Your guide to

EYLEA®

(Aflibercept)

The brochure has been produced for people who have been prescribed EYLEA (aflibercept solution for injection)

EYLEA is used to treat macular oedema secondary to Central Retinal Vein Occlusion (CRVO)

This material is reviewed and approved by the Saudi FDA

EYLEA®
Aflibercept (40mg/ml)

Welcome to your EYLEA guide

Your doctor has prescribed EYLEA because you have been diagnosed with central retinal vein occlusion, or CRVO.

This is a condition that is making it harder for you to see clearly. Treatments like EYLEA can help stop your eyesight from becoming worse, and may improve some of the symptoms you have.

This guide has been made to help answer any questions you may have, so you can get the most out of your treatment.

Within this book you will find:

- Information to help you understand CRVO
  - What is CRVO?
  - What causes CRVO?
  - Advice for living with CRVO

- What to expect from your EYLEA® treatment
  - What is EYLEA?
  - How will I take EYLEA?
  - What if I have questions about EYLEA?

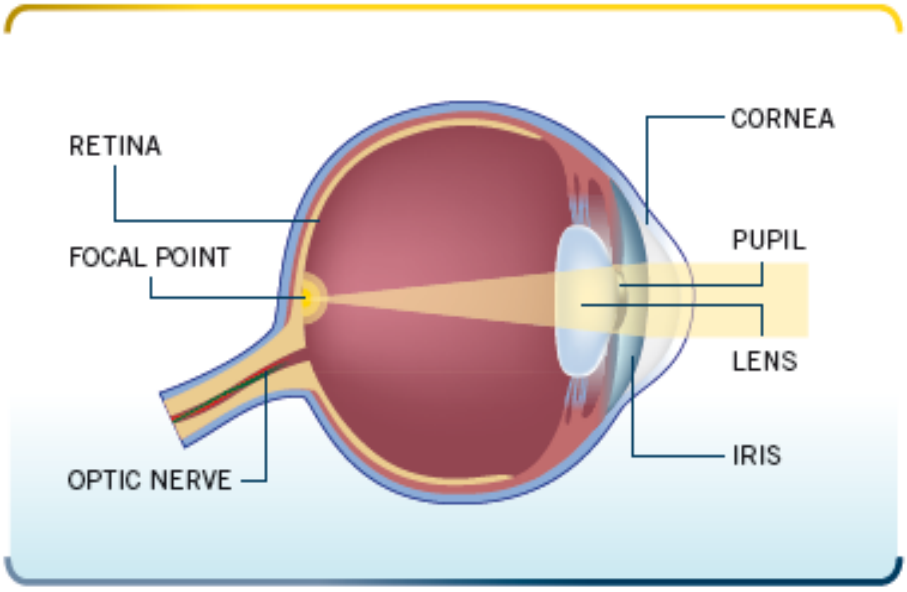
- How to care for your eyes after your EYLEA treatment
  - What should I expect?
  - When do I need to take EYLEA again?
  - Are there side effects with EYLEA?

What is CRVO?

Central retinal vein occlusion is a condition that damages your eyesight by blocking the flow of blood to and from the retina, in the back of your eye.

The retina is where all of the images you see are recorded – it acts like the film in a camera.

The blockage stops blood from flowing in and out of the retina which can damage your eyesight and eventually lead to blindness and a painful eye.



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What causes CRVO?

Central retinal vein occlusion can happen at any age, but is more common in people over 65 years.

In many people with CRVO, a specific cause can't be determined but it often happens as a consequence of other conditions like glaucoma, hypertension (high blood pressure) or diabetes.

Other things that can increase your risk of getting CRVO, or having it get worse, are 'lifestyle' factors including smoking and being overweight. Quitting smoking greatly lowers the risk of damage to your eyes as well as improving your general health. If you are overweight, losing weight and eating healthily can help protect your eyesight. Your general practitioner can help you with quitting smoking and losing weight.

The best things you can do to protect your eyesight is to follow your eye doctor's advice and to make sure you keep all of your scheduled appointments.

