



Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Ranivisio, 10 mg/ml Solution for intravitreal injection

Active ingredient:

Ranibizumab 10 mg/ml

Inactive ingredients and allergens in the medicine – see section 6 "Additional information"

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask 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 you think that their illness is similar.

In addition to the leaflet, the medicine **Ranivisio** has a patient safety information card. This card contains important safety information that you must know and follow before starting treatment and during treatment with **Ranivisio**. Carefully read the patient safety information card and the patient leaflet before you start using the medicine. Keep the card for further review if needed.

1. What is the medicine intended for?

Ranivisio is intended:

- For treatment of patients with neovascular (wet) age-related macular degeneration (AMD)
- For treatment of adult patients with visual impairment due to diabetic macular edema (DME)
- For treatment of visual impairment due to macular edema secondary to retinal vein occlusion (RVO)
- For treatment of visual impairment due to choroidal neovascularization (growth of new, abnormal blood vessels in the vascular layer of the eye) (CNV)
- For treatment of proliferative diabetic retinopathy (PDR)

Therapeutic group: Eye medicines that contradict the growth of new blood vessels (anti-neovascularization).

Ranivisio is used in adults for treatment of several eye diseases that cause vision impairment. These diseases result from damage to the retina (light-sensitive layer at the back of the eye) caused by the conditions that the medicine is intended to treat.

Ranivisio specifically recognizes and binds to a protein called human vascular endothelial growth factor A (VEGF-A) present in the eye. In excess, the protein causes abnormal blood vessel growth and swelling in the eye, which can lead to impairment of vision in diseases such as neovascular (wet) age-related macular degeneration (AMD), vision impairment resulting from diabetic macular edema (DME), vision impairment resulting from proliferative diabetic retinopathy (PDR), vision impairment resulting from macular edema secondary to retinal vein occlusion (RVO), vision impairment resulting from choroidal neovascularization (CNV). By binding to the protein, **Ranivisio** can block its action and prevent the abnormal blood vessel growth and swelling.

In these diseases, **Ranivisio** can help stabilize, and in many cases, improve your vision.

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (ranibizumab), or to any of the other ingredients this medicine contains (see section 6).
- You have an infection in or around the eye.
- You have pain or redness (severe intraocular inflammation) in the eye.

Special warnings regarding the use of the medicine

Consult your doctor before starting treatment with **Ranivisio**.

- **Ranivisio** is given as an injection into the eye. Occasionally, an infection in the internal portion of the eye, pain or redness (inflammation), detachment or tear of one of the layers in the back of the eye (retinal detachment or tear and retinal pigment epithelial detachment or tear) or clouding of the lens (cataract) may occur after **Ranivisio** treatment. It is important to identify and treat such an infection or retinal detachment as soon as possible. Please tell your doctor immediately if you develop signs such as eye pain or an increased sense of discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in your field of vision or an increased sensitivity to light.
- In some patients, the eye pressure may increase for a short period immediately after the injection. You may not notice this; therefore your doctor may monitor this after each injection.
- Inform your doctor if you have a history of eye diseases or eye treatments, or if you have had a stroke or experienced transient signs of a stroke (weakness or paralysis of limbs or face, difficulty speaking or understanding). This information will be taken into account to evaluate if **Ranivisio** is the appropriate treatment for you.

For more detailed information on side effects that could occur during **Ranivisio** treatment, see section 4 "Side effects".

Children and adolescents

The preparation is not intended for children and adolescents.

Drug interactions

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

Pregnancy and breastfeeding

- Women who could become pregnant must use effective contraception during treatment and for at least three additional months after the last injection of **Ranivisio**.
- There is no experience of using **Ranivisio** in pregnant women. **Ranivisio** should not be used during pregnancy, unless the potential benefit from treatment outweighs the potential risk to the unborn child. If you are pregnant, think you may be pregnant or are planning a pregnancy, discuss this with your doctor before treatment with **Ranivisio**.
- Small amounts of **Ranivisio** may pass into breast milk, therefore **Ranivisio** is not recommended for use while breastfeeding. Consult with your doctor or pharmacist before **Ranivisio** treatment.

Driving and using machines

After treatment with **Ranivisio** you may experience temporary blurred vision. If this happens, do not drive or use machines until the blurred vision passes.

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine. **Ranivisio** will be administered to you as a single injection into the eye by your eye doctor, under local anesthesia.

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

For treatment of adults, the usual dosage of an injection is generally: 0.05 ml (which contains 0.5 mg of active ingredient).

