SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

EYLEA® (aflibercept) Injection is a prescription medication administered by injection into the eye. You should not use EYLEA if you have an infection in or around the eye, eye pain or redness, or known allergies to any of the ingredients in EYLEA, including aflibercept.

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
About DR and DME

#1 CAUSE OF NEW CASES OF BLINDNESS
in people 20 to 74 years old

MORE THAN 1 IN 4 people 40 years and older with diabetes had a serious eye condition (such as DME) that may cause vision loss between 2005 and 2008.

DR CASES ALMOST DOUBLED between 2000 and 2010.

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
Take action now
If you have diabetes, you need to keep your eyes as healthy as possible.³ See a retina specialist (a doctor specializing in diseases of the retina) to help manage your eye health.⁵

It’s important to get a dilated eye exam¹
- This eye exam is a test used to diagnose DME and DR in patients with DME
- Allows the retina specialist to see the back of the eye, including the retina, for signs of problems
  - To see the retina, the retina specialist puts drops in the eye to dilate (widen) the pupil (the opening that controls the amount of light coming into the eye)

Get a dilated eye exam at least once a year, and be sure to follow up with your retina specialist on a regular basis.¹
UNDERSTANDING THE DAMAGE BOTH CONDITIONS CAN CAUSE

What is DR?¹

DR is the most common eye condition caused by diabetes. DR happens when too much blood sugar (glucose) damages the blood vessels in the retina (the light-sensitive tissue of the eye). As a result:

- The retina does not get enough blood and nutrients
- Blood vessels can bulge, weaken, and leak blood into the retina
DR can lead to DME¹

DME is a complication of DR. In DME, the macula (the part of the retina responsible for sharp central vision) swells with fluid leaked from the damaged vessels.
DME AND DR IN DME CAN START WITHOUT YOU NOTICING IT

With DME and DR in patients with DME, there may be no symptoms at first. Both conditions can cause vision problems and even blindness.¹

**SYMPTOMS MAY INCLUDE**⁶,⁷

- Blurriness in the center of vision
- Blind spots or patches
- Waviness in the center of vision
- Colors that look dull

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
Share the enclosed card with your loved one so he or she can see how DME and DR in DME might affect your vision.

If you have diabetes—even if you don’t have symptoms of DME or DR in DME—you should get a dilated eye exam at least once a year. Early diagnosis and treatment are important to your eye health.\(^1\)
HOW YOUR DOCTOR DIAGNOSES DME AND DR IN DME

Your retina specialist has different tests for diagnosing DME and DR in DME. Some commonly used tests are described below.

COMMON DIAGNOSTIC TESTS

Visual acuity test
Measures how well you see the letters on an eye chart from a distance.

Dilated eye exam
Your doctor puts drops into your eye to dilate the pupil. He or she can then see the back of the eye, including the retina, for signs of problems.
### COMMON DIAGNOSTIC TESTS

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fundus photography</strong></td>
<td>The image shows the inside of the back of the eye.</td>
</tr>
<tr>
<td><strong>Fluorescein angiography</strong></td>
<td>Dye is used to show the blood vessels in the back of the eye.</td>
</tr>
<tr>
<td><strong>Optical coherence tomography</strong></td>
<td>This shows the layers and thickness of the retina.</td>
</tr>
</tbody>
</table>
TREATMENT WITH EYLEA® (afibercept) INJECTION

EYLEA is a prescription medication approved by the Food and Drug Administration (FDA) for the treatment of DME and DR in patients with DME

- EYLEA has been studied for safety and efficacy in more than 3,000 people with DME, DR in DME, and other eye conditions
- EYLEA is administered by injection into the eye. You should not use EYLEA if you have an infection in or around the eye, eye pain or redness, or known allergies to any of the ingredients in EYLEA, including afibercept
- EYLEA is an anti–vascular endothelial growth factor (anti-VEGF) treatment

What is VEGF?

VEGF is a protein made by the blood vessels that, at high levels, can cause abnormal blood vessels to grow in the eye and leak fluid into the macula. Symptoms of DME and DR in patients with DME happen as the macula swells with fluid. Blocking VEGF helps reduce the fluid leaking into the macula.⁹,¹⁰
SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

Injection into the eye with EYLEA can result in an infection in the eye and retinal detachment (separation of retina from the back of the eye). Inflammation in the eye has been reported with the use of EYLEA.

