Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Eylea 2 mg
Solution for injection into the eye

Each pre-filled syringe contains:
an extractable volume of at least 0.09 mL, equivalent to at least 3.6 mg aflibercept

Inactive ingredients and allergens in this medicine: see section 6 'Additional information' and section 2 under 'Important information about some of this medicine's ingredients'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. 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.

In addition to the patient information leaflet, Eylea also has a patient safety information guide. This guide contains important safety information that you need to know and that you should follow before you start and during treatment with Eylea. Carefully read the patient safety information guide and patient information leaflet before using this medicine. Keep the guide in case you need to read it again.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Eylea is intended to treat adults who have:
- neovascular age-related macular degeneration (wet AMD)
- impaired vision due to macular edema secondary to retinal vein occlusion (branch RVO [BRVO] or central RVO [CRVO])
- impaired vision due to diabetic macular edema (DME)
- impaired vision due to myopic choroidal neovascularisation (myopic CNV).

Therapeutic group: ophthalmologicals / anti angiogenics.

Aflibercept, the active ingredient in Eylea, blocks the activity of a group of factors known as Vascular Endothelial Growth Factor A (VEGF-A) and Placental Growth Factor (PlGF).

In patients with wet AMD and in short-sighted patients who have myopic CNV, these factors, in excess, are involved in the abnormal formation of new blood vessels in the eye. These new blood vessels can cause a leak of blood components into the eye and eventually damage the tissues in the eye that are responsible for vision.

In patients with CRVO, a blockage occurs in the main blood vessel that transports blood away from the retina. VEGF levels rise in response causing leakage of fluid into the retina, which results in swelling of the macula (the portion of the retina responsible for fine vision) called macular edema. When the macula swells with fluid, central vision becomes blurry.

In patients with BRVO, one or more branches of the main blood vessel that transports blood away from the retina is blocked. VEGF levels rise in response causing leakage of fluid into the retina which results in macular edema.

Diabetic macular edema (DME) is a swelling of the retina occurring in patients with diabetes as a result of fluid leaking from blood vessels within the macula. The macula is the portion of retina responsible for fine vision. When the macula swells with fluid, central vision becomes blurry.

Eylea has been shown to stop the growth of new abnormal blood vessels in the eye which often leak fluid or bleed. Eylea can help to stabilize, and in many cases, improve the vision loss related to wet AMD, CRVO, BRVO, DME and myopic CNV.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient (aflibercept) or to any of the other ingredients in this medicine. See section 6 'Additional information' for a list of inactive ingredients.
- You have an active or suspected infection in or around the eye (ocular or periocular infection).
- You have severe inflammation of the eye (indicated by pain or redness).

Special warnings about using this medicine
Before you start Eylea, tell the doctor if:

- you have glaucoma
- you have a history of seeing flashes of light or floaters and if you have a sudden increase in size and number of floaters
- you have had eye surgery within the previous four weeks or have eye surgery scheduled during the next four weeks
- you have a severe form of CRVO or BRVO (ischemic CRVO or BRVO), treatment with Eylea is not recommended

In addition, it is important for you to know that:

- The safety and efficacy of Eylea when administered to both eyes at the same time have not been studied and if used in this way it may lead to an increased risk of experiencing side effects.
- Injections with Eylea may cause an increase in eye pressure (intraocular pressure) in some patients within 60 minutes of the injection. Your doctor will monitor this after each injection.
- If you develop an infection or inflammation inside the eye (endophthalmitis) or other complications, you may have eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, and increased sensitivity to light. It is important to have any symptoms diagnosed and treated as soon as possible.
- Your doctor will check whether you have other risk factors that may increase the chance of a tear or detachment of one of the layers at the back of the eye (retinal detachment or tear, and retinal pigment epithelial detachment or tear), in which case Eylea must be given with caution.
- Eylea should not be used during pregnancy unless the potential benefit outweighs the potential risk to the unborn child.
- Women of childbearing potential have to use effective contraception during treatment and for at least three additional months after the last injection of Eylea.

