EYLEA®

Package Leaflet:
Eylea 40 mg/ml solution for injection in a vial
Aflibercept

This is a medicament
- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT EYLEA IS AND WHAT IT IS USED FOR

Eylea is a solution which is injected into the eye to treat eye conditions in adults called
- neovascular (wet) age-related macular degeneration (wet AMD),
- impaired vision due to macular oedema secondary to central retinal vein occlusion (CRVO).

Aflibercept, the active substance 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, these factors, in excess, trigger the abnormal formation of new blood vessels in the eye. These new blood vessels can cause the leak of blood components into the eye and eventual damage to tissues in the eye responsible for vision. In patients with CRVO, a blockage occurs in the main blood vessel that transports blood away from the retina. VEGF levels are elevated in response causing the leakage of fluid into the retina and thereby swelling of the macula, which is called macular oedema.
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 stabilise, and in many cases, improve the vision loss related to wet AMD and CRVO.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN EYLEA

You will not be given Eylea:
- if you are allergic to aflibercept or any of the other ingredients of this medicine (listed in section 6)
- if you have an active or suspected infection in or around the eye (ocular or periocular infection)

- if you have severe inflammation of the eye (indicated by pain or redness)

Warnings and precautions

Talk to your doctor before you are given Eylea:

- as injection with Eylea may trigger 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 have glaucoma.
- 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 risk factors for a special eye disease (retinal pigment epithelial tears), where Eylea will be given with caution.
- if you have a history of seeing flashes of light or floaters and if you have sudden increase of size and number of floaters.
- if surgery was performed or is planned on your eye within the previous or next four weeks.
- Eylea should not be used in 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 further months after the last injection of Eylea.
- if you have a severe form of CRVO (ischaemic chronic CRVO), the treatment with Eylea is not recommended.
- if you have an eye disease caused by diabetes (diabetic retinopathy).

When injecting VEGF inhibitors, substances similar to those contained in Eylea, into the body and not only into the eye, there is a potential risk of blood clots blocking 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.

If any of the above applies to you, talk to your doctor before you are given Eylea.

Children and adolescents

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

Other medicines and Eylea

Tell your doctor if you are using, have recently used or might use any other medicines.

Pregnancy and breastfeeding

- Women of childbearing potential have to use effective contraception during treatment and for at least three further months after the last injection of Eylea.
- There is no experience of using Eylea in pregnant women. 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.
- Eylea is not recommended during breastfeeding as it is not known whether Eylea passes into human milk. Ask your doctor for advice before starting Eylea treatment.

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 last.

Important information about some of the ingredients of Eylea

This medicine contains less than 1 mmol (23 mg) of sodium per dose which means it is essentially "sodium-free".

3. HOW YOU WILL BE GIVEN EYLEA

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

The recommended dose is 2 mg aflibercept (50 microlitres).

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 anaesthetic to reduce or prevent any pain you might have with the injection.

wet AMD

Patients with wet AMD will be treated with one injection per month for three consecutive doses, followed by one injection every two months.

After the first 12 months of treatment with Eylea, the treatment interval may be extended based on your doctor's examination.
Unless you experience any problems or are advised differently by your doctor, there is no need for you to see your doctor between the injections.
Macular Oedema secondary to CRVO
Your doctor will determine the most appropriate treatment schedule for you. You will start your treatment with a series of monthly Eylea injections.
The intervals between two injections should not be shorter than one month.
If your condition does not improve after the first three months of treatment, your doctor may decide to stop treatment with Eylea.
When your doctor considers your condition has been stable for three months while on treatment, treatment may be stopped. If considered necessary, treatment intervals may be extended beyond one month. If your condition is worsening after discontinuation, treatment should be resumed.
Usually, your doctor will examine you during the injection visits. If treatment intervals are longer than one month, your doctor may decide to examine you more often. You will then have to make additional appointments to see your doctor for examinations between the injections.

If a dose of Eylea is missed

Make a new appointment for an examination and injection.

Stopping treatment with Eylea

Consult your doctor before stopping the treatment.
If you have any further questions on the use of this medicine, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Allergic reactions (hypersensitivity) could potentially occur. These may be serious and require that you contact your doctor immediately.

For patients with wet AMD

With administration of Eylea, there may be some side effects due to the injection procedure. Some of these may be **serious** and include infection or **inflammation inside the eye** (endophthalmitis), clouding of the lens due to injury (traumatic cataract), and **temporary increase of pressure inside the eye** (transient increased intraocular pressure). These serious side effects occurred in less than 1 in every 1,000 injections in clinical studies.
If you get any of these serious side effects, contact your doctor immediately.

For patients with macular oedema secondary to CRVO

With administration of Eylea, there may be some side effects due to the injection procedure. Some of these may be **serious** and include infection or **inflammation inside the eye** (endophthalmitis), **clouding of the lens** (cataract), and **detachment of the gel-like substance inside the eye** from the retina (vitreous detachment). These serious side effects occurred in 3 out of 2,728 injections in clinical studies.
If you get any of these serious side effects, contact your doctor immediately.

List of side effects reported in patients with wet AMD or CRVO

The following is a list of the side effects reported to be possibly related to the injection procedure or to the medicine. Please do not get alarmed, you might not experience any of these. Always discuss any suspected side effects with your doctor.

