Recommendations for treatment with

Prescriber Guide

This Guide provides you important information on EYLEA® 40 mg/ml solution for injection (2 mg aflibercept dose) and EYLEA® 114.3 mg/ml solution for injection (8 mg aflibercept dose), the medication itself and how to correctly administer it to your patients.

Please provide your patients with the EYLEA® patient guide and the Patient Information Leaflet.

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

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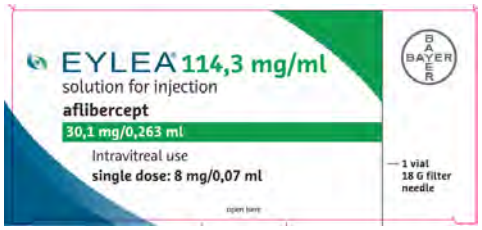
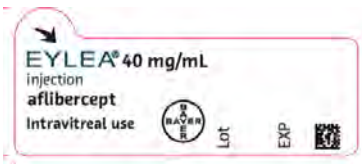
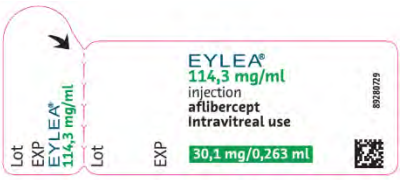
KEY SUMMARY FOR EYLEA

DIFFERENCES BETWEEN EYLEA 40 MG/ML SOLUTION FOR INJECTION (2 MG DOSE) AND EYLEA 114.3 MG/ML SOLUTION FOR INJECTION (8 MG DOSE)

	EYLEA 40 MG/ML	EYLEA 114.3 MG/ML
APPROVED INDICATIONS IN ADULTS*	wAMD, DME, BRVO, CRVO, mCNV	wAMD, DME
DOSE PER INJECTION	2 MG	8 MG
INJECTION VOLUME	0.05 ML	0.07 ML
PRESENTATION	PRE-FILLED SYRINGE AND VIAL	VIAL
PACKAGING		
VIAL		
LABEL ON VIAL		

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).

MA-EYL-SA-0009-1

Contraindications

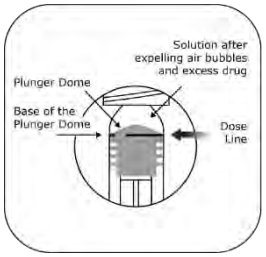
- Hypersensitivity to aflibercept or to any of the excipients listed in section 6.1 of the Summary of Product Characteristics (SmPC)
- Active or suspected ocular or periocular infection
- Active severe intraocular inflammation

Key instructions for use

- The vials and the 40 mg /ml (2 mg dose) EYLEA solution for injection pre-filled syringe contain more than the recommended dose of EYLEA**. Do not inject the entire volume.**
- Ensure proper aseptic technique including broad-spectrum microbicide to minimise the risk of intraocular infection
- For the intravitreal injection, a **30 G x ½ inch injection needle** should be used

- **Pre-filled syringe:** EYLEA 40 mg/ml solution for injection (2 mg dose)
  - Expel excess volume and air bubbles from the pre-filled syringe and adjust the base of the plunger dome **(NOT the tip)** to the dose line before injection
  - Push the plunger slowly and with constant pressure, and do not administer any residual volume remaining in the syringe after injection

✓ **Correct** plunger position



Selected instructions for storage and handling

- **Store EYLEA in the refrigerator** (2°C to 8°C)
- EYLEA is **not licensed for multi-dose**, further compounding or vial splitting. Use of more than one injection from the vial or the pre-filled syringe **can lead to contamination and subsequent infection**

Special warnings and precautions for use

In all cases, instruct patients to immediately report signs and symptoms of adverse events

Adverse event/risk	Measures to minimize risk
Intraocular inflammation including endophthalmitis	Use proper aseptic technique when preparing the injection and during the injection itself Use recommended antiseptic agents Monitor patient after the injection
Transient IOP* increase	Properly prime the syringe by removing excess volume and air bubbles from the syringe before administration Monitor patient's vision and IOP after the injection
Medication error	Properly prime the syringe by removing excess volume and air bubbles from the syringe before administration Monitor patient's vision and IOP after the injection
Retinal pigment epithelial tear	Monitor patient after the injection
Cataract	Measure for correct site of injection, use correct injection technique
Off-label use/misuse	Use medication only for treatment of approved indications and use approved dose
Embryo-fetotoxicity	Instruct patient to use effective contraception during treatment: For at least 3 months after last intravitreal injection of EYLEA 40 mg/ml (2 mg dose) For at least 4 months after last intravitreal injection of EYLEA114.3 mg/ml (8 mg dose) EYLEA 40 mg/ml (2 mg dose) and EYLEA 114.3 mg/ml (8 mg dose) should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.
Exposure during breastfeeding	Eylea is not recommended in patients who are breastfeeding

*Intraocular pressure increase

After the injection

- **Evaluate vision immediately after injection** (hand movement or finger counting)
- **Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure**
- Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay

GENERAL INFORMATION

You must explain to the patient the implications of anti-VEGF treatment. The patient guide is a tool that will help you to communicate to your patient about the disease and treatment. It contains information on the signs and symptoms of adverse reactions and when they should seek immediate medical attention.

