EYLEA®
(aflibercept solution for injection)

Prescriber Guide

This Guide provides you important information on EYLEA®, the medication itself, and how to correctly administer it to your patients.

Please provide your patients with the EYLEA® patient card, which indicates how the patients may access the Patient Guide online including its audio version (read out of the patient guide), and the Patient Information Leaflet on our BERMITS site:
https://www.edumaterial.bayer.com.mt/mt-eylea-patient

Prescriber guide approved by Malta Medicines Authority in January 2022

For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
MA-M_AFL-MT-0002-01

CONTENTS

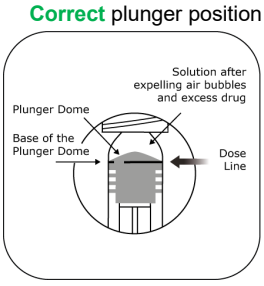
KEY SUMMARY FOR EYLEA

Contraindications

- 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

Key instructions for use

- The vial and pre-filled syringe contain more than the recommended dose of Eylea. **Don't inject the entire volume.**
- Ensure proper aseptic technique including broad-spectrum microbicide to minimize risk of intraocular infection
- For the intravitreal injection, a **30 G x ½ inch injection needle** should be used
- **Pre-filled syringe:**
  - Expel excess volume and air bubbles from the pre-filled syringe and adjust the base of the plunger dome 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



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 patients after the injection
Transient IOP increase	Properly prime the syringe by removing excess volume and air bubbles from syringe before administration Monitor patients vision and IOP after the injection
Medication error	
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-foetotoxicity	Instruct patient to use effective contraception during treatment for at least 3 months after last injection Do not use in patients who are pregnant unless the potential benefit outweighs the potential risk to the foetus
Exposure during breastfeeding	Eylea is not recommended in patients who are breastfeeding

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

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. This includes the signs and symptoms of adverse events and when they should seek immediate medical attention. The patient guide is a tool that will help you to communicate to your patient about the disease and treatment. It contains the information on the signs and symptoms of adverse events and when the patient should seek immediate medical attention. This guide is available upon request to Bayer, and you should distribute it to your patients. It is available as a booklet and as an audio guide option for your patients.

ABOUT EYLEA

- EYLEA is a 40 mg/mL solution for injection, in a vial or in a pre-filled syringe
- **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 is indicated for adults (18 years and older) for the treatment of:

- neovascular (wet) age-related macular degeneration (AMD)
- visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)
- visual impairment due to diabetic macular oedema (DME)
- visual impairment due to myopic choroidal neovascularisation (myopic CNV)

Dosing recommendations:

- The recommended dose for EYLEA is 2 mg aflibercept, equivalent to 0.05 mL
- The posology recommendations for wAMD, RVO, DME and myopic CNV are different to each other
- Refer to the approved Summary of Product Characteristics for Eylea (SmPC) for complete information on dosing recommendations for EYLEA.
    - The SmPC is a document that describes the properties of Eylea, and the approved conditions of use. It is an important source of information for healthcare professionals on how to use Eylea safely and effectively. It is located at https://www.ema.europa.eu/en/documents/product-information/eylea-epar-product-information_en.pdf

IMPORTANT SAFETY INFORMATION ABOUT EYLEA

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 during the week following injection** 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 aflibercept (equivalent to 0.05 mL). Expel the excess volume and air bubbles from the syringe prior to injection.

- Always check that the excess volume and air bubbles in the pre-filled syringe are eliminated before use: the base of the plunger dome (not the tip of the dome) must be aligned with the black dose line on the syringe (refer to figures shown in INSTRUCTIONS FOR USE OF EYLEA section).
- Carefully depress the plunger rod
- 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

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 myopic CNV 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

There are no data on the use of aflibercept in pregnant women. Also, it is not known whether aflibercept is excreted in breast milk. A risk to the breast-fed child cannot be excluded. 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.

Pregnancy
EYLEA should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus, although the systemic exposure after ocular administration is very low.

Breast-feeding
EYLEA is not recommended during breast-feeding.

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

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 adverse events.

STORAGE AND HANDLING OF EYLEA

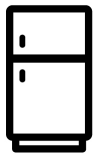
The solution is clear and colourless to pale yellow. It is an iso-osmotic solution.
Inspect the solution visually before use, for any foreign particulate matter and/or unusual colour (the solution can be pale yellow, which is normal**) or any variation in physical appearance. If any of these are observed,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

Do not split a vial/pre-filled syringe into more than one dose. Each vial/pre-filled syringe is for single 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 pre-filled syringe contains more than the recommended 0.05 mL dose of EYLEA. **The excess volume and any air bubbles in the syringe must be expelled before injecting the patient with the recommended dose**

Each vial contains more than the recommended 0.05 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.**

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 from light.
	Prior to use, 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 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.