How is CRVO treated?

There are several treatment options for CRVO and they work in different ways.

Some of these treatments work by shrinking and sealing up these weak blood vessels to prevent them from becoming blocked. Other treatments focus on reducing swelling and managing pain.

Since no two people are alike, there is no one-size-fits-all solution.

Your doctor will choose a treatment best-suited for your individual needs.

What is EYLEA?

EYLEA is a type of treatment known as an anti-VEGF.

This is an abbreviation for anti-vascular endothelial growth factor, which is a description of how EYLEA works to protect your vision. EYLEA blocks a particular protein used to develop new blood vessels in your eye. By stopping this from happening, EYLEA can keep weak blood vessels from being made which in turn can help improve your eyesight or stop it from getting worse.

EYLEA is a solution (a liquid) that is injected into the eye. While it is understandable to worry about an injection, most people who have EYLEA treatment say that the injection is painless and it sounds worse than it really is.

Who is EYLEA for?

EYLEA is for people who have been diagnosed with CRVO.
Before your EYLEA treatment starts, make sure to tell your doctor or nurse if you:

- Have an infection in or around your eye
- If you currently have redness in your eye or if there is any pain in your eye
- Think you may be allergic to iodine, any pain killers or any of the ingredients in EYLEA
- Have had any issues or problems with eye injections before
- Have glaucoma or a history of high pressure in your eye
- If you see, or have seen, flashes of light or 'floaters' in your vision
- Are taking any medications, with or without a prescription
- Are pregnant, planning to become pregnant or breastfeeding. There is no experience of using EYLEA in pregnant women. EYLEA should not be used during pregnancy, discuss this with your doctor before treatment with EYLEA. Women of child bearing potential should use effective contraception during their treatment and for at least three months after the last injection of EYLEA.
- Had or will have eye surgery within 4 weeks before or after EYLEA treatment

How can I get ready for my EYLEA appointment?

Your doctor may ask you to take eye-drops for a few days before your appointment. After your treatment, your vision may be blurry so you should not drive home. Plan to have a friend or family member take you to your appointment or arrange another way to get there and home again. On the day of your appointment, do not wear any makeup.

What can I expect at my EYLEA appointment?

Your doctor or nurse will get you ready for your EYLEA treatment. These people are highly trained professionals with experience in treating CRVO. They understand that the treatment procedure may sound frightening and they will take extra care to make sure you are relaxed and comfortable.

You will be given eyedrops which act as a local pain killer and an eyewash will be used to clean your eye and the skin around it. Your face will be covered by a special drape and your eye will be held open. The eye drops will blur your vision so you will not see the needle.

An experienced doctor will give the injection into the white of your eye. Most people say the injection is painless and some say they feel a slight pressure. The whole procedure may feel a bit uncomfortable, but is over in a few minutes.

What if I have concerns or questions?

If you have any concerns or questions, your doctor or nurse are the best people to speak to. They are very experienced and they know your individual situation so can provide you with the answers you need.

Don't worry about asking questions or voicing any concerns. Your doctor or nurse can give you answers and reassurance.

What can I expect after my EYLEA® appointment?

Your doctor may give you some eye tests after your injection. This may include a puff of air that measures the pressure inside your eye. After your injection, your vision will be blurry so you should not plan to drive until after your vision returns to normal.

In the next few days you may get a bloodshot eye or see moving spots in your vision. Both of these should clear within a few days and if they don't, or if they get worse, you should contact your doctor.

Some people might feel a little bit of pain or discomfort in their eye after their injection. If this does not go away or gets worse, you should contact your doctor.

When do I need to come back for another appointment?

Your doctor will arrange your next EYLEA appointment with you. Your treatment schedule will be created to best meet your individual needs.

Remember, your doctor or nurse is always the best person to speak to if you have questions about your treatment.

Speak with your doctor before stopping your EYLEA treatment.

When you get a new appointment, don't forget to record it in your calendar

Does EYLEA have side effects?