The Summary of Product Characteristics, or SmPC, describes the properties of EYLEA and the approved indications for use. It is an important source of information for healthcare professionals on how to use EYLEA safely and effectively. Refer to the approved SmPC for EYLEA for complete information on posology and dosing recommendations for EYLEA 40 mg/ml solution for injection (2 mg dose) and Eylea 114.3 mg/ml solution for injection (8 mg dose).

ABOUT EYLEA

EYLEA is for intravitreal injection only. It must only be administered by a qualified physician experienced in administering intravitreal injections and familiar with the handling of the vial/pre-filled syringe

	EYLEA 40 mg/ml	**EYLEA 114.3 mg/ml**
Presentation	Pre-filled syringe and vial	Vial
Approved indications in adult (18 years and older) patients		
Neovascular (wet) AMD	Yes	Yes
Visual impairment due to diabetic macular oedema (DME)	Yes	Yes
Visual impairment due to macular oedema secondary to retinal vein occlusion (RVO), branch (BRVO) or central (CRVO)	Yes	No
Visual impairment due to myopic choroidal neovascularisation (mCNV)	Yes	No
Recommended dose	2 mg	8 mg
Volume to inject	50 microliters or 0.05 ml	70 microliters or 0.07 ml
Posology for approved indications	The posology recommendations for wAMD, RVO, DME and mCNV are different to each other Refer to the SmPC for complete information on posology and dosing for EYLEA 40 mg/ml and for EYLEA 114.3 mg/ml	

IMPORTANT SAFETY INFORMATION ABOUT EYLEA

Contraindications
EYLEA is contraindicated in the following:

- Hypersensitivity to aflibercept or to any of the excipients listed in section 6.1 of the SmPC
- Active or suspected ocular or periocular infection
- Active severe intraocular inflammation

Special warnings and precautions for use

Intravitreal injection-related reactions
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract.

- **Always use proper aseptic injection techniques** when administering EYLEA
- **Monitor patients following injections as per local practice** to permit early treatment if an infection occurs
- **Instruct patients to immediately report any signs and symptoms** suggestive of endophthalmitis or any of the adverse reactions mentioned above

The pre-filled syringe and the vial contain more than the recommended dose of 2 mg or 8 mg aflibercept (equivalent to 0.05 ml/0.07 ml). Expel the excess volume and air bubbles from the syringe prior to injection.

- Administer the recommended dose and do not inject any residual volume, as increased injection volume can lead to clinically relevant intraocular pressure elevation

Increase in intraocular pressure
Transient increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including injections with EYLEA.

- **Monitor your patient after the injection procedure** and take special precaution in patients with poorly controlled glaucoma (do not inject EYLEA while the intraocular pressure is ≥30 mm Hg)
- Refer to the post-injection care section for further instructions

Immunogenicity
EYLEA is a therapeutic protein and has potential for immunogenicity.

- **Instruct patients to report any signs or symptoms of intraocular inflammation** (e.g. pain, photophobia or redness), which may be attributable to hypersensitivity
- Refer to the post-injection care section for further instructions

Systemic effects
Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors and there is a theoretical risk that these may relate to VEGF inhibition.

- Exercise caution when treating patients with CRVO, BRVO, DME or mCNV, and wAMD with a history of stroke, transient ischaemic attacks or myocardial infarction within the last 6 months as there are limited data on safety of EYLEA in these groups

Special populations

The following recommendations are made:

- **Women of childbearing potential**
  Use effective contraception during treatment and **for at least 3 months** after the last intravitreal injection of EYLEA 40 mg/ml (2 mg dose).
  Use effective contraception during treatment and for at least 4 months after the last intravitreal injection of EYLEA 114.3 mg/ml (8 mg dose).

- **Pregnancy**
  EYLEA 2 mg and EYLEA 8 mg should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.

- **Breast-feeding**
  Based on very limited human data, aflibercept may be excreted in human milk at low levels. Aflibercept is a large protein molecule and the amount of medication absorbed by the infant is expected to be minimal. The effects of aflibercept on a breast-fed newborn/infant is unknown. As a precautionary measure, breast-feeding is not recommended during the use of Eylea.

Post-injection care
Immediately after intravitreal injection:

- Evaluate the patient's vision (hand movement or finger counting)

- Monitor the patient for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or conducting a tonometry test. Sterile equipment for paracentesis should be readily available if anterior chamber paracentesis needs to be done.

- Instruct the patient to report any signs and symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

- Instruct the patient to report any signs or symptoms after the injection that get worse over time.

Adverse Drug Reactions

Adverse drug reactions are the same for EYLEA 40 mg/ml (2 mg dose) and EYLEA 114.3 mg/ml (8 mg dose).

Key signs and symptoms of adverse reactions include:

Transient increased intraocular pressure	Patients may experience vision changes such as temporary vision loss, eye pain, halos around lights, red eye, nausea and vomiting
Tear of the retinal pigment epithelium	Patients may experience acute decrease in (central) vision, blind spot (central scotoma), and distorted vision with deviation of either vertical or horizontal lines (metamorphopsia)
Tear or detachment of the retina	Patients may experience sudden flashes of light, a sudden appearance or an increase of the number of vitreous floaters, a curtain over a portion of their visual field and vision changes
Intraocular inflammation including endophthalmitis	Patients may experience eye pain or increased discomfort, worsening eye redness, photophobia or sensitivity to light, swelling, and vision changes, such as a sudden decrease in vision or blurring of vision
Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities	Patients may experience less vivid lines and shapes, shadows and colour vision than before, and vision changes

See section 4.8 of the SmPC for full list of potential adverse reactions.