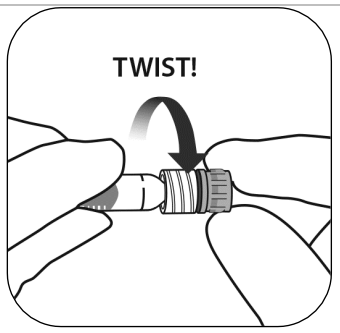
INSTRUCTIONS FOR USE OF EYLEA

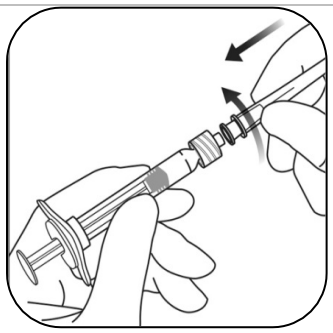
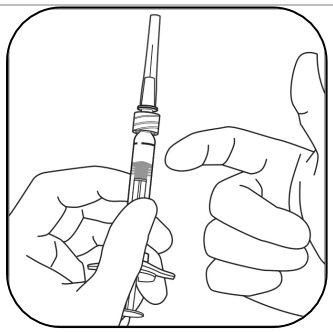
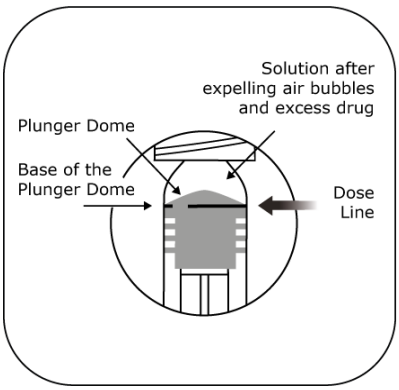
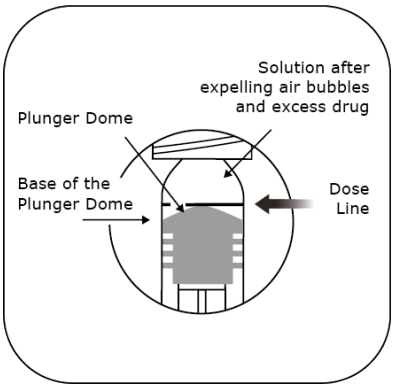
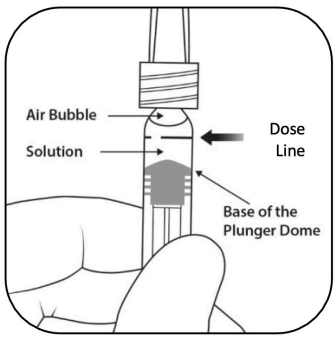
General preparation for injection

- 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, sterile 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

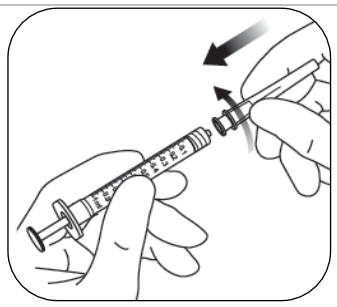
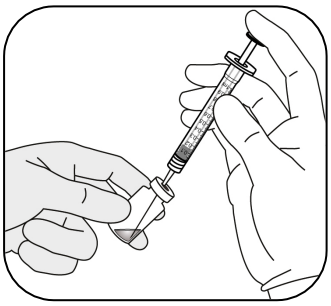
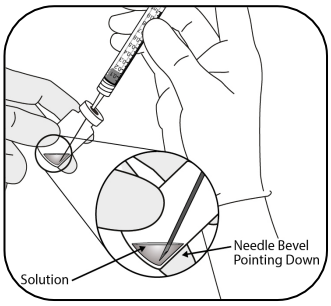
Note: the EYLEA pre-filled syringe is a glass syringe with a rubber plunger that requires slightly more force to depress compared with plastic syringes (such as those used with the vial presentation). **Become familiarised with this syringe before using it on patients.**

