NOVARTIS

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

The medicine is dispensed with a doctor's prescription only

# LUCENTIS®, 10 mg/ml

Solution for intraocular injection
Vial

**Active ingredient:**
Ranibizumab 10 mg/ml

Inactive and allergenic ingredients in the preparation: See section 6 'Further Information'.

**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 or your baby. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

## 1. WHAT IS THE MEDICINE INTENDED FOR?

Lucentis 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 retinopathy of prematurity (ROP)
- For treatment of proliferative diabetic retinopathy (PDR)

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

Lucentis 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.

Lucentis is used in babies born prematurely for treatment of retinopathy of prematurity, a disease causing vision impairment due to damage to the back of the eye.

Lucentis 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), or visual impairment caused by retinal disease (retinopathy) in babies born prematurely (ROP). By binding to the protein, Lucentis can block its action and prevent the abnormal blood vessel growth and swelling.

In these diseases, Lucentis can help stabilize, and in many cases, improve your or your baby's vision.

## 2. BEFORE USING THE MEDICINE

**Do not use the medicine if:**

- You or your baby is sensitive (allergic) to the active ingredient ranibizumab or to any of the additional ingredients contained in the medicine (see section 6 'Further information')
- You or your baby has an infection in or around the eye
- You or your baby has pain or redness (severe intraocular inflammation) in the eye

**Special warnings regarding use of the medicine**

Consult your or your baby's doctor before starting treatment with Lucentis.
- Lucentis 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 Lucentis 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. **Please tell your baby's doctor immediately if the baby develops signs such as eye pain or worsening eye redness.**
- In some patients, the eye pressure may increase for a short period immediately after the injection. You may not notice this; therefore, your or your baby's 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 Lucentis is the appropriate treatment for you.

For more detailed information on side effects that could occur during Lucentis treatment, see section 4 'Side effects'.

**Children and adolescents:**
The preparation is not intended for children and adolescents.
The preparation is intended for the treatment of babies born prematurely with retinopathy of prematurity (ROP).

**Drug interactions:**
**If you are taking, or have recently taken, or if you may take, other medicines, including non-prescription medicines and nutritional supplements, or if your baby is receiving, or has recently received, or may receive, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.**

**Pregnancy and breast-feeding:**
- Women who could become pregnant must use effective contraception during treatment and for at least three additional months after the last injection of Lucentis.
- There is no experience of using Lucentis in pregnant women. Lucentis 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 Lucentis.
- Small amounts of Lucentis may pass into breast milk, therefore Lucentis is not recommended for use while breast-feeding. Consult with your doctor or pharmacist before Lucentis treatment.

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

## 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.
Lucentis will be administered to you or to your baby as a single injection into the eye by your or your baby's eye doctor, under local anesthesia.
The dosage and treatment regimen 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).

**For treatment of babies born prematurely,** the usual dosage of an injection is generally: 0.02 ml (which contains 0.2 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 or your baby's eye carefully to prevent infection. The doctor will also give you or your baby local anesthesia to reduce or prevent any pain you or your baby may experience with the injection.
**The treatment in adults** begins with one injection of Lucentis per month.
**The treatment in babies born prematurely** begins with one injection of Lucentis in each eye (some babies may need treatment in one eye).
The doctor will monitor the condition of your or your baby's eye and, depending on how you or your baby responds to the treatment, will decide if and when you or your baby needs to receive further treatment.
Detailed instructions on how to use Lucentis are provided in English at the end of the leaflet, in the section 'How to prepare and administer Lucentis'.

**Elderly (age 65 years and over)**
Can be used in people over the age of 65 without dosage adjustment.

**Do not exceed the recommended dosage.**

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.
Adhere to the treatment regimen 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 Lucentis treatment**
If you are considering stopping your or your baby's Lucentis treatment, go to your next appointment and discuss this with the doctor. The doctor will advise you and will decide how long you or your baby should be treated with Lucentis.

**Do not take medicines in the dark! Check the label and the dose <u>each time</u> 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 Lucentis 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 use of Lucentis may be the result of the medicine itself or from the injection procedure, and mostly affect the eye.

<u>Adult patients</u>
**The most serious side effects are listed below:**

**Common serious side effects** (effects that occur in 1-10 in 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 in 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 user in 10)
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 Lucentis treatment are listed below:**

**Common side effects** (effects that occur in 1-10 in 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 in 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.

<u>Babies born prematurely</u>
**The side effects most commonly observed in babies born prematurely are described below:**
Visual side effects include: Bleeding in the back of the eye (retinal bleeding), bleeding in the eye or at the site of injection, and bloodshot eye (conjunctival bleeding).
Non-visual side effects include: Sore throat, nasal congestion and runny nose, low red blood cell count (with symptoms such as tiredness, breathlessness, pale skin), cough, urinary tract infection, allergic reactions such as rash and skin reddening.

**Additional side effects that have been observed with Lucentis in adults may also occur in babies born prematurely and are listed below:**

The most serious side effects in adults are listed below:

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

**Uncommon serious side effects** (effects that occur in 1-10 in 1,000 users): Blindness, infection of the eyeball (endophthalmitis) with inflammation of the inside of the eye.
It is important to identify and treat serious side effects such as infection of the eyeball or retinal detachment as soon as possible. **Tell the doctor immediately if your baby develops signs such as eye pain or worsening eye redness.**

Other side effects in adults are listed below:

**Very common side effects** (effects that occur in more than 1 user in 10)
Visual side effects include: Inflammation of the eye, visual disturbances, eye pain, small particles or spots in field of vision (floaters), 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: Headache and joint pain.