Management of adverse reactions

In case of any adverse reactions that concern your patient, your patient must have immediate access to an ophthalmologist.

Appropriate management of ALL adverse reactions, including those associated with the intravitreal injection, should be carried out according to clinical practice and/or following standardised guidelines.

Healthcare Professionals are asked to report any suspected adverse reactions.
See section 4.8 of the SmPC for how to report suspected adverse reactions.

STORAGE AND HANDLING OF EYLEA

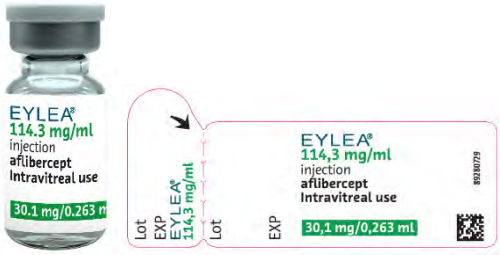
The solution is clear and colourless to pale yellow. It is an iso-osmotic solution.
Inspect the solution visually before use for any foreign particulate matter and/or unusual colour (the solution can be pale yellow, which is normal**) or any variation in physical appearance. If any of these are observed, discard the product.**

The EYLEA 40 mg/ml (2 mg dose) vial looks different to the EYLEA 114.3 mg/ml (8 mg dose) vial to allow for easy identification. Please take this into consideration when selecting the product to be injected to the patient (please see pictures below).

Do not split a vial/pre-filled syringe into more than one dose. Each vial/pre-filled syringe is for single eye use only. Extraction of multiple doses from a single vial/pre-filled syringe may increase the risk of contamination and subsequent infection in the patient.

Each EYLEA 40 mg/ml solution for injection in a <u>pre-filled syringe</u> (2 mg dose) contains **more than the recommended 0.05 ml dose of aflibercept. The excess volume and any air bubbles in the syringe must be expelled before injecting the patient with the recommended dose.**

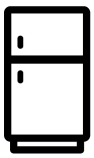
Each EYLEA 40 mg/ml solution for injection in a <u>vial</u> (2 mg dose) **contains more than the recommended 0.05 ml dose of aflibercept. The excess volume and any air bubbles in the disposable syringe must be discarded before injecting the patient with the recommended dose.**



Each EYLEA 114.3 mg/ml solution for injection in a <u>vial</u> (8 mg dose) **contains more than the recommended 0.07 ml dose of EYLEA. The excess volume and any air bubbles in the disposable syringe must be discarded before injecting the patient with the recommended dose.**

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).

Special precautions for storage

	Store in a refrigerator (2–8°C).
	Do not freeze.
	Keep the pre-filled syringe in its blister and in the outer carton in order to protect it from light. Keep the vial in the outer carton in order to protect it from light.
	Prior to use EYLEA 40 mg/ml (2 mg dose), the unopened vial or blister of EYLEA may be kept at room temperature (below 25°C) for up to 24 hours.

The inside of the sealed EYLEA 40 mg/ml (2 mg dose) solution for injection in a pre-filled syringe blister packaging is sterile. Do not open the pre-filled syringe blister outside the clean administration room.

After opening the blister or vial, proceed under aseptic conditions.

INSTRUCTIONS FOR USE OF EYLEA

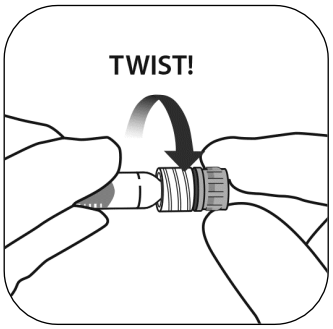
General preparation for injection

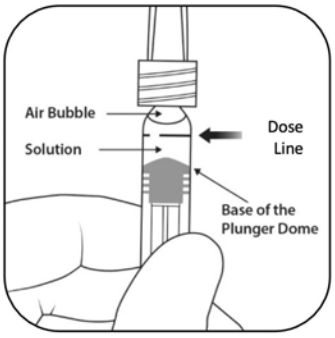
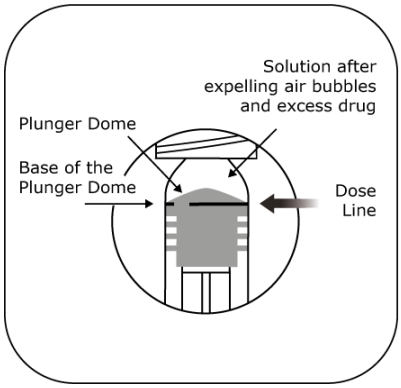
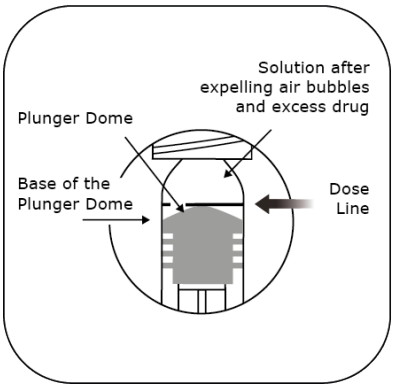
- Intravitreal injections must be carried out according to medical standards and applicable guidelines by **a qualified physician experienced in administering intravitreal injections and familiar with the handling** of the vial/pre-filled syringe
- Surgical hand disinfection, aseptic gloves, a sterile drape and a sterilised eyelid speculum (or equivalent) are recommended
- For the intravitreal injection, a **30 G x ½ inch injection needle** should be used