The systemic use of VEGF inhibitors, substances similar to those in Eylea, is potentially related to the risk of blood clots that block blood vessels (arterial thromboembolic events) which may lead to heart attack or stroke. There is a theoretical risk of such events following injection of Eylea into the eye. There are limited data about the safety of treating patients who have CRVO, BRVO, DME and myopic CNV who have had a stroke or a transient ischemic attack or a heart attack within the last 6 months. If any of these apply to you, Eylea will be given with caution.

There is only limited experience in the treatment of:

- patients with DME due to type I diabetes
- patients with diabetes who have very high average blood sugar values (glycated hemoglobin [HbA1c] over 12%)
- patients with diabetes who have an eye disease caused by diabetes called proliferative diabetic retinopathy

There is no experience in the treatment of:

- patients with acute infections
- patients with other eye conditions such as a detachment of the retina or a hole in the macula
- patients with diabetes who have uncontrolled high blood pressure
- non-Asian patients with myopic CNV
- patients previously treated for myopic CNV

- myopic CNV patients with damage outside the central part of the macula (extrafoveal lesions)

If any of the above apply to you, your doctor will consider this lack of information when treating you with Eylea.

Children and adolescents
The use of Eylea in children or adolescents under 18 years old has not been studied because wet AMD, CRVO, BRVO, DME, and myopic CNV occur mainly in adults. Therefore, its use in this age group is not relevant.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Also tell your doctor or pharmacist if you might begin taking any other medicines.

Pregnancy, breastfeeding, and fertility
Women of childbearing potential have to use effective contraception during treatment and for at least three additional months after the last injection of Eylea.

There is no experience using Eylea in pregnant women. Animal studies have shown toxicity to the fetus. Eylea should not be used during pregnancy unless the potential benefit outweighs the potential risk to the unborn child. If you are pregnant or planning to become pregnant, discuss this with your doctor before treatment with Eylea.

Small amounts of Eylea may pass into human milk. The effect on breastfed newborns/infants is unknown.
The use of Eylea is not recommended during breastfeeding. If you are a breastfeeding woman, consult your doctor before starting treatment with Eylea.

The results of animal studies that included systemic exposure to high doses have shown that aflibercept may damage fertility in men and women. These effects are not expected after injection into the eye with very low systemic exposure.

Driving and using machines
After your injection with Eylea, you may experience some temporary visual disturbances. Do not drive or use machines as long as these disturbances last.

Important information about some of this medicine's ingredients
Eylea contains:
- less than 1 millimole sodium (23 mg) per dose, which means that it is essentially 'sodium-free'.
- 0.015 mg of polysorbate 20 in each injection of a single dose of 0.05 ml, which is equivalent to 0.3 mg/ml. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

A doctor experienced in giving eye injections will inject Eylea into your eye under aseptic (clean and sterile) conditions.

Only your doctor will determine your dose and how you should take this medicine.
The usually recommended dose is 2 mg aflibercept (0.05 mL).
Eylea is given as an injection into your eye (intravitreal injection).

Before the injection your doctor will use a disinfectant eyewash to clean your eye carefully to prevent infection. Your doctor will also give you a local anesthetic to reduce or prevent any pain you might have with the injection.

Do not exceed the recommended dose.

Wet age-related macular degeneration (wet AMD)
Patients with wet AMD are treated with one injection per month for three consecutive doses, followed by an additional injection after two months.

If your condition has been stable, your doctor will then decide whether the interval between injections can remain two months or whether it will be gradually extended by 2-week or 4-week periods. If your condition gets worse, your doctor may decide to shorten the interval between injections.

Unless you experience any problems or are advised differently by your doctor, there is no need for you to see your doctor between injections.

Macular edema secondary to retinal vein occlusion (branch retinal vein occlusion [BRVO] or central retinal vein occlusion [CRVO])
Your doctor will determine a treatment schedule that is best for you. You will start your treatment with a series of monthly Eylea injections.