Just like any medicine, whether it is by prescription or over the counter, EYLEA has the potential to cause side effects. Not everyone who takes EYLEA will experience a side effect.

Side effects may include:

- Infection inside the eye: Eye pain or increased discomfort. Worsening eye redness, sensitivity to light, swelling and vision changes such as sudden decrease in vision or blurring of vision.
- Clouding of the lens (cataract): Seeing shadows, less vivid lines and shapes or less colour vision.
- Increase in eye pressure: Seeing halos around lights. Experiencing a red eye, nausea, vomiting and vision changes.
- Tear or detachment of a layer of the retina: Sudden flashes of light, a sudden appearance or an increase of floaters, a curtain like effect over a portion of the visual area, and vision changes.

Contact your doctor immediately if you think you have experienced any of these side effects.

For a full list of side effects, refer to your Patient Information Leaflet included with your patient brochure.

Living with CRVO

Being diagnosed with CRVO and experiencing problems with your eyesight can be an anxious time. It is normal to worry and feel uncertain about your future, but your diagnosis doesn't mean you can no longer live a full life. You can continue to enjoy family, friends and interests with some small changes.

Some helpful adjustments include:

- Tell friends and family that you have CRVO and it affects your vision
- Use brighter lighting
- Organise your surroundings so everything has a place
- Carry and use a torch and magnifying lenses when about
- Read large print books and newspapers and try audio books

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

Please report any adverse events to the
National Pharmacovigilance and Drug Safety Centre
SFDA call center: 19999
E-Mail: npc.drug@sfda.gov.sa
Online: https://ade.sfda.gov.sa/Home/Report

Or

Pharmacovigilance department in Bayer Saudi LLC:
Bayer Saudi Arabia LLC.
Al Kamal Import Office
Ittihad St. P.O Box 15369
21444 Jeddah, Saudi Arabia
Tel.: +966 126573015
Fax: +9661 2 6534992
Email: pv.me@bayer.com
For medical inquiries: med-info.me@bayer.com

EYLEA®

Package Leaflet: Information for the patient
Eylea 40 mg/mL solution for injection in a vial
aflibercept

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 retinal vein occlusion (branch RVO (BRVO) or central RVO (CRVO)),
- impaired vision due to diabetic macular oedema (DME).
- impaired vision due to myopic choroidal neovascularisation (myopic CNV).

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 and 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 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 causing a swelling of the macula, (the portion of the retina responsible for fine vision), which is called macular oedema. 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 are elevated in response causing the leakage of fluid into the retina and thereby causing macular oedema.
Diabetic macular oedema is a swelling of the retina occurring in patients with diabetes due to leaking of fluid 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 stabilise, and in many cases, improve the vision loss related to wet AMD, CRVO, BRVO, DME and myopic CNV.

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:
- if you have glaucoma.
- if you have a history of seeing flashes of light or floaters and if you have a 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.
- if you have a severe form of CRVO or BRVO (ischaemic CRVO or BRVO), treatment with Eylea is not recommended.

Furthermore, 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 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 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.

The systemic use of VEGF inhibitors, substances similar to those contained in Eylea, is potentially related to the 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. There are limited data on safety in treating patients with CRVO, BRVO, DME and myopic CNV who have had a stroke or a mini-stroke (transient ischaemic 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.
- diabetics with very high average blood sugar values (HbA1c over 12%).
- diabetics with 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.
- diabetics with uncontrolled high blood pressure.
- non-Asian patients with myopic CNV.
- patients previously treated for myopic CNV.
- patients with damage outside the central part of the macula (extrafoveal lesions) for myopic CNV.

If any of the above applies 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 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.

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

Pregnancy and breast-feeding
- 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 breast-feeding 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 sodium (23 mg) per dosage unit, that is to say 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 another injection after a further two months.
Your doctor will then decide whether the treatment interval between injections may be kept at every two months or be gradually extended in 2- or 4-weekly intervals if your condition has been stable. If your condition worsens, the interval between injections can be shortened.
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 RVO (branch RVO or central RVO)
Your doctor will determine the most appropriate treatment schedule 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 worsen with a longer treatment interval, your doctor will shorten the interval accordingly.
Based on your response to treatment your doctor will decide on the schedule for follow up examinations and treatments.