Pre-filled syringe 40 mg/ml (2 mg dose), solution for injection

Note: the EYLEA pre-filled syringe is a glass syringe with a rubber plunger that requires slightly more force to depress compared with plastic syringes (such as those used with the vial presentation). **Become familiarised with this syringe before using it on patients.**

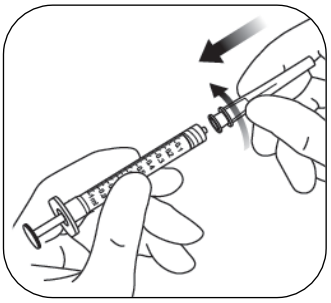
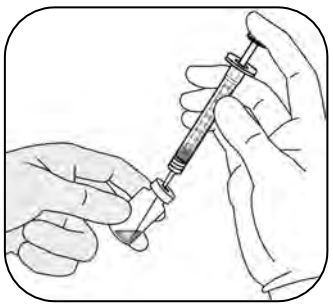
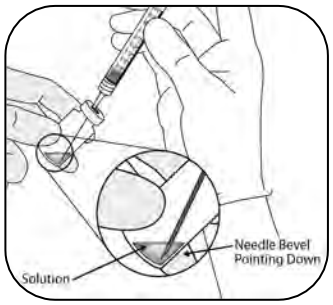
The pre-filled syringe and contents must be inspected before using. Do not use the pre-filled syringe if any part is damaged or loose. Do not use it if the syringe cap is detached from the Luer Lock. Look for any particulate matter and/or unusual colour or any variation in physical appearance. If any of these are observed, discard the product.

1	<u>Prepare the pre-filled syringe for administration</u> It is important to prepare the pre-filled syringe using aseptic technique. An assistant should carry out the following steps: Remove the carton containing the pre-filled syringe from the refrigerator. Open the carton and remove the blister containing the syringe. The blister must not be placed on an aseptic surface because the outside surface of the blister is not sterile. The inside of the sealed blister and the pre-filled syringe are sterile. Carefully peel open the blister. **Aseptic technique must be used once the blister is opened.** The qualified physician carries out the remainder of the steps with sterile technique including the use of aseptic gloves (white gloves in pictures) when handling: with two fingers, remove the pre-filled syringe from the blister, visually inspect the syringe and place the syringe in an aseptic tray until ready for assembly.
2	<u>Remove the syringe cap</u> Hold the syringe in one hand while using the other hand to grasp the syringe cap with the thumb and forefinger. **Twist off – do not snap off – the syringe cap.** 
3	**Do not pull back the plunger.** This may compromise the sterility of the product.

4	<u>Attach the needle</u> Using aseptic technique, **firmly twist the 30 G x ½ inch injection needle onto the Luer-lock syringe tip.** 
5	<u>Check for bubbles</u> Holding the syringe with the needle pointing upwards, **check the solution for bubbles. If bubbles are present, gently tap the syringe with your finger until the bubbles rise to the top.** 
6	<u>Eliminate air bubbles and excess drug</u> **Correct handling of the prefilled syringe is important in order to avoid the risk of medication errors. This includes removal of the excess volume and air bubbles, in order to avoid overdosing.** Remove the air bubbles and excess drug from the syringe by slowly depressing the plunger rod to align the base of the plunger dome (not the tip of the dome) with the dose line on the syringe. Remember that the feel with this syringe is different from disposable syringes. The remaining volume after aligning to the dose line ensures an injection volume of 0.05 ml.  **Accurate positioning of the plunger is critical. Incorrect plunger positioning can lead to delivering more or less than the labelled dose.** ✓ **Correct** plunger position  ✗ **Incorrect** plunger position 

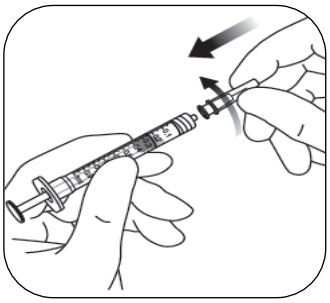
7	Inject EYLEA **Inject the solution into the eye carefully with constant pressure on the plunger. Do not apply additional pressure once the plunger has reached the bottom of the syringe.** **Do not administer any residual solution observed in the syringe**.
8	**Dispose of any unused medicinal product or waste material in accordance with local regulations.**

