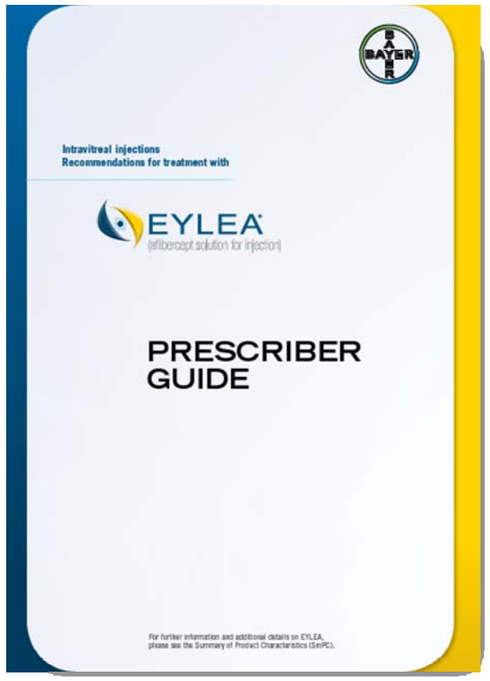
Visual	Translated Content
Front Cover 	**Intravitreal injections** **Recommendations for treatment with** EYLEA (aflibercept solution for injection) **Prescriber Guide** For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).
Page 2 	CD **Intravitreal Injection Procedure Video** For further information and additional details on EYLEA, please see the Summary of Product Characteristics (SmPC).

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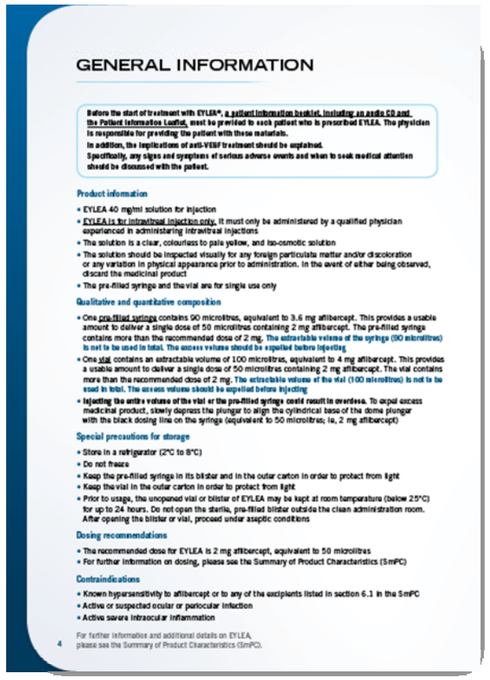
EYLEA
(aflibercept solution for injection)


GENERAL INFORMATION

Before the start of treatment with EYLEA®, a patient information booklet, including an audio CD and the Patient Information Leaflet, must be provided to each patient who is prescribed EYLEA. The physician is responsible for providing the patient with these materials.
In addition, the implications of anti-VEGF treatment should be explained.
Specifically, any signs and symptoms of serious adverse events and when to seek medical attention should be discussed with the patient.

Product information
- EYLEA 40 mg/ml solution for injection
- EYLEA is for intravitreal injection only. It must only be administered by a qualified physician experienced in administering intravitreal injections
- The solution is a clear, colourless to pale yellow, and iso-osmotic solution
- The solution should be inspected visually for any foreign particulate matter and/or discoloration or any variation in physical appearance prior to administration. In the event of either being observed, discard the medicinal product
- The pre-filled syringe and the vial are for single use only

Qualitative and quantitative composition
- One pre-filled syringe contains 90 microlitres, equivalent to 3.6 mg aflibercept. This provides a usable amount to deliver a single dose of 50 microlitres containing 2 mg aflibercept. The pre-filled syringe contains more than the recommended dose of 2 mg. The extractable volume of the syringe (90 microlitres) is not to be used in total. The excess volume should be expelled before injecting
- One vial contains an extractable volume of 100 microlitres, equivalent to 4 mg aflibercept. This provides a usable amount to deliver a single dose of 50 microlitres containing 2 mg aflibercept. The vial contains more than the recommended dose of 2 mg. The extractable volume of the vial (100 microlitres) is not to be used in total. The excess volume should be expelled before injecting
- Injecting the entire volume of the vial or the pre-filled syringe could result in overdose. To expel excess medicinal product, slowly depress the plunger to align the cylindrical base of the dome plunger with the black dosing line on the syringe (equivalent to 50 microlitres; ie, 2 mg aflibercept)

Special precautions for storage
- Store in a refrigerator (2°C to 8°C)
- Do not freeze
- Keep the pre-filled syringe in its blister and in the outer carton in order to protect from light
- Keep the vial in the outer carton in order to protect from light
- Prior to usage, the unopened vial or blister of EYLEA may be kept at room temperature (below 25°C) for up to 24 hours. Do not open the sterile, pre-filled blister outside the clean administration room. After opening the blister or vial, proceed under aseptic conditions