The interval between two injections should not be shorter than one month.

Your doctor may decide to stop treatment with Eylea if you are not benefiting from continued treatment.

Your treatment will continue with monthly injections until your condition is stable. Three or more monthly injections may be needed.

Your doctor will monitor your response to treatment and may continue your treatment by gradually increasing the interval between your injections to maintain a stable condition. If your condition starts to get worse with a longer interval between injections, your doctor will shorten the interval accordingly.

Based on your response to treatment your doctor will decide on a schedule for follow up examinations and treatments.

Diabetic macular edema (DME)
Patients with DME are treated with one injection per month for the first five consecutive doses followed by an injection every two months.

Unless you experience any problems or are advised differently by your doctor, there is no need for you to see your doctor between injections.

After the first 12 months of treatment with Eylea, the treatment interval may be extended based on your doctor's examination. Your doctor will decide on the schedule for follow up examinations.

Your doctor may decide to stop treatment with Eylea if it is determined that you are not benefiting from continued treatment.

Myopic choroidal neovascularisation (myopic CNV)
Patients with myopic CNV are treated with a single injection. You will receive additional injections only if the tests your doctor orders show that your condition has not improved.

The interval between two injections should not be shorter than one month.

If your condition goes away and then comes back, your doctor may re-start the treatment.
Your doctor will decide on the schedule for follow up examinations.

If you have accidentally taken a higher dose
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you miss an Eylea injection
Make a new appointment for an examination and injection.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop treatment with this medicine
Consult your doctor before you stop treatment.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

Like with all medicines, using Eylea may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Consult a doctor immediately if you experience any **allergic reaction** (hypersensitivity). Allergic reactions may occur. **They may be serious and require you to call your doctor immediately.**

With administration of Eylea, there may be some side effects affecting the eyes which are due to the injection procedure. Some of these may be **serious** and include **blindness, a serious infection or inflammation inside the eye** (endophthalmitis), **detachment, tear or bleeding of the light-sensitive layer at the back of the eye** (retinal detachment or tear), **clouding of the lens** (cataract), **bleeding in the eye** (vitreous hemorrhage), **detachment of the gel-like substance inside the eye from the retina** (vitreous detachment), and **increase of pressure inside the eye**. See in section 2 under 'Special warnings about using this medicine'. These serious side effects affecting the eyes occurred in less than 1 in 1,900 injections that were given in clinical studies.

If you experience a sudden decline in your vision, or an increase in pain and redness in your eye after your injection, **contact your doctor immediately**.

List of reported side effects
Following is a list of side effects reported to be possibly related to the injection procedure or the medicine.

Very common side effects (may affect more than 1 in 10 people):
- eyesight deteriorates
- bleeding in the back of the eye (retinal haemorrhage)
- bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye
- eye pain

Common side effects (may affect up to 1 in 10 people):
- detachment or tear of one of the layers in the back of the eye which cause flashes of light with floaters, sometimes progressing to loss of vision (retinal pigment epithelial tear*/detachment, retinal tear/detachment)
  *Conditions known to be associated with wet AMD; observed in wet AMD patients only.
- degeneration of the retina (causing disturbed vision)
- bleeding in the eye (vitreous hemorrhage)
- certain forms of clouding of the lens (cataract)
- damage to the front layer of the eyeball (the cornea)
- increase in eye pressure
- spots moving in your vision (floaters)
- detachment of the gel-like substance inside the eye from the retina (vitreous detachment, resulting in flashes of light and floaters)
- a feeling of having something in the eye
- increased tear production