Vial 40 mg/ml (2mg dose) and 114.3 mg/ml (8mg dose) solution for injection

1	<u>Inspect the vial, and remove the vial cap</u> It is important to prepare the syringe with EYLEA from the vial, using aseptic technique. Note in the pictures that darker/grey gloves are not aseptic and white gloves are aseptic. An assistant should carry out the following steps (assistant is shown with darker/grey gloves in the images): Remove the carton containing the vial from the refrigerator. Open the carton and remove the vial. **Check the carton, the vial and label to ensure the correct EYLEA solution is chosen.** The vial should not be placed on an aseptic surface because the outside surface of the vial is not sterile. The inside of the vial is sterile. Visually inspect the vial and contents. Remove the plastic cap and disinfect the outer part of the rubber vial stopper.	
2	<u>Attach the filter needle</u> The qualified physician should carry out the remaining steps using aseptic technique, including the use of aseptic gloves: Using aseptic technique, screw on the 18 G, 5-micron filter needle supplied in the carton to a 1 ml sterile Luer-lock syringe.	
3	<u>Insert needle into vial</u> Insert the filter needle into the centre of the vial stopper until the needle is completely inserted into the vial and the needle tip touches the bottom or bottom edge of the vial.	
4	<u>Draw up the solution</u> Withdraw all of the EYLEA vial contents into the syringe, keeping the vial in an upright position, slightly inclined to ease complete withdrawal. To avoid the introduction of air, ensure the bevel of the filter needle is submerged in the liquid. Continue to tilt the vial during withdrawal, keeping the bevel of the filter needle submerged in the liquid. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.	
5	<u>Remove the filter needle</u> Unscrew and properly dispose the filter needle. **Do not use the filter needle for intravitreal injection.**	

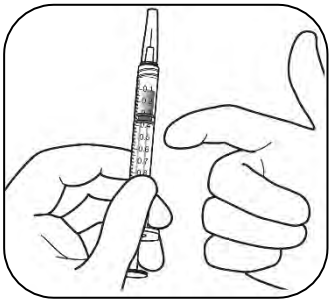
6 Attach the injection needle

Using aseptic technique, **firmly twist a 30 G x ½ inch injection needle** to the Luer-lock syringe tip.



7 Check for air bubbles

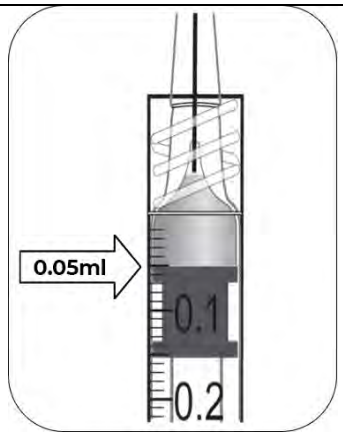
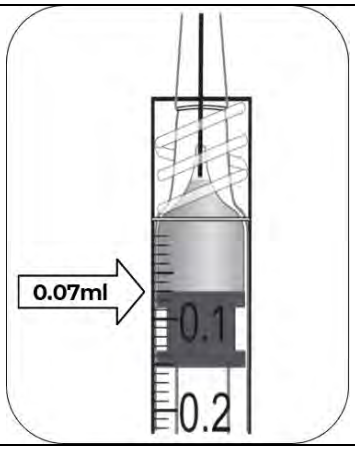
Holding the syringe with the needle pointing upwards, visually inspect the contents of the syringe. **Check the solution for bubbles. If bubbles are present, gently tap the syringe with your finger until the bubbles rise to the top.**

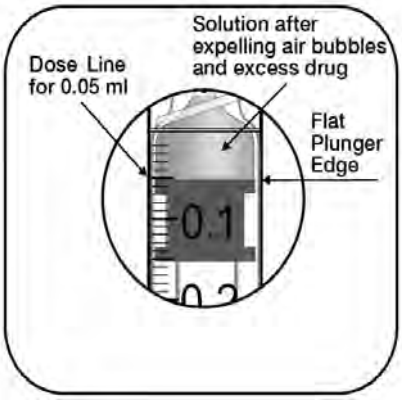
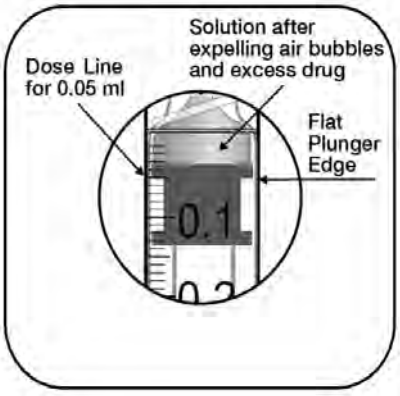


8 Eliminate air bubbles and excess drug

Correct handling of the filled syringe is important in order to avoid the risk of medication errors. This includes removal of the excess volume and air bubbles, in order to avoid overdosing.

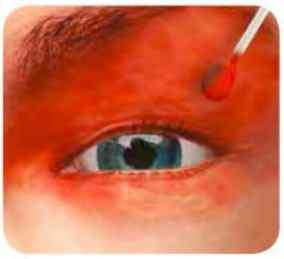
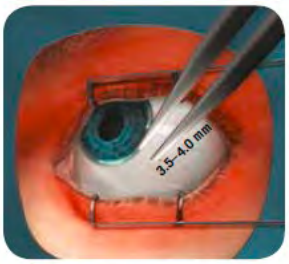
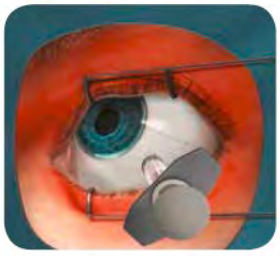
Attention! The EYLEA 2 mg dose uses 0.05 ml volume of EYLEA 40 mg/ml solution. The EYLEA 8 mg dose uses 0.07 ml volume of EYLEA 114.3 mg/ml solution.