Dosing recommendations
- The recommended dose for EYLEA is 2 mg aflibercept, equivalent to 50 microlitres
- For further information on dosing, please see the Summary of Product Characteristics (SmPC)

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

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

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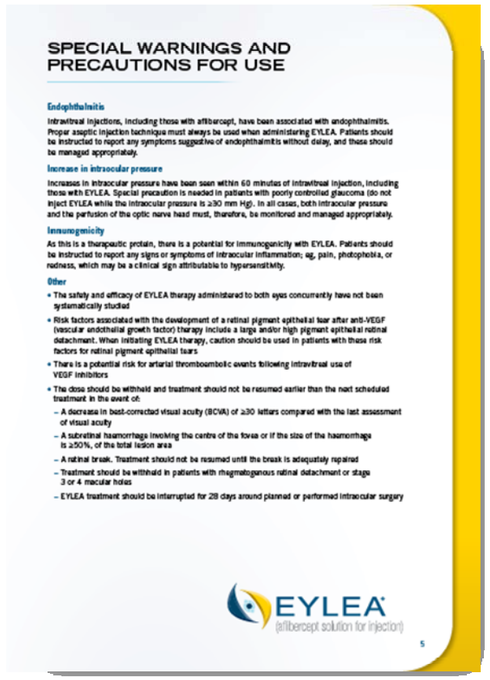
SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Endophthalmitis

Intravitreal injections, including those with aflibercept, have been associated with endophthalmitis. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis without delay, and these should be managed appropriately.

Increase in intraocular pressure

Increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including those with EYLEA. Special precaution is needed in patients with poorly controlled glaucoma (do not inject EYLEA while the intraocular pressure is ≥30 mm Hg). In all cases, both intraocular pressure and the perfusion of the optic nerve head must, therefore, be monitored and managed appropriately.

Immunogenicity

As this is a therapeutic protein, there is a potential for immunogenicity with EYLEA. Patients should be instructed to report any signs or symptoms of intraocular inflammation; eg, pain, photophobia, or redness, which may be a clinical sign attributable to hypersensitivity.

Other

- The safety and efficacy of EYLEA therapy administered to both eyes concurrently have not been systematically studied
- Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF (vascular endothelial growth factor) therapy include a large and/or high pigment epithelial retinal detachment. When initiating EYLEA therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears
- There is a potential risk for arterial thromboembolic events following intravitreal use of VEGF inhibitors
- The dose should be withheld and treatment should not be resumed earlier than the next scheduled treatment in the event of:
  - A decrease in best-corrected visual acuity (BCVA) of ≥30 letters compared with the last assessment of visual acuity
  - A subretinal haemorrhage involving the centre of the fovea or if the size of the haemorrhage is ≥50%, of the total lesion area
  - A retinal break. Treatment should not be resumed until the break is adequately repaired
  - Treatment should be withheld in patients with rhegmatogenous retinal detachment or stage 3 or 4 macular holes
  - EYLEA treatment should be interrupted for 28 days around planned or performed intraocular surgery

EYLEA (aflibercept solution for injection)

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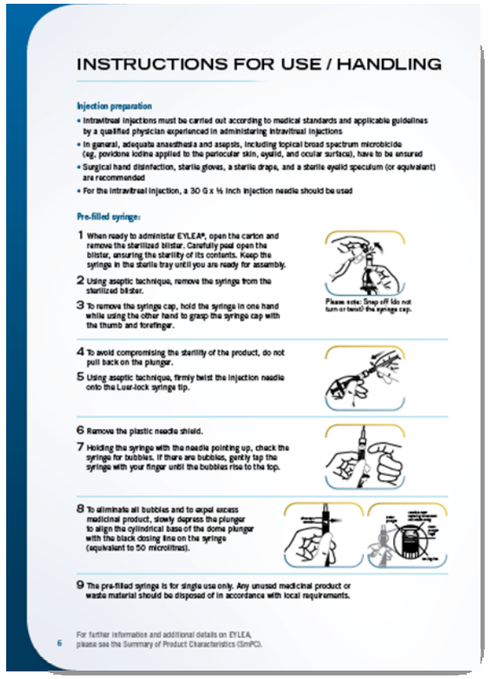

INSTRUCTIONS FOR USE/HANDLING

Injection preparation

• Intravitreal injections must be carried out according to medical standards and applicable guidelines by a qualified physician experienced in administering intravitreal injections
• In general, adequate anaesthesia and asepsis, including topical broad spectrum microbicide (eg, povidone iodine applied to the periocular skin, eyelid, and ocular surface), have to be ensured
• Surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent) are recommended
• For the intravitreal injection, a 30 G x ½ inch injection needle should be used

Pre-filled syringe:

1 When ready to administer EYLEA®, open the carton and remove the sterilized 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 sterilized 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 forefinger.
[*Content below visual*: “Please note: Snap off (do not turn or twist) 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 Remove the plastic needle shield.