Diabetic macular oedema (DME)
Patients with DME will be treated with one injection per month for the first five consecutive doses followed by one injection every two months thereafter.
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.
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 CNV
Patients with myopic CNV will be treated with one single injection. You will receive further injections only if your doctor's examinations reveal 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 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**.
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 haemorrhage), **detachment of the gel-like substance inside the eye from the retina** (vitreous detachment) and **increase of pressure inside the eye**, see section 2. These serious side effects affecting the eyes occurred in less than 1 in 1,900 injections in clinical studies.
If you experience a sudden decrease in vision, or an increase in pain and redness in your eye after your injection, **contact your doctor immediately**.

List of side effects reported:
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***):**
- deterioration of eyesight
- 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, resulting in flashes of light with floaters sometimes progressing to a loss of vision (retinal pigment epithelial tear* / detachment, retinal detachment/tear)
- degeneration of the retina (causing disturbed vision)
- bleeding in the eye (vitreous haemorrhage)
- certain forms of clouding of the lens (cataract)
- damage to the front layer of the eyeball (the cornea)
- increase in eye pressure
- moving spots in vision (floaters)
- detachment of the gel-like substance inside the eye from the retina (vitreous detachment, resulting in flashes of light with 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

* 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)**
- 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)

**Allergic reactions like rash, itching (pruritus), hives (urticaria), and a few cases of severe allergy (anaphylactic/anaphylactoid) reactions were reported

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

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 with wet AMD receiving blood thinners. This increased incidence was comparable between patients treated with ranibizumab and Eylea.
The systemic use of VEGF inhibitors, substances similar to those contained in Eylea, is potentially related to the 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.
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.
To report any side effect(s):
The National Pharmacovigilance Centre (NPC).
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

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 - 8°C). Do not freeze.
- The unopened vial may be stored outside the refrigerator below 25° C for up to 24 hours. Contains no preservatives, discard any unused portion in accordance with local requirement.
- Store in the original package 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 (E 432) (0.3 mg/ml), sodium dihydrogen phosphate monohydrate (for pH adjustment) (1.104 mg/ml), disodium hydrogen phosphate heptahydrate (for pH adjustment) (0.537 mg/ml), sodium chloride (2.338 mg/ml), sucrose (50 mg/ml), water for injections.

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 vial + 1 filter needle.

Manufacturer
Bulk manufacturer
Regeneron Pharmaceuticals Inc
81 Columbia Turnpike RENSSELAER NEW YORK 12144 United States

Final Release
Bayer AG
Müllerstraße 178
13353 Berlin, Germany.

Marketing Authorisation Holder
Bayer AG
Kaiser-Wilhelm-Allee 1
51368 Leverkusen, Germany.

This leaflet was last revised in January, 2021.

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

The following information is intended for healthcare professionals only:

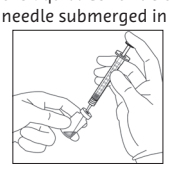
The vial should only be used for the treatment of a single eye.
The solution should be inspected visually for any foreign particulate matter and/or discolouration or any variation in physical appearance prior to administration. In the event of either being observed, discard the medicinal product.
The unopened vial may be stored outside the refrigerator 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.

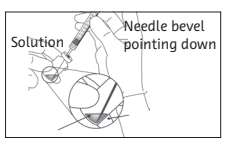
Instructions for use of vial:

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

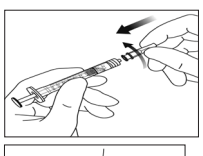
2. Attach the 18 G, 5-micron filter needle supplied in the carton to a 1 mL sterile Luer-lock syringe.

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.