EYLEA 2 mg dose	EYLEA 8 mg dose
Use 0.05 ml volume of EYLEA 40 mg/ml solution	Use 0.07 ml of EYLEA 114.3 mg/ml solution
Eliminate all air bubbles and expel excess drug by slowly depressing the plunger rod to align the flat plunger edge with the **0.05 ml line on the syringe for the 40 mg/ml mg vial.**	Eliminate all air bubbles and expel excess drug by slowly depressing the plunger rod to align the flat plunger edge with the **0.07 ml line on the syringe for the 114.3 mg/ml mg vial.**
	

	Accurate positioning of the plunger is critical. Incorrect plunger positioning can lead to delivering more or less than the recommended dose, refer to the example below for 0.05 ml volume and the same applies for 0.07 ml volume. ✓ **Correct** plunger position for 0.05 ml volume  ✗ **Incorrect** plunger position for 0.05 ml volume 
9	**Dispose of any unused medicinal product or waste material in accordance with local regulations.**

Injection procedure

For further information on intravitreal injection procedure, sterile techniques (including periocular and ocular disinfection) and anaesthesia, please refer to local and/or national clinical guidelines.

1	Administer topical anaesthesia.	
2	Apply disinfectant (e.g. 5% povidone iodine solution or equivalent) to the eyelids, eyelid margins and into the conjunctival sac. The disinfectant should be on the surface for the length of time recommended in local practice guidelines Eye dilation prior to the injection procedure is **not** necessary.	
3	A disinfectant (e.g. 10% povidone iodine solution or equivalent) should also be applied to the periocular skin, eyelids and eyelashes, avoiding extensive pressure to the periocular glands. The disinfectant should be on the surface for the length of time recommended in local practice guidelines	
4	Cover with sterile drape and insert sterile lid speculum. A second application of disinfectant, e.g., 5% povidone iodine solution, may be made to the conjunctival sac. Disinfectant should be on the surface for the length of time recommended in local practice guidelines	
5	Tell patient to look away from the injection site. Position the eye adequately. At an area of 3.5–4.0 mm posterior to the limbus, mark an injection site.	
6	Insert the injection needle into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe. Inject the recommended dose, with careful and constant pressure on the plunger. Do not apply additional pressure once the plunger has reached the bottom of the syringe. Do not inject any residual volume remaining in the syringe after the injection. Use a different scleral site for subsequent injections.	

Eylea ® *40 mg/ml solution for injection -* ***Composition****: The active substance is Aflibercept. One vial delivers a dose of 2 mg Aflibercept (0.05 mL) -* ***Indications****: Eylea* ® *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 neovascularization (myopic CNV). Aflibercept blocks the activity of Vascular Endothelial Growth Factor A (VEGF-A) and Placental Growth Factor (PlGF).* ***Usage:*** *Eylea* ® *to be injected into the eye under aseptic (clean and sterile) conditions. The recommended dose is 2 mg Aflibercept (0.05 mL). by a doctor experienced in giving eye injections. Eylea* ® *is given as an injection into eye (intravitreal injection). Before the injection the doctor will use disinfectant eyewash to clean the eye carefully to prevent infection. The doctor will also give a local anesthetic to reduce or prevent any pain the patient might have with the injection.* ***Wet AMD****: Patients with wet AMD will be treated with one injection per month for 3 consecutive doses, followed by another injection after a further two months. Doctor will then decide whether the treatment interval between injections may be kept at every 2 months or be gradually extended in 2- or 4-weekly intervals if condition has been stable. If condition worsens, the interval between injections can be shortened. Unless any problems or are advised differently by doctor, there is no need to see doctor between the injections.* ***Macular oedema secondary to RVO (branch RVO or central RVO)****. start treatment with a series of monthly Eylea* ® *injections. The interval between two injections should not be shorter than one month. Doctor may decide to stop treatment with Eylea* ®*, if not benefiting from continued treatment. treatment will continue with monthly injections until condition is stable. 3 or more monthly injections may be needed. doctor will monitor the response to treatment and may continue treatment by gradually increasing the interval between injections to maintain a stable condition. If condition starts to worsen with a longer treatment interval, doctor will shorten the interval accordingly. Based on response - doctor will decide on the schedule for follow up examinations and treatments.* ***Diabetic macular oedema (DME)*** *Patients with DME will be treated with 1 injection per month for the first five consecutive doses followed by one injection every 2 months thereafter. Unless any problems or are advised differently by doctor, there is no need to see doctor between the injections. Treatment interval may be kept at every two months or adjusted to your condition, based on your doctor's examination. doctor may decide to stop treatment with Eylea* ® *if it is not benefiting from continued treatment.* ***Myopic CNV*** *Patients with myopic CNV will be treated with one single injection. receive further injections only if doctor's examinations reveal that condition has not improved. The interval between 2 injections should not be shorter than one month. If condition goes away and then comes back, doctor may re-start the treatment. doctor will decide on the schedule for follow up examinations.* ***Contraindications****: Allergy to aflibercept or any of the other ingredients of this medicine****,*** *Active or suspected infection in or around the eye (ocular or periocular infection), Severe inflammation of the eye (indicated by pain or redness)* ***Warnings & Precautions:*** *Doctor should be consulted before taking Eylea* ® *if the patient has any of the following: Glaucoma. A history of seeing flashes of light or floaters and a sudden increase of size and number of floaters, if surgery was performed or is planned on eye within the previous or next 4 weeks, in case of severe form of CRVO or BRVO (ischemic CRVO or BRVO), treatment with Eylea* ® *is not recommended. Furthermore, it is important 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. This will be monitored by the doctor after each injection, if the patient develops an infection or inflammation inside the eye (endophthalmitis) or other complications, the patient 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. Doctor will check whether the patient has 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 3 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 ischemic attack) or a heart attack within the last 6 months. If any of these apply to the patient, 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 patient, this lack of information when treating with Eylea* ® *should be considered.* ***Children & adolescents****: The use of Eylea* ® *in children or adolescents under 18 has not been studied because wet AMD, CRVO, BRVO, DME & myopic CNV occur mainly in adults. Therefore, its use in this age group is not relevant.****Other medicines & Eylea*** ®***:*** *The doctor should be informed if the patient has 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 woman is pregnant or planning to become pregnant, doctor should be consulted before treatment with Eylea* ®*. Eylea* ® *is not recommended during breastfeeding as it is not known whether Eylea* ® *passes into human milk. doctor should be consulted for advice before starting Eylea* ® *treatment.* ***Driving and using machines:*** *After injection with Eylea* ®*, the patient may experience some temporary visual disturbances. The patient should not drive or use machines as long as these last.* ***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 immediate doctor consultation. 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, If the patient experience a sudden decrease in vision, or an increase in pain and redness in the eye after injection, Doctor should be consulted immediately.* ***List of side effects reported: Very common side effects:*** *deterioration of eyesight, bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye, eye pain, bleeding in the back of the eye (retinal hemorrhage).* ***Common side effects:*** *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 hemorrhage), 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.* ***Reporting of side effects:*** *Doctor should be consulted in case of any side effect. This includes any possible side effects not listed in this leaflet. Reporting side effects 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*