Very common side effects (*may affect more than 1 in 10 people*):

- bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye (conjunctival haemorrhage)
- eye pain

Common side effects (*may affect up to 1 in 10 people*):

- decreased sharpness of vision (retinal pigment epithelium tear, detachment of the retinal pigment epithelium)*
- disturbed vision (retinal degeneration)
- bleeding in the eye (vitreous haemorrhage)
- certain forms of clouding of the lens (cataract, cataract nuclear, cataract subcapsular)
- damage to the front layer of the eyeball (corneal erosion, corneal abrasion)
- increase in eye pressure (increased intraocular pressure)
- blurred vision
- moving spots in vision (vitreous floaters)

- swelling of the front layer of the eyeball (corneal oedema)
- detachment of the gel-like substance inside the eye from the retina (vitreous detachment)
- injection site pain
- a feeling of having something in the eye (foreign body sensation in eyes)
- increased tear production (lacrimation increased)
- swelling of the eyelid (eyelid oedema)
- bleeding at the injection site (injection site haemorrhage)
- redness of the eye (conjunctival hyperaemia, ocular hyperaemia)

*) Conditions known to be associated with wet AMD; observed in wet AMD patients only.

Uncommon side effects (*may affect up to 1 in 100 people*):
- allergic reactions (hypersensitivity)
- inflammation inside the eye (endophthalmitis)
- decreased sharpness of vision (retinal detachment, retinal tear)
- inflammation in the iris of the eye (iritis)
- inflammation of certain parts of the eye (iridocyclitis, anterior chamber flare)
- certain forms of clouding of the lens (cataract cortical, lenticular opacities)
- damage of the front layer of the eyeball (corneal epithelium defect)
- injection site irritation
- strange feeling in the eye
- eyelid irritation

Rare side effects (*may affect up to 1 in 1,000 people*):
- inflammation of certain parts of the eye (vitritis, uveitis)
- pus in the eye (hypopyon)

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

The use of systemic VEGF inhibitors, substances similar to those contained in Eylea, is potentially related to risk of arterial thromboembolic events (of blood clots blocking blood vessels) 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 for an immune reaction (formation of antibodies) with Eylea.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE EYLEA

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C). Do not freeze.
- Prior to usage, the unopened vial may be stored at room temperature (below 25°C) for up to 24 hours.
- Keep the vial in its outer carton in order to protect from light.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away any medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Eylea contains
- The active substance is: aflibercept. One vial contains 100 microlitres, equivalent to 4 mg aflibercept. One vial delivers a dose of 2 mg aflibercept in 50 microlitres.
- The other ingredients are: polysorbate 20, sodium dihydrogen phosphate monohydrate (for pH adjustment), disodium hydrogen phosphate heptahydrate (for pH adjustment), sodium chloride, sucrose, water for injection.

What Eylea looks like and contents of the pack

Eylea is a solution for injection (injection) in a vial (4 mg/100 microlitres). The solution is colourless to pale yellow.

Pack size of 1.

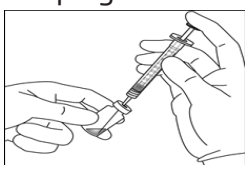
Manufacturer

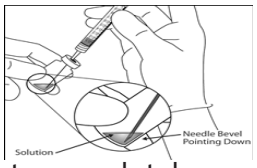
Bulk manufacturer
Regeneron Pharmaceuticals Inc
81 Columbia Turnpike RENSSELAER NEW YORK 12144 United States
Final Release
Bayer Pharma AG
D 13342 - Berlin
Germany
This leaflet was last revised in August 2013
The following information is intended for healthcare professionals only:
Each vial should only be used for the treatment of a single eye.
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.
Prior to usage, the unopened vial of Eylea may be kept at room temperature (below 25°C) for up to 24 hours.
After opening the vial, proceed under aseptic conditions.
For the intravitreal injection, a 30 G x ½ inch injection needle should be used.
Instructions for use of vials:

1. Remove the plastic cap and disinfect the outer part of the rubber stopper of the vial.

2. Attach the 18 G, 5-micron filter needle supplied in the carton to a 1 ml sterile Luer-lock syringe.

3. Push the filter needle into the centre of the vial stopper until the needle is completely inserted into the vial and the tip touches the bottom or bottom edge of the vial.
4. Using aseptic technique withdraw all of the Eylea vial contents into the syringe, keeping the vial in an upright position, slightly inclined to ease complete withdrawal.To deter the introduction of air, ensure the bevel of the filter needle is submerged into the liquid. Continue to tilt the vial during withdrawal keeping the bevel of the filter needle submerged in the liquid.

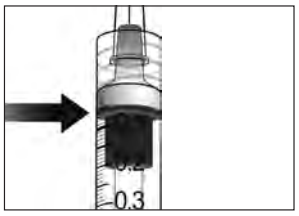


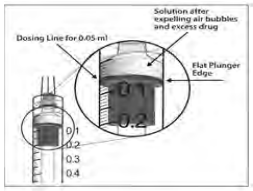


5. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.
6. Remove the filter needle and properly dispose of it.
   Note: Filter needle is not to be used for intravitreal injection.
7. Using aseptic technique, firmly twist a 30 G x ½ inch injection needle onto the Luer-lock syringe tip.

8. When ready to administer Eylea, remove the plastic needle shield.
9. 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.

10. Eliminate all bubbles and expel excess medicinal product by slowly depressing the plunger so that the plunger tip aligns with the line that marks 0.05 ml on the syringe.





11. The vials are for single use only.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements