HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use EYLEA safely and effectively. See full prescribing information for EYLEA.

EYLEA[®] (aflibercept) Injection For Intravitreal Injection Initial U.S. Approval: 2011

RECENT MAJOR CHANGES Indications and Usage, Macular Edema Following Retinal Vein Occlusion (RVO) (1.2) 10/2014 Indications and Usage, Diabetic Macular Edema (DME) (1.3) 7/2014 Dosage and Administration, Macular Edema Following 10/2014 Retinal Vein Occlusion (RVO) (2.3) 10/2014 Dosage and Administration, Diabetic Macular Edema 10/2014 Dosage and Administration, Diabetic Macular Edema 7/2014 Dosage and Administration, Preparation for 7/2014 Administration (2.5) 1/2014

• Warnings and Precautions, Thromboembolic Events (5.3) 10/2014

-INDICATIONS AND USAGE -

- EYLEA is indicated for the treatment of patients with:
- Neovascular (Wet) Age-Related Macular Degeneration (AMD) (1.1)
- Macular Edema Following Retinal Vein Occlusion (RVO) (1.2)
- Diabetic Macular Edema (DME) (1.3)

- Neovascular (Wet) Age-Related Macular Degeneration (AMD)
 The recommended dose for EYLEA is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first 3 months, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). (2.2)
- Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks. (2.2)

Macular Edema Following Retinal Vein Occlusion (RVO)

 The recommended dose for EYLEA is 2 mg (0.05 mL) administered by intravitreal injection once every 4 weeks (monthly). (2.3)

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 - 1.2 Macular Edema Following Retinal Vein Occlusion (RVO)
 - 1.3 Diabetic Macular Edema (DME)

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- 2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD)
- 2.3 Macular Edema Following Retinal Vein Occlusion (RVO)
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- 4 CONTRAINDICATIONS
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 - 4.3 Hypersensitivity

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WARNINGS AND PRECAUTIONS

- 5.1 Endophthalmitis and Retinal Detachments
- 5.2 Increase in Intraocular Pressure

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5.3 Thromboembolic Events

ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity

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Diabetic Macular Edema (DME)

- The recommended dose for EYLEA is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). (2.4)
- Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks. (2.4)

----- DOSAGE FORMS AND STRENGTHS-

40 mg/mL solution for intravitreal injection in a single-use vial (3)

- Ocular or periocular infection (4.1)
- Active intraocular inflammation (4.2)
- Hypersensitivity (4.3)

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. (5.1)
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection. (5.2)
- There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. (5.3)

- ADVERSE REACTIONS -

The most common adverse reactions (\geq 5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous floaters, intraocular pressure increased, and vitreous detachment. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Regeneron at 1-855-395-3248 or FDA at 1-800-FDA-1088 or <u>www.fda.gov/medwatch</u>.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2014

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*Sections or subsections omitted from the full prescribing information are not listed

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EYLEA is indicated for the treatment of patients with:

- 1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)
- **1.2** Macular Edema Following Retinal Vein Occlusion (RVO)
- **1.3 Diabetic Macular Edema (DME)**

2 DOSAGE AND ADMINISTRATION

2.1 Important Injection Instructions

For ophthalmic intravitreal injection. EYLEA must only be administered by a qualified physician.

2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks [*see Clinical Studies (14.1)*].

2.3 Macular Edema Following Retinal Vein Occlusion (RVO)

The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection once every 4 weeks (monthly) [*see Clinical Studies (14.2), (14.3)*].

2.4 Diabetic Macular Edema (DME)

The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks [*see Clinical Studies (14.4*)].

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2.5 **Preparation for Administration**

EYLEA should be inspected visually prior to administration. If particulates, cloudiness, or discoloration are visible, the vial must not be used.

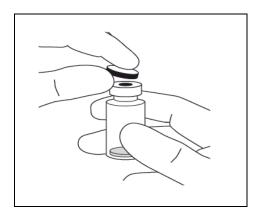
Using a septic technique, the intravitreal injection should be performed with a 30-gauge x $\frac{1}{2}$ -inch injection needle.

Vial

The glass vial is for single use only.

1. Remove the protective plastic cap from the vial (see Figure 1).

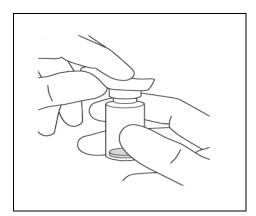
Figure 1:



2. Clean the top of the vial with an alcohol wipe (see Figure 2).

Figure 2:

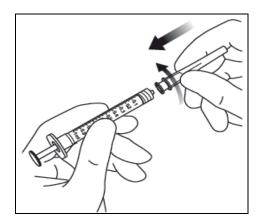
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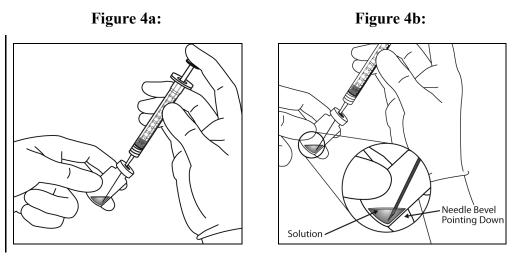
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3. Remove the 19-gauge x 1¹/₂-inch, 5-micron, filter needle from its pouch and remove the 1-mL syringe supplied in the carton from its pouch. Attach the filter needle to the syringe by twisting it onto the Luer lock syringe tip (see Figure 3).

Figure 3:



- 4. Push the filter needle into the center of the vial stopper until the needle is completely inserted into the vial and the tip touches the bottom or bottom edge of the vial.
- 5. Using aseptic technique withdraw all of the EYLEA vial contents into the syringe, keeping the vial in an upright position, slightly inclined to ease complete withdrawal. To deter the introduction of air, ensure the bevel of the filter needle is submerged into the liquid. Continue to tilt the vial during withdrawal keeping the bevel of the filter needle submerged in the liquid (see Figures 4a and 4b).

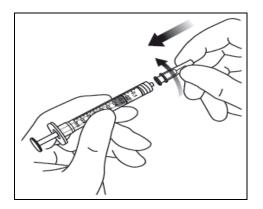


- 6. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.
- 7. Remove the filter needle from the syringe and properly dispose of the filter needle. **Note**: Filter needle is **not** to be used for intravitreal injection.

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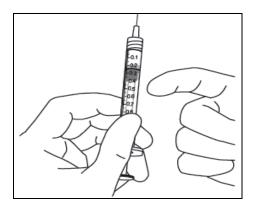
8. Remove the 30-gauge x ¹/₂-inch injection needle from the plastic pouch and attach the injection needle to the syringe by firmly twisting the injection needle onto the Luer lock syringe tip (see Figure 5).

Figure 5:



- 9. When ready to administer EYLEA, remove the plastic needle shield from the needle.
- 10. 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 (see Figure 6).

Figure 6:



11. To eliminate all of the bubbles and to expel excess drug, SLOWLY depress the plunger so that the plunger tip aligns with the line that marks 0.05 mL on the syringe (see Figures 7a and 7b).

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