EYLEA is given by injection into the eye and works by blocking VEGF. EYLEA blocks VEGF by trapping it between its molecular arms.
IMPROVEMENTS IN DME AND DR IN PATIENTS WITH DME

EYLEA® (aflibercept) Injection for the treatment of DME

- 862 people who had DME participated in 2 clinical studies
  - People received EYLEA every 8 weeks (after 5 initial monthly doses) or EYLEA every 4 weeks or were treated with laser (control)
- Both studies measured the number of letters on the eye chart people could read before and after EYLEA treatment at 1 and 2 years

EYLEA improved vision at 1 year—improvement was maintained through 2 years

On average in the 2 clinical studies:
- People treated with EYLEA saw about 10 more letters on the eye chart compared with the number of letters they saw before treatment
- People treated with laser saw only about 1 more letter on the eye chart compared with the number of letters they saw before treatment

These results are from 2 clinical studies; your individual results may vary.
EYLEA® (aflibercept) Injection also helped make DR less severe in some patients with DME at 2 years

In the 2 clinical studies, EYLEA
- Reduced the severity of DR
- Reversed some damage from DR in DME

Timely treatment with EYLEA can make a difference for patients with DR in DME.

SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

In some patients, injections with EYLEA may cause a temporary increase in eye pressure within 1 hour of the injection. Sustained increases in eye pressure have been reported with repeated injections, and your doctor may monitor this after each injection.
In the 2 clinical studies, people treated with EYLEA could see, on average, about 10 more letters on the eye chart at 1 year and 2 years than before treatment. These results are from 2 clinical studies; your individual results may vary.

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

There is a potential risk of serious and sometimes fatal side effects related to blood clots, leading to heart attack or stroke in patients receiving EYLEA.

ON AVERAGE, AT 1 AND 2 YEARS AFTER TREATMENT WITH EYLEA® (aflibercept) INJECTION IN THE STUDIES

More than a third of people treated with EYLEA in the studies improved by at least 15 letters (3 lines) on the eye chart at 1 year.
DOSING AND POSSIBLE SIDE EFFECTS

Dosing
EYLEA® (aflibercept) Injection is a prescription medicine approved for the treatment of patients with DME and DR in patients with DME

- The recommended dose for DME and DR in patients with DME is the same: 2 mg of EYLEA administered by injection into the eye every 2 months (8 weeks) following 5 initial monthly (4 weeks) injections
  — EYLEA may be dosed once per month, but additional benefit was not seen
- EYLEA was studied in adults of various ages and in some adults with kidney disease, with no changes in dosing needed
- After 5 initial monthly doses, patients may need only half as many injections with EYLEA

Your doctor will decide what EYLEA dosing schedule is right for you.
Possible Side Effects

- Injection into the eye with EYLEA® (aflibercept) Injection can result in an infection in the eye and retinal detachment (separation of retina from the back of the eye). Inflammation in the eye has been reported with the use of EYLEA.

- In some patients, injections with EYLEA may cause a temporary increase in eye pressure within 1 hour of the injection. Sustained increases in eye pressure have been reported with repeated injections, and your doctor may monitor this after each injection.

- There is a potential risk of serious and sometimes fatal side effects related to blood clots, leading to heart attack or stroke in patients receiving EYLEA.

- Serious side effects related to the injection procedure with EYLEA are rare but can occur including infection inside the eye and retinal detachment.

- The most common side effects reported in patients receiving EYLEA are increased redness in the eye, eye pain, cataract, floaters (moving spots) in the field of vision, increased pressure in the eye, and vitreous (gel-like substance) detachment.

- It is important that you contact your doctor right away if you think you might be experiencing any side effects.
IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

- EYLEA® (aflibercept) Injection is a prescription medication administered by injection into the eye. You should not use EYLEA if you have an infection in or around the eye, eye pain or redness, or known allergies to any of the ingredients in EYLEA, including aflibercept.

- Injection in the eye with EYLEA can result in an infection in the eye or retinal detachment (separation of retina from the back of the eye). Inflammation in the eye has been reported with the use of EYLEA.

- In some patients, injections with EYLEA may cause a temporary increase in eye pressure within 1 hour of the injection. Sustained increases in eye pressure have been reported with repeated injections, and your doctor may monitor this after each injection.

- There is a potential risk of serious and sometimes fatal side effects related to blood clots, leading to heart attack or stroke in patients receiving EYLEA.

Please see enclosed full Prescribing Information.
• Serious side effects related to the injection procedure with EYLEA® (aflibercept) Injection are rare but can occur including infection inside the eye and retinal detachment.

• The most common side effects reported in patients receiving EYLEA are increased redness in the eye, eye pain, cataract, floaters (moving spots) in the field of vision, increased pressure in the eye, and vitreous (gel-like substance) detachment.

• It is important that you contact your doctor right away if you think you might be experiencing any side effects.

• EYLEA is for prescription use only. For additional safety information, please talk to your doctor and see the full Prescribing Information for EYLEA.

• You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
PREPARING FOR YOUR INJECTION

**Before your appointment**

- Ask your doctor’s office how long the appointment might be
- Arrange for someone to drive you to and from the appointment
- Bring with you
  - A list of questions (don’t be afraid to ask them)
  - A list of all prescription and over-the-counter medicines you take and when you take them
  - Dark glasses (your eyes may be sensitive to light afterwards)

**Did you know?**

You may be eligible for transportation to and from your appointment through Rides in Sight, a transportation-referral service.

Call 1-855-607-4337 or visit www.ridesinsight.org.
During your appointment

Your doctor will
- Discuss the procedure with you
- Examine, wash, and numb your eye
- Administer the injection
- Check your eye pressure after the injection

After your appointment

- You may have some temporary visual problems. Do not drive or operate heavy machinery
- You may have a temporary increase in eye pressure. Your doctor should check for this
- Your eyes may be sensitive to light (wear dark glasses)

SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (afibercept) INJECTION

Serious side effects related to the injection procedure with EYLEA are rare but can occur including infection inside the eye and retinal detachment.
LEARN HOW EYLEA4U® CAN HELP YOU

EYLEA4U can provide patient support for EYLEA® (aflibercept) Injection in many ways

If you need help with the cost of EYLEA, these EYLEA4U patient support programs may be available to help you, if you are eligible:

- EYLEA Co-Pay Card Program
- Referral to Independent Co-Pay Assistance Foundations
- Patient Assistance Program

YOUR EYLEA4U SUPPORT SPECIALIST IS READY TO:

- Answer your questions and explain your options
- Provide support and information on EYLEA
- Help you enroll in programs that may be right for you

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
SELECT IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

The most common side effects reported in patients receiving EYLEA are increased redness in the eye, eye pain, cataract, floaters (moving spots) in the field of vision, increased pressure in the eye, and vitreous (gel-like substance) detachment.

We’re Here 4 U!

Get in touch with an EYLEA4U® Support Specialist today.

Call 1-855-EYLEA4U (1-855-395-3248) and press Option 4, Monday through Friday, 9 AM to 8 PM Eastern Time.

Visit www.EYLEA.com for more information and resources.
The following organizations have information and resources on DME and DR in patients with DME:

**American Academy of Ophthalmology**
www.aao.org | 1-415-561-8500

**American Association of Diabetes Educators**
www.diabeteseducator.org | 1-800-338-3633

**American Diabetes Association**
www.diabetes.org | 1-800-DIABETES (1-800-342-2383)

**American Society of Retina Specialists**
www.asrs.org | 1-312-578-8760

**Diabetes Sight Risk**
www.diabetessightrisk.com

**Discovery Eye Foundation**
www.discoveryeye.org | 1-310-623-4466

**Lighthouse International**
www.lighthouse.org | 1-800-284-4422

*Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.*
National Diabetes Information Clearinghouse
www.diabetes.niddk.nih.gov | 1-800-860-8747

National Eye Institute
www.nei.nih.gov/health/diabetic | 1-301-496-5248

Prevent Blindness America
www.preventblindness.org | 1-800-331-2020

Rides in Sight
www.ridesinsight.org | 1-855-607-4337

VisionAware
www.visionaware.org

While Regeneron Pharmaceuticals does provide financial support to patient support organizations, Regeneron does not endorse any specific patient organization. The information provided by Regeneron Pharmaceuticals or these organizations is meant for informational purposes only and is not meant to replace a physician’s medical advice.
There are things you can do

In addition to treatment, you can

- Control blood sugar and blood pressure through diet, exercise, and (in some cases) medication
- Join a support group in your area
- See a low vision specialist about lifestyle changes and vision aids

Did you know?
A low vision specialist provides advice and guidance on lifestyle changes you may need to make because of low vision.

Ask your doctor any questions about your condition and your treatment plan

- Should I meet with a low vision specialist?
- How might my condition continue affecting my vision?
- What are the side effects of treatment?
- How often do I need to get treated?
- How long do I need to be on treatment?

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.
Pull out the Amsler grid to help check your vision

- Routinely checking your vision at home is important\textsuperscript{15}
- Use the enclosed Amsler grid as a tool to help check your vision

Report any changes in your vision to your doctor right away.

These vision aids can help many people with low vision perform everyday tasks\textsuperscript{14}

- Magnifying glasses
- Sound alerts on smartphones
- Special computer screens with bigger type sizes
- Better lighting (less glare, more contrast)

Please see Important Safety Information on pages 18-19 and enclosed full Prescribing Information.

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REGENERON

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EYLEA® (aflibercept) Injection
For Intravitreal Injection

1 INDICATIONS AND USAGE

1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)
1.2 Macular Edema Following Retinal Vein Occlusion (RVO)
1.3 Diabetic Macular Edema (DME)
1.4 Diabetic Retinopathy (DR) in Patients with DME

1.4 Diabetic Retinopathy (DR) in Patients with DME

2 DOSAGE AND ADMINISTRATION

2.1 Important Injection Instructions
2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD)
2.3 Macular Edema Following Retinal Vein Occlusion (RVO)
2.4 Diabetic Macular Edema (DME)
2.5 Diabetic Retinopathy (DR) in Patients with DME
2.6 Preparation for Administration
2.7 Injection Procedure

2.7 Injection Procedure

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

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**FULL PRESCRIBING INFORMATION**

1 **INDICATIONS AND USAGE**

EYLEA is indicated for the treatment of:

1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)
1.2 Macular Edema Following Retinal Vein Occlusion (RVO)
1.3 Diabetic Macular Edema (DME)
1.4 Diabetic Retinopathy (DR) in Patients with DME

2 **DOSE 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 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)].

2.5 Diabetic Retinopathy (DR) in Patients with 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 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 (14.5)].

2.6 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 aseptic technique, the intravitreal injection should be performed with a 30-gauge x ½-inch injection needle.

Vial

The glass vial is for single use only.

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

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

Figure 1:

Figure 2:

3. Remove the 19-gauge x ½-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).

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).

Figure 4a:

Figure 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.

8. Remove the 30-gauge x ½-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).

Figure 7a:

Figure 7b:
2.7 Injection Procedure
The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a topical broad-spectrum microbiode should be given prior to the injection.

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, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay [see Patient Counseling Information (17)].

Each vial should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before EYLEA is administered to the other eye.

After injection, any unused product must be discarded.

3 DOSAGE FORMS AND STRENGTHS
Single-use, glass vial designed to provide 0.05 mL of 40 mg/mL solution (2 mg) for intravitreal injection.

4 CONTRAINDICATIONS
4.1 Ocular or Periocular Infections
EYLEA is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation
EYLEA is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity
EYLEA is contraindicated in patients with known hypersensitivity to aflibercept or any of the excipients in EYLEA. Hypersensitivity reactions may manifest as severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS
5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments [see Adverse Reactions (6.1)]. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately [see Dosage and Administration (2.7) and Patient Counseling Information (17)].

5.2 Increase in Intraocular Pressure
Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA [see Adverse Reactions (6.1)]. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular endothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately [see Dosage and Administration (2.7)].

5.3 Thromboembolic Events
There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in the Warnings and Precautions (5) section of the labeling:

- Endophthalmitis and retinal detachments
- Increased intraocular pressure
- Thromboembolic events

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.

A total of 2711 patients treated with EYLEA constituted the safety population in seven phase 3 studies. Among those, 2110 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous floaters, intraocular pressure increased, and vitreous detachment.

