" and in section 2 "Important information about some of the ingredients of the medicine".

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 the treatment of your ailment. 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 use by adults over the age of 18.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for the reduction of intraocular pressure in adults (over 18 years of age) in cases of glaucoma or intraocular hypertension in patients who do not fully respond to treatment for intraocular pressure with a single medicine.

Therapeutic group:
Brimonidine tartrate – alpha-2 adrenergic receptor agonist.
Brinzolamide – carbonic anhydrase inhibitor.
Both ingredients work together to reduce intraocular pressure.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:
- You have a known sensitivity (allergy) to brinzolamide or brimonidine tartrate or to any of the other ingredients of the medicine (see section 6 "Further Information").
- You are sensitive (allergic) to medicines from the sulphonamide group (such as: medicines for the treatment of diabetes, for the treatment of infections and diuretics).
- You are taking medicines that inhibit the enzyme monoamine oxidase (such as medicines for the treatment of depression or Parkinson's disease) or certain anti-depressants. You must inform the doctor if you are taking any anti-depressants.
- You suffer from severe kidney problems.
- You suffer from excessive acidity of the blood (caused by an increased level of chlorine, known as hyperchloraemic acidosis).
- In children and infants under the age of 2 years.

Special warnings regarding use of the medicine

Before treatment with Simbrinza, tell the doctor or pharmacist if you are suffering, or have suffered in the past, from:
- Liver problems.
- High intraocular pressure called narrow-angle glaucoma.
- Dry eyes or corneal problems.
- Coronary heart disease (characterized by symptoms such as chest pain or a feeling of pressure in the chest, difficulty breathing or choking), heart failure, high or low blood pressure.
- Depression.
- Impaired or poor blood circulation (such as Raynaud's disease, Raynaud's syndrome or cerebral insufficiency).
- If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using Simbrinza or other similar medicines.

Extra caution is required when using Simbrinza in the following situations:
Serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with brinzolamide treatment. Stop using Simbrinza and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Do not use this preparation while you are wearing soft contact lenses. Take out the lenses before using the preparation - see in section 2 "Important information about some of the ingredients of the medicine".

Children and adolescents
Simbrinza is not intended for use in children and adolescents under the age of 18, as the medicine has not been studied in this age group. It is especially important not to use in children under the age of 2 years (see in section 2 –"Do not use this medicine if"), as it is likely to be unsafe.

Drug interactions
If you are taking, may take, or have recently taken, other medicines in addition to Simbrinza, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Simbrinza can affect or be affected by other medicines you are using, including other eye drops for the treatment of glaucoma. Tell the doctor or pharmacist, especially if you are taking:
- medicines to lower blood pressure.
- heart medicines, including digoxin (to treat heart diseases).
- other medicines to treat glaucoma that also treat altitude sickness, such as: acetazolamide, methazolamide and dorzolamide.
- medicines that can affect the metabolism, such as chlorpromazine, methylphenidate and reserpine.
- antivirals (including medicines to treat AIDS [HIV]) or antibiotics.
- medicines to treat fungi and yeasts.
- monoamine oxidase inhibitors or antidepressants, including amitriptyline, nortriptyline, clomipramine, mianserin, venlafaxine and duloxetine.
- anesthetics.
- sedatives, opiates, barbiturates.
- likewise, inform the doctor about any change in the dosage of your current medicines.

Use of the medicine and alcohol consumption
If you consume alcohol on a regular basis, consult the doctor or pharmacist before using the medicine. Simbrinza may be affected by drinking alcohol.

Pregnancy and breastfeeding
Pregnancy:
Consult the doctor before using the medicine if you are pregnant, think you are pregnant or are planning a pregnancy.
During treatment with Simbrinza, it is recommended to use effective contraception for women who may become pregnant.
The use of Simbrinza during pregnancy is not recommended. Do not use the medicine unless explicitly instructed by the doctor.
Breastfeeding:
The medicine may pass into breast milk. If you are breastfeeding, it is not recommended to use Simbrinza.

Driving and operating machinery
Use of the medicine may cause blurred or disturbed vision for a period of time immediately after use. The medicine may also cause dizziness, drowsiness or fatigue in some patients. Do not drive or operate machinery until the symptoms have passed.

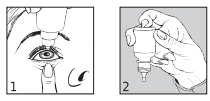
Important information about some of the ingredients of the medicine
The medicine contains 0.15 mg of the preservative benzalkonium chloride in every 5 ml, which is equivalent to 0.03 mg/ml. Benzalkonium chloride may be absorbed by soft contact lenses and can discolor the contact lenses. Remove contact lenses before using this medicine, and reinsert them at least 15 minutes after instilling the medicine into the eye. Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or a disorder of the cornea (the transparent layer at the front of the eye). If you experience an abnormal sensation in the eye, stinging or eye pain after using the medicine, refer to your doctor.

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 about 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 each treated eye, twice a day, at fixed times.

Do not exceed the recommended dose
Attention: Do not swallow or inject the medicine! This medicine is intended for use in the eyes only.

Instructions for use:
Shake well before use.
To avoid contamination, do not allow the tip of the bottle to come into contact with any surface (including the eye itself). Keep the bottle tightly closed.
The bottle of drops may not be full; this is to allow better control of the drip rate.



How to use the drops:

First, wash your hands. Twist off the bottle cap. After the cap is removed, if the tamper evident snap collar is loose, remove it before use. Hold the bottle between your thumb and finger, with the opening pointing downwards.

Do not touch the dropper with your fingers when opening or closing the bottle, as you could contaminate the medicine.