- swelling of the eyelid
- bleeding at the injection site
- redness of the eye

Uncommon side effects (may affect up to 1 in 100 people):
- allergic reactions (hypersensitivity)**
  ** Allergic reactions like rash, itching, hives, and a few cases of severe allergy (anaphylactic/anaphylactoid) reactions were reported.
- serious inflammation or infection inside the eye (endophthalmitis)
- inflammation in the iris or other parts of the eye (iritis, uveitis, iridocyclitis, anterior chamber flare)
- abnormal sensation in the eye
- eyelid irritation
- swelling of the front layer of the eyeball (cornea)

Rare side effects (may affect up to 1 in 1,000 people):
- blindness
- clouding of the lens due to injury (traumatic cataract)
- inflammation of the gel-like substance inside the eye
- pus in the eye

Side effects of unknown frequency (the frequency of these effects has not been established yet):
- inflammation of the white part of the eye associated with redness and pain (scleritis)

In the clinical trials, there was an increased incidence of bleeding from small blood vessels in the outer layers of the eye (conjunctival hemorrhage) in patients with wet AMD receiving blood thinners. This increased incidence was similar in patients treated with ranibizumab and in patients treated with Eylea.

The systemic use of VEGF inhibitors, substances similar to those in Eylea, is potentially related to the risk of blood clots that block blood vessels (arterial thromboembolic events) which may lead to heart attack or stroke. There is a theoretical risk of such events following injection of Eylea into the eye.

As with all therapeutic proteins, there is a possibility of an immune reaction (formation of antibodies) to Eylea.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions
- Store in the refrigerator (2°C to 8°C). Do not freeze.
- The unopened wrapper can be stored before use at room temperature (below 25°C) for up to 24 hours.
- Keep the pre-filled syringe in its wrapper and in the outer carton to protect it from light.
- Do not throw away any medicine via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient, this medicine also contains:
  Sucrose, sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, polysorbate 20, water for injection.

  See section 2 'Important information about some of this medicine's ingredients'

- What the medicine looks like and contents of the pack:
  Eylea is a solution for injection in a pre-filled syringe. The solution is colorless to light yellow.
- Each pack contains 1 pre-filled syringe.
- Registration holder's name and address: Bayer Israel Ltd., 36 Hacharash Street, Hod Hasharon 45240.
- Manufacturer's name and address: Bayer AG, Berlin, Germany.
- Revised in May 2025.
- Registration number of the medicine in the Ministry of Health's National Drug Registry:
  151 12 33800 00

Information for healthcare professionals only:

Instructions for use of pre-filled syringe:

The pre-filled syringe should only be used **for the treatment of a single eye**.

Do not open the sterile pre-filled syringe blister outside the clean administration room.

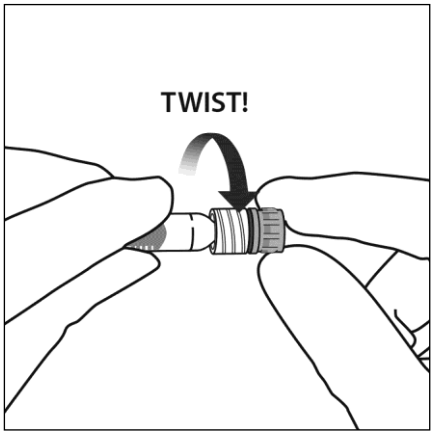
The pre-filled syringe contains more than the recommended dose of 2 mg aflibercept (equivalent to 0.05 mL). The excess volume must be discarded prior to administration.

The solution should be inspected visually for any foreign particulate matter and/or discolouration or any variation in physical appearance prior to administration. In the event of either being observed, discard the medicinal product.

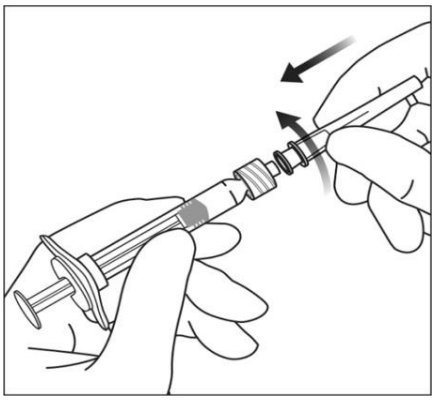
The unopened blister may be stored outside the refrigerator below 25° C for up to 24 hours. After opening the blister, proceed under aseptic conditions.
For the intravitreal injection, a 30 G x ½ inch injection needle should be used.