**Common side effects** (effects that occur in 1-10 in 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 the eye), small marks on the surface of the eye, blurred vision, 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: Anxiety, nausea.

**Uncommon side effects** (effects that occur in 1-10 in 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 site of injection, 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 or your baby suffers 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 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 package and on the label of the vial. The expiry date refers to the last day of that month.

**Storage conditions:**
Store in the original package to protect from light.
Store refrigerated (2°C - 8°C).
Do not freeze.
Prior to use, the unopened vial may be kept at room temperature (25°C) for up to 24 hours.

## 6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
α,α-trehalose dihydrate, L-histidine HCl monohydrate, L-histidine, Polysorbate 20, Water for injection.

What the medicine looks like and the contents of the package:
Lucentis is a solution for injection in a vial (0.23 ml).
The solution is aqueous, clear to slightly opalescent, colorless to pale brownish-yellow.
Each 1 ml contains 10 mg ranibizumab.
One vial contains 2.3 mg ranibizumab in 0.23 ml solution.

There are three pack types, but not all may be marketed:
<u>Vial-only pack</u>
The pack contains one glass vial of ranibizumab, with a gray rubber stopper. The vial is for single use only.

<u>Vial + filter needle pack</u>
The pack contains one glass vial of ranibizumab, with a gray rubber stopper and one blunt filter needle (18 G, 5 µm) to draw up the contents of the vial. All components are for single use only.

<u>Vial + injection kit pack</u>
The pack contains one glass vial of ranibizumab, with a gray rubber stopper, one blunt filter needle (18 G, 5 µm) to draw up the contents of the vial, one injection needle (30G) and a plastic syringe (1 ml) to draw up the contents of the vial and inject into the eye. All components are for single use only.

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

Revised in May 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
136 75 31520

**המידע הבא מיועד לאנשי הצוות הרפואי בלבד:** אנא עיינו גם בפרק 3 'כיצד תשתמש בתרופה?'.

**المعلومات التالية مخصصة لأفراد الطاقم الطبي فقط:** يرجى منكم أيضاً قراءة الفقرة 3 "كيفية إستعمال الدواء؟" بتمعن.

**The following information is intended for medical healthcare professionals only:** Please also read section 3 "How should you use the medicine?".

## כיצד להכין ולהזריק לוסנטיס
## كيفية تحضير وحقن لوسينتيس
## How to prepare and administer Lucentis

Single-use vial for intravitreal use only.

**Adults:** Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections.

**Preterm infants:** Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections in preterm infants.

Lucentis 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 and 0.02 ml for preterm infants), 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.

Vial-only pack

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 or 0.02 ml mark)
- an injection needle (30G x ½″).

These medical devices are not included within the Lucentis pack.

Vial + filter needle pack

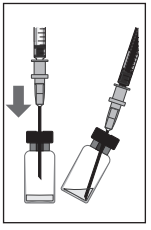
All components are sterile and for single use only. Any component with packaging showing signs of damage or tampering must not be used. The sterility cannot be guaranteed unless the component packaging seal remains intact. Re-use may lead to infection or other illness/injury.

For preparation and intravitreal injection, the following medical devices for single use are needed:
- a 5 µm filter needle (18G x 1½″, 1.2 mm x 40 mm, provided)
- a 1 ml sterile syringe (including a 0.05 ml or 0.02 ml mark, not included within the Lucentis pack)
- an injection needle (30G x ½″; not included within the Lucentis pack)

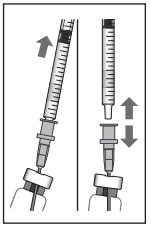
Vial + injection kit

All components are sterile and for single use only. Any component with packaging showing signs of damage or tampering must not be used. The sterility cannot be guaranteed unless the component packaging seal remains intact. Re-use may lead to infection or other illness/injury.

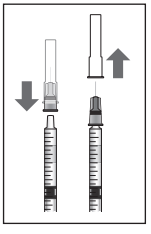
To prepare Lucentis for intravitreal administration, please adhere to the following instructions:



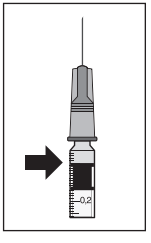
1. Before withdrawal, remove the vial cap and clean the vial septum (e.g. with 70% alcohol swab).
2. Assemble a 5 µm filter needle (18G x 1½″, 1.2 mm x 40 mm, 5 µm) onto a 1 ml syringe using aseptic technique. Push the blunt filter needle into the center of the vial stopper until the needle touches the 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 appropriate mark on the syringe. The dose for adults is 0.05 ml. The dose for preterm infants is 0.02 ml. The syringe is ready for injection.
   Note: Do not wipe the injection needle. Do not pull back on the plunger.

**Adults:** 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.

**Preterm infants:** The injection needle should be inserted 1.0 to 2.0 mm posterior to the limbus, with the needle pointing towards the optic nerve. The injection volume of 0.02 ml is then delivered.

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.