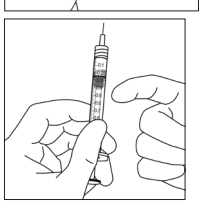




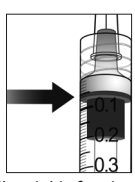
5. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.
6. Remove the filter needle and properly dispose of it.
Note: Filter needle is not to be used for intravitreal injection.
7. Using aseptic technique, firmly twist a 30 G x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

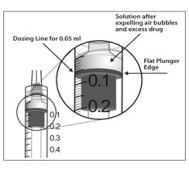


8. Holding the syringe with the needle pointing up, check the syringe for bubbles.
If there are bubbles, gently tap the syringe with your finger until the bubbles rise to the top.



9. 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.





10. The vial is for single use only. Extraction of multiple doses from a single vial 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

Bayer

EYLEA®

Package Leaflet: Information for the patient
Eylea 40 mg/mL solution for injection in a pre-filled syringe
aflibercept

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 retinal vein occlusion (branch RVO (BRVO) or central RVO (CRVO)),
- ▶ impaired vision due to diabetic macular oedema (DME).
- ▶ impaired vision due to myopic choroidal neovascularisation (myopic CNV).

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 and 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 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 causing a swelling of the macula, (the portion of the retina responsible for fine vision), which is called macular oedema. 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 are elevated in response causing the leakage of fluid into the retina and thereby causing macular oedema.
Diabetic macular oedema is a swelling of the retina occurring in patients with diabetes due to leaking of fluid 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 stabilise, and in many cases, improve the vision loss related to wet AMD, CRVO, BRVO, DME and myopic CNV.

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:
- ▶ if you have glaucoma.
- ▶ if you have a history of seeing flashes of light or floaters and if you have a 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.
- ▶ if you have a severe form of CRVO or BRVO (ischaemic CRVO or BRVO), treatment with Eylea is not recommended.

Furthermore, 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 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 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.

The systemic use of VEGF inhibitors, substances similar to those contained in Eylea, is potentially related to the 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.
There are limited data on safety in treating patients with CRVO, BRVO, DME and myopic CNV who have had a stroke or a mini-stroke (transient ischaemic 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.
- ▶ diabetics with very high average blood sugar values (HbA1c over 12%).
- ▶ diabetics with 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.
- ▶ diabetics with uncontrolled high blood pressure.
- ▶ non-Asian patients with myopic CNV.
- ▶ patients previously treated for myopic CNV.
- ▶ patients with damage outside the central part of the macula (extrafoveal lesions) for myopic CNV.

If any of the above applies 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 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.

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

Pregnancy and breast-feeding
- ▶ 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 breast-feeding 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 sodium (23 mg) per dosage unit, that is to say 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 (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 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 another injection after a further two months .
Your doctor will then decide whether the treatment interval between injections may be kept at every two months or be gradually extended in 2- or 4-weekly intervals if your condition has been stable. If your condition worsens, the interval between injections can be shortened.
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 RVO (branch RVO or central RVO)
Your doctor will determine the most appropriate treatment schedule 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 worsen with a longer treatment interval, your doctor will shorten the interval accordingly.
Based on your response to treatment your doctor will decide on the schedule for follow up examinations and treatments.

Diabetic macular oedema (DME)
Patients with DME will be treated with one injection per month for the first five consecutive doses followed by one injection every two months thereafter.
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.
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 CNV
Patients with myopic CNV will be treated with one single injection. You will receive further injections only if your doctor's examinations reveal 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 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.**
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 haemorrhage), **detachment of the gel-like substance inside the eye from the retina** (vitreous detachment) and **increase of pressure inside the eye**, see section 2. These serious side effects affecting the eyes occurred in less than 1 in 1,900 injections in clinical studies.
If you experience a sudden decrease in vision, or an increase in pain and redness in your eye after your injection, **contact your doctor immediately**.