The interval between two doses injected into the same eye should be at least four weeks. All injections will be administered by the eye doctor.

Before the injection, the doctor will wash your eye carefully to prevent infection. The doctor will also give you local anesthesia to reduce or prevent any pain you may experience with the injection.

The treatment in adults begins with one injection of **Ranivisio** per month.

The doctor will monitor the condition of your eye, and depending on how you respond to the treatment, will decide if and when you need to receive further treatment.

Detailed instructions on how to use **Ranivisio** are provided in English at the end of the leaflet, in the section "How to prepare and administer **Ranivisio** to adults".

Elderly (age 65 years and over)

Can be used in people over the age of 65 without dosage adjustment.

Do not exceed the recommended dose.

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

Continue with the treatment as recommended by the doctor.

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

Before stopping Ranivisio treatment

If you are considering stopping your **Ranivisio** treatment, go to your next appointment and discuss this with the doctor.

The doctor will advise you and will decide how long you should be treated with **Ranivisio**.

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

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

4. Side effects

Like any medicine, the use of **Ranivisio** 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.

Side effects related to the use of **Ranivisio** may be the result of the medicine itself or from the injection procedure, and mostly affect the eye.

The most serious side effects are listed below:

Common serious side effects (effects that occur in 1-10 out of 100 users): Detachment or tear of the layer in the back of the eye (retinal detachment or tear), resulting in flashes of light with floaters, progressing to a temporary loss of sight or clouding of the lens (cataract).

Uncommon serious side effects (effects that occur in 1-10 out of 1,000 users): Blindness, infection of the eyeball (endophthalmitis) with inflammation of the inside of the eye.

The symptoms you might experience are pain or increased discomfort in the eye, worsening eye redness, blurred or decreased vision, an increased number of small particles in the field of vision or increased sensitivity to light. **Refer to the doctor immediately if you develop any of these side effects.**

The most frequently reported side effects are listed below:

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

Visual side effects include: Inflammation of the eye, bleeding in the back of the eye (retinal bleeding), visual disturbances, eye pain, small particles or spots in your field of vision (floaters), bloodshot eye, eye irritation, sensation of a foreign body in the eye, increased tear production, inflammation or infection of the eyelid margins, dry eye, redness or itching of the eye and increased eye pressure.

Non-visual side effects include: Sore throat, nasal congestion, runny nose, headache and joint pain.

Other side effects which may occur following Ranivisio treatment are listed below:

Common side effects (effects that occur in 1-10 out of 100 users):

Visual side effects include: Decreased visual acuity, swelling of a section of the eye (uvea, cornea), inflammation of the cornea (the front part of eye), small marks on the surface of the eye, blurred vision, bleeding at the site of injection, bleeding in the eye, discharge from the eye with itching, redness and swelling (conjunctivitis), light sensitivity, eye discomfort, swelling of the eyelid, eyelid pain.

Non-visual side effects include: Urinary tract infection, low red blood cell count (with symptoms such as tiredness, breathlessness, dizziness, pale skin), anxiety, cough, nausea, allergic reactions such as rash, hives, itching and skin reddening.

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

Visual side effects include: Inflammation and bleeding in the front part of the eye, pus sac on the eye, changes in the central part of the eye surface, pain or irritation at the injection site, abnormal sensation in the eye, irritation of the eyelid.

Reporting side effects

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 the doctor.

Side effects can be reported to the Ministry of Health by clicking the link

"דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the link:

<https://sideeffects.health.gov.il>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants 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) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in refrigerator (2°C - 8°C). Do not freeze. Store the vial in the outer carton in order to protect from light. Prior to use, the unopened vial may be kept at

room temperature (25°C) for up to 24 hours. After transfer to syringe the solution can be kept at room temperature (25°C) for up to 8 hours.

6. Additional information

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

α,α-trehalose dihydrate, histidine hydrochloride monohydrate, histidine, polysorbate 20, water for injection.

What the medicine looks like and what the package contains:

Ranivisio is a solution for injection in a vial (0.23 ml).

The solution is clear to slightly opalescent. Each 1 ml contains 10 mg ranibizumab.

One vial contains 2.3 mg ranibizumab in 0.23 ml solution.

The pack contains one glass vial of ranibizumab with a rubber seal. The vial is for single use only.

Manufacturer name and address: Bioeq AG, Zug, Switzerland

Revised in June 2024 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:

176-24-37973-00

Registration holder: Dexcel Ltd., 1 Dexcel street, Or Akiva 3060000, Israel

The following information is intended for healthcare professionals only:

Please also read section 3 "How to use the medicine?".