- Please refer to Package Insert Leaflet (PIL) in your country for further product data & details
Marketing Authorization Holder: *Bayer AG Kaiser-Wilhelm-Allee 1 - 51368 Leverkusen, Germany* ***SA PIL Revised: Nov. 2022***

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
PP-EYL-ALL-1295-1

Eylea ® PFS: *A prefilled Syringe with* ***Aflibercept 40 mg/ml*** *as one pre-filled syringe contains an extractable volume of at least 0.09 mL, equivalent to at least 3.6 mg aflibercept which delivers a dose of 2 mg aflibercept in 0.05 mL to block the activity of a group of factors known as Vascular Endothelial Growth Factor A (VEGF-A) and Placental Growth Factor (PlGF).* ***Indications:*** *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).* ***The recommended dose****: is 2 mg aflibercept (0.05 mL),* *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 2 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, but to not less than every two months in the first year of treatment.* *Macular Oedema secondary to RVO (branch RVO or central RVO): 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. 3 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 -* ***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, accurate positioning of the plunger is very important, because incorrect plunger positioning can lead to delivering more or less than the labelled dose. 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 -* ***Contraindications:*** *if you are allergic to aflibercept or any of the other ingredients of this medicine, 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:*** *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 or 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: *Injections with Eylea ® may cause an increase in eye pressure (intraocular pressure) in some patients within 60 minutes of the 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, 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 3 further months after the last injection of 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.* ***- 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 ®. Eylea ® should not be used during pregnancy unless the potential benefit outweighs the potential risk to the unborn child.* ***Driving & 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.* ***- 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 - 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. 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: Very common side effects****: deterioration of eyesight, bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye* ***or*** *eye pain -* ***- Common side effects:****: 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, allergy, swelling of the eyelid, bleeding at the injection site, redness of 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. - The systemic use of VEGF inhibitors is potentially related to the risk of blood clots blocking blood vessels (arterial thromboembolic events) which may lead to heart attack or stroke - 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): Fax: +966-11-205-7662* ***-*** *SFDA Call Center: 19999****,*** *E-mail: npc.drug@sfda.gov.sa****,*** *Website: https://ade.sfda.gov.sa*

- For full product prescribing data, please refer to package insert leaflet (PIL)

Marketing Authorisation Holder: *Bayer AG* ***-*** *51368 Leverkusen, Germany* ***KSA PIL version:*** *July 2021*