Instructions for use of pre-filled syringe:

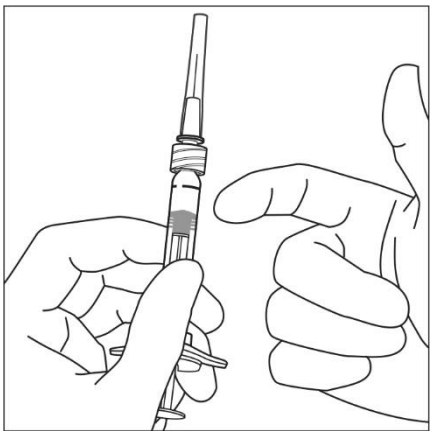
1. When ready to administer Eylea, open the carton and remove the sterilised blister. Carefully peel open the blister ensuring the sterility of its contents. Keep the syringe in the sterile tray until you are ready for assembly.
2. Using aseptic technique, remove the syringe from the sterilised blister.
3. To remove the syringe cap, hold the syringe in one hand while using the other hand to grasp the syringe cap with the thumb and fore finger. Please note: You should twist off (do not snap off) the syringe cap.



4. To avoid compromising the sterility of the product, do not pull back on the plunger.
5. Using aseptic technique, firmly twist the injection needle onto the Luer-lock syringe tip.

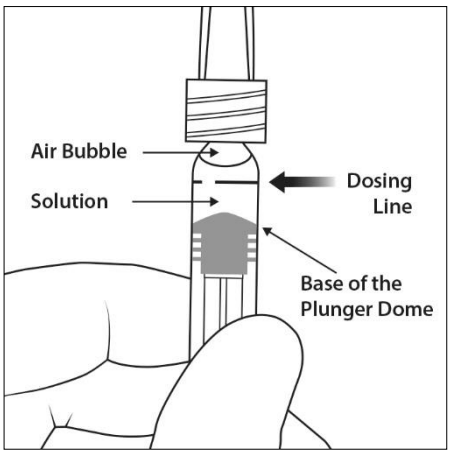


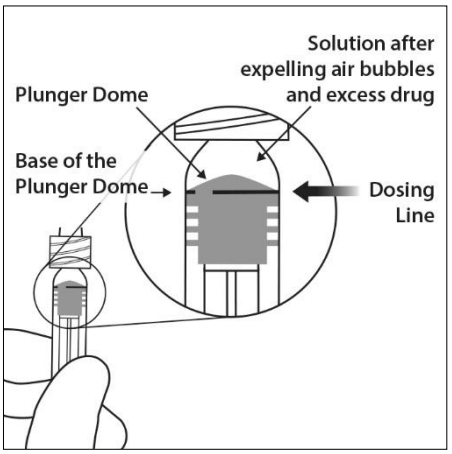
6. Holding the syringe with the needle pointing up, check the syringe for bubbles. If there are bubbles, gently tap the syringe with your finger until the bubbles rise to the top.



7. Eliminate all bubbles and **expel excess medicinal product by slowly depressing the plunger to align the base of the plunger dome** (not the tip of the dome) **with the dosing line on the syringe** (equivalent to 0.05 mL i.e. 2 mg aflibercept).

   Note: This accurate positioning of the plunger is very important, because incorrect plunger positioning can lead to delivering more or less than the labelled dose





8. Inject while pressing the plunger carefully and with constant pressure. Do not apply additional pressure once the plunger has reached the bottom of the syringe. Do not administer any residual solution observed in the syringe.

9. The pre-filled syringe is for single use only. Extraction of multiple doses from a pre-filled syringe may increase the risk of contamination and subsequent infection. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.