How to prepare and administer Ranivisio to adults

Single-use vial for intravitreal use only.

Ranivisio must be administered by a qualified ophthalmologist experienced in intravitreal injections.

Ranivisio should be inspected visually for particulate matter and discoloration prior to administration.

The injection procedure should be carried out under aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent) and the availability of sterile paracentesis (if required). The patient's medical history for hypersensitivity reactions should be carefully evaluated prior to performing the intravitreal procedure. Adequate anaesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid and ocular surface should be administered prior to the injection, in accordance with local practice.

Since the volume contained in the vial (0.23 ml) is greater than the recommended dose (0.05 ml for adults), a portion of the volume contained in the vial must be discarded prior to administration.

Use of more than one injection from a vial can lead to product contamination and subsequent ocular infection.

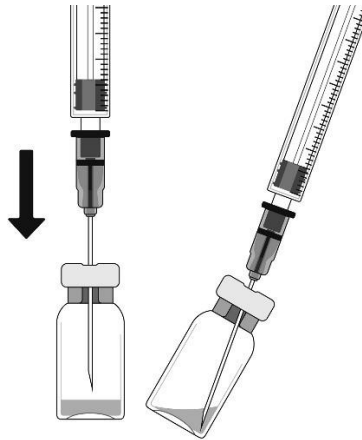
The vial is for single use only. After injection, any unused product must be discarded. Any vial showing signs of damage or tampering must not be used. The sterility cannot be guaranteed unless the packaging seal remains intact.

For preparation and intravitreal injection, the following medical devices for single use are needed:

- a 5 µm filter needle (18G)
- a 1 ml sterile syringe (including a 0.05 ml mark)
- an injection needle (30G x ½").

These medical devices are not included within the **Raniviso** pack.

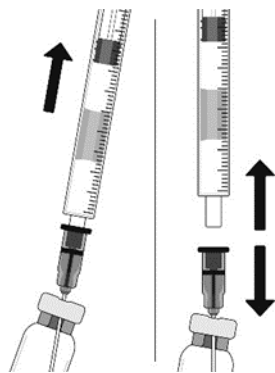
To prepare **Raniviso** for intravitreal administration to adult patients, please adhere to the following instructions:



1. Before withdrawal, remove the vial cap and clean the vial septum (e.g. with 70% alcohol swab).

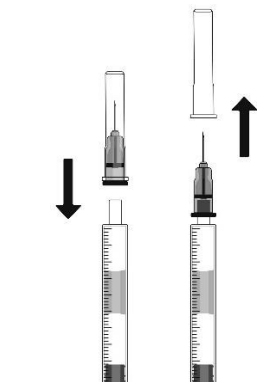
2. Assemble a 5 µm filter needle (18G x 1½", 1.2 mm x 40 mm, 5 µm) onto a 1 ml syringe using aseptic technique. Push the blunt filter needle into the centre of the vial stopper until the needle touches the bottom edge of the vial.

3. Withdraw all the liquid from the vial, keeping the vial in an upright position, slightly inclined to ease complete withdrawal.



4. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.

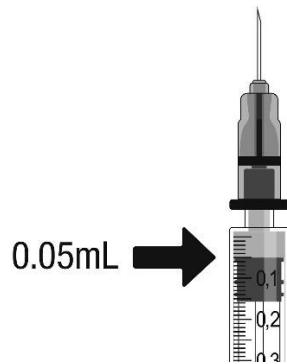
5. Leave the blunt filter needle in the vial and disconnect the syringe from the blunt filter needle. The filter needle should be discarded after withdrawal of the vial contents and should not be used for the intravitreal injection.



6. Aseptically and firmly assemble an injection needle (30G x ½", 0.3 mm x 13 mm) onto the syringe.

7. Carefully remove the cap from the injection needle without disconnecting the injection needle from the syringe.

Note: Grip at the hub of the injection needle while removing the cap.



8. Carefully expel the air along with the excess solution from the syringe and adjust the dose to the 0.05 ml mark on the syringe. The syringe is ready for injection.

Note: Do not wipe the injection needle. Do not pull back on the plunger.

The injection needle should be inserted 3.5-4.0 mm posterior to the limbus into the vitreous cavity, avoiding the horizontal meridian and aiming towards the center of the globe. The injection volume of 0.05 ml is then delivered; a different scleral site should be used for subsequent injections.

After injection, do not recap the needle or detach it from the syringe. Dispose of the used syringe together with the needle in a sharps disposal container or in accordance with local requirements.