List of side effects reported:
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)**:**
- ▶ deterioration of eyesight
- ▶ 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, resulting in flashes of light with floaters sometimes progressing to a loss of vision (retinal pigment epithelial tear* /detachment, retinal detachment/tear)
- ▶ degeneration of the retina (causing disturbed vision)
- ▶ bleeding in the eye (vitreous haemorrhage)
- ▶ certain forms of clouding of the lens (cataract)
- ▶ damage to the front layer of the eyeball (the cornea)
- ▶ increase in eye pressure
- ▶ moving spots in vision (floaters)
- ▶ detachment of the gel-like substance inside the eye from the retina (vitreous detachment, resulting in flashes of light with 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

* 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)**
- ▶ 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)

**Allergic reactions like rash, itching (pruritus), hives (urticaria), and a few cases of severe allergy (anaphylactic/anaphylactoid) reactions were reported

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

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 with wet AMD receiving blood thinners. This increased incidence was comparable between patients treated with ranibizumab and Eylea.
The systemic use of VEGF inhibitors, substances similar to those contained in Eylea, is potentially related to the 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.
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.

To report any side effect(s):
Saudi Arabia:
The National Pharmacovigilance Centre (NPC).
SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

Kuwait:
Hotline: 1810005
Email: health@moh.gov.kw
Website: www.moh.gov.kw/kdfc/
P.O.Box: 5 Safat, 13001 Kuwait

Other Countries:
Please contact the relevant competent authority

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.
- ▶ The unopened blister may be stored outside the refrigerator below 25 °C for up to 24 hours.
- ▶ Store in the original package 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 pre-filled syringe contains an extractable volume of at least 0.09 mL, equivalent to at least 3.6 mg aflibercept. One pre-filled syringe delivers a dose of 2 mg aflibercept in 0.05 mL.
- ▶ The other ingredients are: polysorbate 20 (E 432), sodium dihydrogen phosphate monohydrate (for pH adjustment), disodium hydrogen phosphate heptahydrate (for pH adjustment), sodium chloride, sucrose, water for injections.

What Eylea looks like and contents of the pack
Eylea is a solution for injection (injection) in a pre-filled syringe. The solution is colourless to pale yellow.
Pack size of 1 pre-filled syringe.

Bulk manufacturer
Regeneron Pharmaceuticals Inc
81 Columbia Turnpike
Rensselaer, New York 12144, United States

Final Release
Bayer AG
Müllerstraße 178
13353 Berlin, Germany.

Marketing Authorisation Holder
Bayer AG
51368 Leverkusen, Germany.

This leaflet was last revised in July 2021.

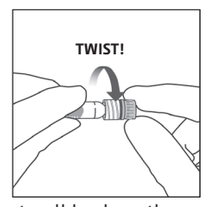
This is a medicament
- ▶ A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- ▶ Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- ▶ The doctor and the pharmacist 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.

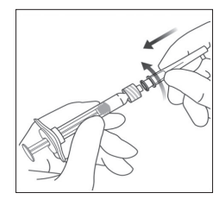
Council of Arab Health Ministers
Union of Arab Pharmacists

The following information is intended for healthcare professionals only:
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.

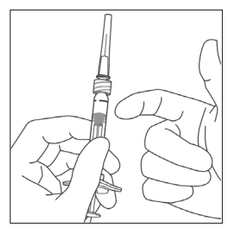
Instructions for use of pre-filled syringe:
1. When ready to administer Eylea, open the carton and remove the sterilised blister. Carefully peel open the blister ensuring the sterility of its contents. Keep the syringe in the sterile tray until you are ready for assembly.
2. Using aseptic technique, 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.



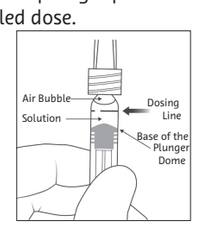
4. To avoid compromising the sterility of the product, do not pull back on the plunger.
5. Using aseptic technique, firmly twist the injection needle onto the Luer-lock syringe tip

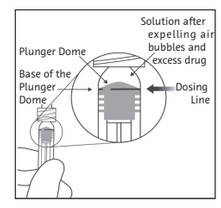


6. Holding the syringe with the needle pointing up, check the syringe for bubbles. If there are bubbles, gently tap the syringe with your finger until the bubbles rise to the top.



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 black 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.

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