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
PP-EYL-ALL-1295-1

Eylea ® 8 mg: Composition: *1 ml solution contains 114.3 mg of the* ***active substance aflibercept*** *- Each vial contains 0.263 ml usable amount to deliver a single dose of 0.07 ml* ***containing 8 mg aflibercept for intravitreal injection*** *-* ***Indications:*** *To treat eye disorders in adults called: Wet age-related macular degeneration* ***(wet AMD)*** *& Visual impairment due to diabetic macular oedema* ***(DME)*** *-* ***How Eylea works:*** *Eylea belongs to a group of medicines called anti-neovascularisation agents which stops growth of new abnormal blood vessels in the eye to stabilise and often improve vision –* ***Dosage:*** *The recommended dose is 8 mg aflibercept per injection: Patient to receive 1 injection every month for the first 3 months - After that, you may receive injections up to every 5 months. Your doctor will decide on the frequency based on the condition of your eye -* ***Before the injection:*** *your doctor will use a disinfectant eyewash to clean your eye carefully to prevent infection and a local anaesthetic eye drop to numb the eye to reduce or prevent pain from the injection -* ***If you missed a dose of Eylea****: Make a new appointment with your doctor as soon as possible -* ***Before stopping Eylea treatment:*** *Speak with your doctor before stopping treatment. Stopping treatment may increase your risk of vision loss and your vision may worsen –* ***Contraindications:*** *If are allergic to aflibercept or any of the other ingredients of this medicine, if you have an infection in or around the eye or if you have pain or redness in your eye (severe eye inflammation) -* ***Warnings and precautions:*** *Talk to your doctor* ***before receiving*** *Eylea if you: have glaucoma – an eye condition caused by high pressure in the eye****,*** *have a history of seeing flashes of light or dark floating spots and if their size or number suddenly increases* ***or*** *had eye surgery in the last 4 weeks or eye surgery is planned in the next 4 weeks -* ***Tell your doctor immediately if you develop****: Redness of the eye, eye pain, increased discomfort, blurred or decreased vision &/or increased sensitivity to light (These may be symptoms of an inflammation or infection and your doctor may stop giving you Eylea)* ***- 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 such use may increase risk of experiencing side effects, injections with Eylea may cause an increase in eye pressure in some patients within 60 minutes of the injection. Your doctor will monitor this after each injection, your doctor will check for other risk factors that may increase the chance of a tear or detachment of one of the layers at the back of the eye. In such cases your doctor will give you Eylea with caution, women who could become pregnant must use effective birth control during treatment and for at least 4 months after the last injection of Eylea -* ***The use of substances similar to those contained in Eylea is potentially related to the risk of blood clots blocking blood vessels, which may lead to heart attack or stroke.*** *Theoretically, this could also happen after an injection of Eylea into the eye. If you had a stroke, a mini-stroke or a heart attack within the last 6 months, your doctor will give you Eylea with caution -* ***Children and adolescents:*** *The use of Eylea in children or adolescents under 18 has not been studied because the diseases indicated 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 who could become pregnant must use effective birth control during treatment and for at least 4 months after the last injection of Eylea - There is no experience on the use of Eylea in pregnant women - Women should not receive Eylea during pregnancy unless the potential benefit to the woman outweighs the potential risk to the unborn child - Small amounts of Eylea may pass into human milk. The effect on breastfed newborns/infants are unknown. Eylea is not recommended during breastfeeding -* ***Therefore, if you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you receive this medicine - Driving and using machines:*** *After receiving Eylea, you may experience some temporary vision problems. Do not drive or use machines as long as these last -* ***Possible side effects:*** *Like all medicines, this medicine can cause side effects, although not everybody gets them -* ***The side effects of Eylea injection are either from the medicine itself or from the injection procedure and mostly affect the eye - Contact your doctor immediately if you have any of the following: Common side effect (****which may affect up to 1 in 10 people): Clouding of the lens (cataract), bleeding in the back of the eye (retinal haemorrhage), increase of pressure inside the eye, bleeding inside the eye (vitreous haemorrhage), moving spot in your vision (vitreous floaters), detachment of the gel like substance inside the eye (vitreous detachment), reduced sharpness of vision, eye pain, bleeding inside the eye (conjunctival haemorrhage) &/or damage to the clear layer of the eyeball in front of the iris (punctate keratitis) -* ***Uncommon side effect (****which may affect up to 1 in 100 people): Certain forms of clouding of the lens (cataract subcapsular), detachment, tear or bleeding of the light-sensitive layer at the back of the eye, resulting in flashes of light with floaters, sometimes progressing to a loss of vision (retinal detachment or tear), allergic reactions, 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;), inflammation in the iris, of other parts of the eye, or the gel like substance inside the eye (iritis, iridocyclitis, vitritis), certain forms of clouding of the lens (cataract cortical/nuclear), damage to the front layer of the eyeball (corneal abrasion/erosion), blurred vision, eye pain at injection site, a feeling of having something in the eye, increased tear production, bleeding at the injection site &/or redness of the eye -* ***Besides the above, the following side effects may occur although they have not been reported in clinical studies:*** *Redness of the eye (ocular hyperaemia), degeneration of the light sensitive membrane at the back of the eye (retinal degeneration), abnormal sensation in eye, clouding of the lens (lenticular opacities), clouding of the lens due to injury (traumatic cataract), damage to the surface of the clear front layer of the eye (corneal epithelium defect), inflammation of other parts of the eye (anterior chamber flare), eyelid irritation, serious inflammation or infection inside the eye (endophthalmitis), pus in the eye (hypopyon) &/or severe allergic reactions*
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): SFDA: *The National Pharmacovigilance Centre (NPC) - SFDA Call Center: 19999 - Email: npc.drug@sfda.gov.sa - Website: https://ade.sfda.gov.sa*

- Please refer to local product package insert leaflet (PIL) for all product details

Marketing Authorisation Holder: *Bayer AG - Kaiser-Wilhelm-Allee 1 - 51368 Leverkusen, Germany* ***KSA PIL Version Jan. 2024***

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
PP-EYL-ALL-1295-1

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

For further details, Please contact:

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** For Safety Reporting: www.safetrack-public.bayer.com or pv.me@bayer.com