7 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.

8 To eliminate all bubbles and to expel excess medicinal product, slowly depress the plunger to align the cylindrical base of the dome plunger with the black dosing line on the syringe (equivalent to 50 microlitres).
[Content in images: “Air bubble”, “Solution”, “Dome plunger”, “Solution after expelling air bubbles and excess drug”, “Dome plunger edge”, “dosing line”]

9 The pre-filled syringe is for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

For further information and additional details on EYLEA,
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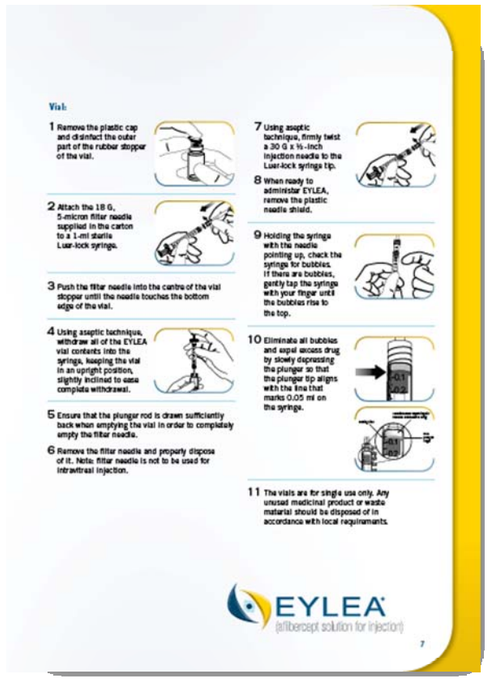

Vial:

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 touches the 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.

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 to the Luer-lock syringe tip.

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

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

10 Eliminate all bubbles and expel excess drug by slowly depressing the plunger so that the plunger tip aligns with the line that marks 0.05 ml on the syringe.
[Content in image: “Dosing line”, “Solution after expelling air bubbles and excess drug”, “Flat plunger edge”]

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

EYLEA
(aflibercept solution for injection)

INJECTION PROCEDURE

1 Administer topical anaesthesia.

2 Instill disinfectant (ie, 5% povidone iodine solution) according to manufacturer's guidance.

3 Apply disinfectant (ie, 10% povidone iodine solution) to periocular skin, lids, and eyelashes, avoiding extensive pressure to eye glands.

4 Cover with sterile drape and insert sterile lid speculum.

5 Tell your patient to look away from the injection site. Position the eye adequately. At an area 3.5 to 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. The injection volume of 0.05 ml is then delivered; a different scleral site should be used for subsequent injections.

For further information on the intravitreal injection procedure, please see:

• Evolving guidelines for intravitreous injections. Aiello LP, Brucker AJ, Chang S, et al. *Retina.* 2004;24(5 Suppl):S3-S19.

• Guidelines for Intravitreal Injections Procedure 2009. The Royal College of Ophthalmologists. Available at: http://www.rcophth.ac.uk/page.asp?section=451. Accessed September 7, 2012.

• Guidelines for intravitreal injections. Korobelnik JF, Weber M, Cohen SY, et al. *J Fr Ophtalmol.* 2009;32(4):288-289.

• Intravitreal Injection Procedure Video (page 2)

For further information and additional details on EYLEA,
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AFTER 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. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, sterile equipment for paracentesis should be available

• Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (eg, eye pain, redness of the eye, photophobia, blurring of vision) without delay

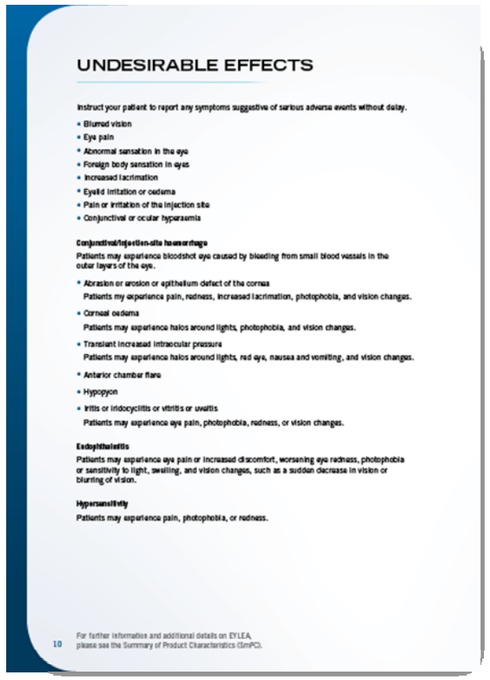
• Most ophthalmologic societies recommend application of antibiotic eyedrops after intravitreal injections. Please take this into consideration

• Please inform your patients that they could experience:

– Bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye (conjunctival haemorrhage)
– Moving spots in their vision (vitreous floaters)
– Eye pain

These conditions normally go away a few days after the injection. Please advise your patients to seek medical attention if these conditions do not go away in a few days or get worse.