Tilt your head back. With your index finger, pull the lower eyelid down, to create a type of "pocket". Instill the medicine into the "pocket" that has been formed (Figure 1). Do this in front of a mirror if it helps.

Do not squeeze the bottle; gently pressing at the base of the bottle is sufficient to extract a drop (Figure 2).

Do not touch your eye or eyelid, surrounding areas or other surfaces with the dropper. This action could contaminate the drops.

Immediately after applying the drop into the eye, close your eye and by using your middle finger, press on the corner of the eye near the nose, for 2 minutes. This action helps prevent absorption of the medicine in your body, thus helping to prevent side effects.

If the treatment is intended for both eyes, repeat the same steps for the other eye. There is no need to close and shake the bottle again before instilling the drops into the other eye.

Close the bottle well immediately after use.

If you are using other eye drops in addition to Simbrinza, wait at least 5 minutes between taking this medicine and taking other drops for treating the eye.

If a drop misses the eye, try again.

After using the medicine, wash your hands thoroughly to clean them from any remnants of the medicine.

To prevent the spread of infection, do not use the same medicine container for more than one person.

If you used a larger amount than necessary, rinse your eyes with warm water. Do not apply more drops until it is time for the next dose.

If you took an overdose, or if an adult/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.

Adults who accidentally swallowed medicines containing brimonidine experienced a decrease in heart rate, a decrease in blood pressure with a possible subsequent rise in blood pressure, heart failure, breathing difficulties and effects on the nervous system. In this case, refer to a doctor immediately.

Severe side effects have been reported in children who accidentally swallowed medicines containing brimonidine. The signs included sleepiness, floppiness, low body temperature, pallor and breathing difficulties. In this case, refer to a doctor immediately.

If you forgot to take this medicine at the required time, take the next dose as planned, but do not under any circumstances take two doses together in order to make up for the forgotten dose. Do not exceed a dosage of one drop in the treated eye, twice a day.

Adhere to the treatment regimen as recommended by the doctor.

If you stop taking the medicine

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist. If you stop using Simbrinza, the intraocular pressure will not be controlled, which can cause vision loss.

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 Simbrinza 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.

Stop using the medicine and contact the doctor immediately if you experience any of the following side effects, as they could be signs of a reaction to the medicine. The frequency of allergic reaction to the medicine is unknown (it is not possible to estimate from the existing data).

- Serious skin effects, including rash or redness or itching of the body or the eyes.
- Breathing difficulties.
- Chest pain, irregular heart rate.

Refer to the doctor immediately if you experience extreme fatigue or dizziness.

The following side effects were observed with Simbrinza and other medicines containing brinzolamide or brimonidine alone.

Stop using Simbrinza and seek medical attention immediately if you notice any of the following symptoms:

- Reddish non-elevated, target-like or circular patches on the trunk (back, chest, abdomen, pelvis), often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis).

Common side effects - effects that occur in 1-10 in 100 users:

In the eyes: Allergic conjunctivitis (eye allergy), eye surface inflammation, eye pain, sensation of discomfort in the eye, blurred vision or visual disturbances, eye redness.

General side effects: Dizziness, drowsiness, dry mouth, bad taste in mouth.

Uncommon side effects - effects that occur in 1-10 in 1,000 users:

In the eyes: Eye surface damage with loss of cells, inflammation of the eyelid, sediments on the surface of the eye, sensitivity to light, swelling of the eye (effect on the cornea or eyelid), dry eyes, eye discharge, watery eyes, eyelid redness, abnormal or decreased sensation in the eye, tired eyes, reduced vision, double vision, medicine particles in the eyes.

General side effects: Decreased blood pressure, chest discomfort, irregular heart rate, slow or fast heart rate, palpitations, sleeping difficulties (insomnia), nightmares, depression, general weakness, headache, dizziness, nervousness, irritability, general feeling of discomfort, memory loss, shortness of breath, nosebleed, cold symptoms, dry throat or nose, sore throat, throat irritation, cough, runny nose, stuffy nose, sneezing, sinus infection, chest congestion, ringing in the ears, indigestion, intestinal gas or stomachache, nausea, diarrhea, vomiting, unusual sensation in the mouth, increased skin allergy symptoms, rash, unusual sensation in the skin, hair loss, general itching, increased blood chlorine levels, or decreased red blood cell count as can be seen in blood tests, pain, back pain, muscle pain or cramps, kidney pain such as lower back pain, decreased libido, sexual dysfunction in men.

Very rare side effects - effects that occur in less than 1 user in 10,000:

In the eyes: Decreased pupil size.

General side effects: Fainting, increased blood pressure.

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

In the eyes: Decreased growth of eyelashes.

General side effects: Tremor, decreased sensation, loss of sense of taste, abnormal liver function values as seen in blood tests, swelling of the face, joint pain, frequent urination, chest pain, swelling of the limbs, reddish non-elevated, target-like or circular patches on the trunk (back, chest, abdomen, pelvis), often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes, which can be preceded by fever and flu-like symptoms. These serious skin rashes can be potentially life-threatening (Stevens-Johnson syndrome, toxic epidermal necrolysis), asthma.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this 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: store below 25°C.
- After first opening, can be used for 4 weeks. The bottle should be discarded 4 weeks after opening. Write the opening date on the carton.

6. FURTHER INFORMATION

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

Propylene glycol, carbomer 974P, boric acid, mannitol, sodium chloride, tyloxapol, benzalkonium chloride, hydrochloric acid and/or sodium hydroxide, purified water.

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

A plastic bottle containing 5 ml of a white to creamy-white suspension.

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

Revised in January 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 158 81 34867