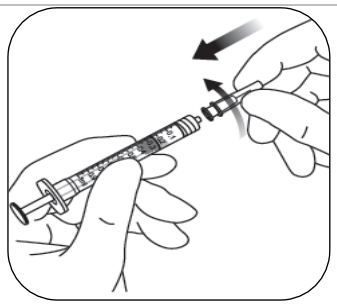
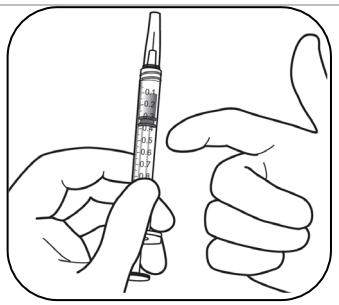
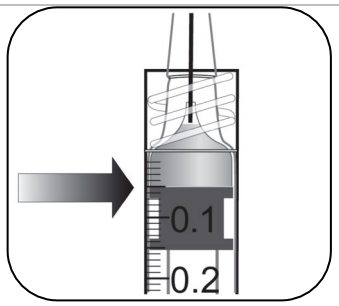
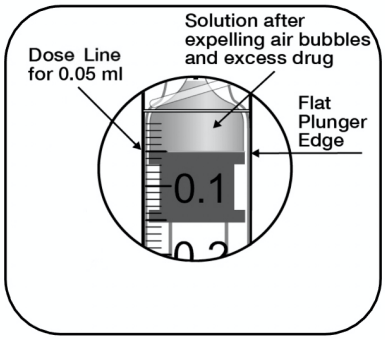
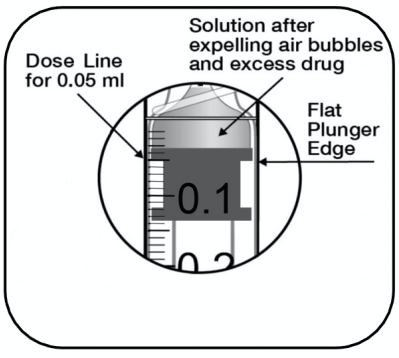
1	<u>Prepare the pre-filled syringe for administration</u> It is important to prepare the pre-filled syringe using aseptic technique. An assistant should carry out the following steps: Remove the carton containing the pre-filled syringe from the refrigerator. Open the carton and remove the blister containing the syringe. The blister must not be placed on a sterile 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 sterile gloves when handling: With two fingers, remove the pre-filled syringe from the blister. Visually inspect the syringe. Place the syringe in a sterile 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 black 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.**

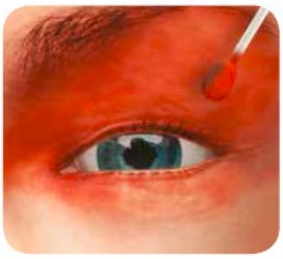
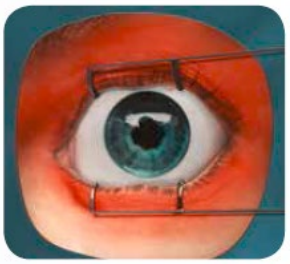
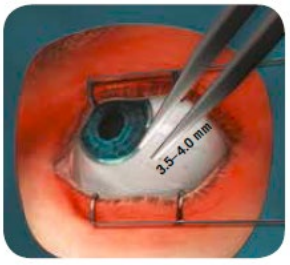
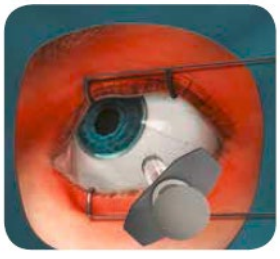
Vial

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. An assistant should carry out the following steps (assistant is shown with darker gloves in the images): Remove the carton containing the vial from the refrigerator. Open the carton and remove the vial. The vial should not be placed on a sterile 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 sterile technique, including the use of sterile 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 of the filter needle. **Do not use the filter needle for intravitreal**	

	injection.
6	<u>Attach the injection needle</u> Using aseptic technique, **firmly twist a 30 G x ½ inch injection needle** to the Luer-lock syringe tip. 
7	<u>Check for air bubbles</u> 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	<u>Eliminate air bubbles and excess drug</u> **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.** 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. Accurate positioning of the plunger is critical. Incorrect plunger positioning can lead to delivering more or less than the recommended dose.  ✓ **Correct** plunger position  ✗ **Incorrect** plunger position 
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 at least 30 seconds. 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 at least 30 seconds.	
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 at least 30 seconds.	
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.

Local Safety Information

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal, and sent by post or email to:
P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000
E: postlicensing.medicinesauthority@gov.mt
Or
E: pv@alfredgera.com

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