EYLEA
(aflibercept solution for injection)



UNDESIRABLE EFFECTS

Instruct your patient to report any symptoms suggestive of serious adverse events without delay.

• Blurred vision
• Eye pain
• Abnormal sensation in the eye
• Foreign body sensation in eyes
• Increased lacrimation
• Eyelid irritation or oedema
• Pain or irritation of the injection site
• Conjunctival or ocular hyperaemia

Conjunctival/injection-site haemorrhage

Patients may experience bloodshot eye caused by bleeding from small blood vessels in the outer layers of the eye.

• Abrasion or erosion or epithelium defect of the cornea
Patients my experience pain, redness, increased lacrimation, photophobia, and vision changes.

• Corneal oedema
Patients may experience halos around lights, photophobia, and vision changes.

• Transient increased intraocular pressure
Patients may experience halos around lights, red eye, nausea and vomiting, and vision changes.

• Anterior chamber flare

• Hypopyon

• Iritis or iridocyclitis or vitritis or uveitis
Patients may experience eye pain, photophobia, redness, or vision changes.

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.

Hypersensitivity

Patients may experience pain, photophobia, or redness.

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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.

• Vitreous floaters or haemorrhage

Vitreous detachment
Patients may experience sudden flashes of light and a sudden appearance/increase in the number of vitreous floaters.

• Retinal tear
• Retinal degeneration

Retinal detachment

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.

• Tear or detachment of the retinal pigment epithelium

In the wet AMD phase 3 studies, there was an increased incidence of conjunctival haemorrhage in patients receiving antithrombotic agents. This increased incidence was comparable between patients treated with ranibizumab and EYLEA®.

Arterial thromboembolic events (ATEs) are adverse events potentially related to systemic VEGF inhibition. There is a theoretical risk of ATES following intravitreal use of VEGF inhibitors.

As with all therapeutic proteins, there is a potential for immunogenicity with EYLEA.

Make sure that, in any case of any adverse event that concerns your patient, your patient has immediate access to an ophthalmologist.

Appropriate action and treatment of serious adverse events should be carried out according to established clinical practice.

Overdose

In clinical trials, doses of up to 4 mg in monthly intervals have been used, and isolated cases of overdoses with 8 mg occurred.

Overdosing with increased injection volume may increase intraocular pressure. Therefore, in case of overdosage, intraocular pressure should be monitored and, if deemed necessary by the treating physician, adequate treatment should be initiated.

EYLEA®
(aflibercept solution for injection)

SAFETY INFORMATION

Any suspected adverse drug reactions can be reported to:

Medicines Authority
Post-licensing Directorate,
203, Level 3,
Rue D'Argens,
Gżira GŻR 1368, MALTA,

or at:
http://www.medicinesauthority.gov.mt/pub/adr.doc
Telephone Number: +356 2343 9000

Or

Alfred Gera & Sons Ltd,
Triq il-Masġar,
Qormi QRM 3217,
MALTA,

or at
pv@alfredgera.com
Tel: +356 21446205

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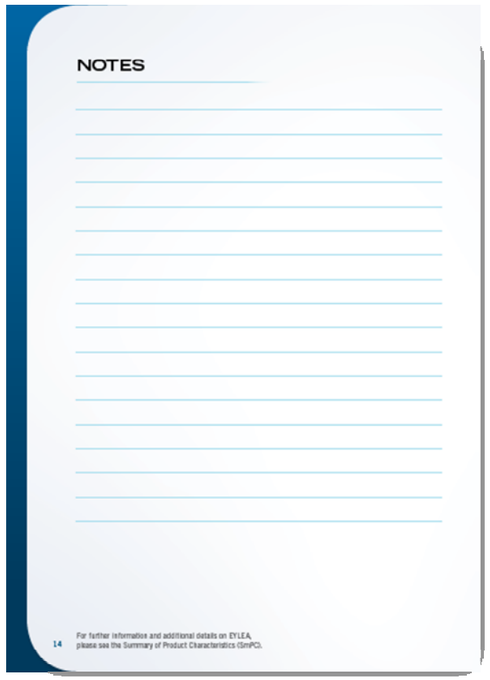

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For more information about EYLEA®,
visit **www.EYLEA.com**

<website currently under review—
reference subject to local LMR approval>

EYLEA®
(aflibercept solution for injection)

BAYER

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www.bayerhealthcare.com
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