Neovascular (Wet) Age-Related Macular Degeneration (AMD)
The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, active-controlled clinical studies (VIEW1 and VIEW2) for 12 months [see Clinical Studies (14.1)].

Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>EYLEA (N=1824)</th>
<th>Active Control (ranibizumab) (N=595)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctival hemorrhage</td>
<td>25%</td>
<td>28%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Cataract</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Laceration</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Ocular hyperemia</td>
<td>4%</td>
<td>8%</td>
</tr>
<tr>
<td>Corneal epithelium defect</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Detachment of the retinal pigment epithelium</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Foreign body sensation in eyes</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Laceration increased</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Intraocular inflammation</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Retinal pigment epithelium tear</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Injection site hemorrhage</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Corneal edema</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, and endophthalmitis.

Macular Edema Following Retinal Vein Occlusion (RVO)
The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following CRVO in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following BRVO in one clinical study (VIBRANT) [see Clinical Studies (14.2), (14.3)].

Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>CRVO (N=218)</th>
<th>BRVO (N=91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye pain</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>Corneal epithelium defect</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Ocular hyperemia</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Foreign body sensation in eyes</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Laceration increased</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Intraocular inflammation</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Cataract</td>
<td>&lt;1%</td>
<td>1%</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>&lt;1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay [see Patient Counseling Information (17)]. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately [see Dosage and Administration (2.7) and Patient Counseling Information (17)].
Table 3: Most Common Adverse Reactions (≥1%) in DME Studies

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Baseline to Week 52</th>
<th>Baseline to Week 100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EYLEA (N=287)</td>
<td>Control (N=287)</td>
</tr>
<tr>
<td></td>
<td>(N=578)</td>
<td></td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>28%</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>31%</td>
<td>21%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Cataract</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>19%</td>
<td>17%</td>
</tr>
<tr>
<td>Vitreous floaters</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>Corneal epithelium defect</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>Intraocular pressure increased</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>Vitreous detachment</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>Foreign body sensation in eyes</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Lacrimation increased</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Intraocular inflammation</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>&lt;1%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunohasassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assay used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.

In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Aflibercept produced embryo-fetal toxicity when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days at subcutaneous doses ≥0.1 mg per kg. Adverse embryo-fetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastrochisis, cleft palate, exodacruxy, intestinal atresia, spina bifida, echogonochepagocle, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternbeame, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal NO Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Aflibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was less than 0.1 mg per kg. Administration of the lowest dose assessed in rabbits (0.1 mg per kg) resulted in systemic exposure (AUC) that was approximately 10 times the systemic exposure observed in humans after an intravitreal dose of 2 mg. There are no adequate and well-controlled studies in pregnant women. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Females of reproductive potential should use effective contraception prior to the initial dose, during treatment, and for at least 3 months after the last intravitreal injection of EYLEA.

8.3 Nursing Mothers

It is unknown whether aflibercept is excreted in human milk. Because many drugs are excreted in human milk, a risk to the breastfed child cannot be excluded. EYLEA is not recommended during breastfeeding. A decision must be made whether to discontinue nursing or to discontinue treatment with EYLEA, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and effectiveness of EYLEA in pediatric patients have not been established.

8.5 Geriatric Use

In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.
Detailed results from the analysis of the VIEW1 and VIEW2 studies are shown in ranibizumab 0.5 mg Q4 group. EYLEA 2Q4 groups were shown to have efficacy that was clinically equivalent to the maintained vision, defined as losing fewer than 15 letters of visual acuity at week 24 in both studies, the primary efficacy endpoint was the proportion of patients who gained at least 15 letters in BCVA compared to baseline. At week 24, the EYLEA 2 mg Q4 group was superior to the control group for the primary endpoint.

Results from the analysis of the COPERNICUS and GALILEO studies are shown in Table 5 and Figure 9 below.

### Table 4: Efficacy Outcomes at Week 52 (Full Analysis Set with LOCF) in VIEW1 and VIEW2 Studies

<table>
<thead>
<tr>
<th>VIEW1</th>
<th>VIEW2</th>
</tr>
</thead>
<tbody>
<tr>
<td>EYLEA 2 mg Q8 weeks</td>
<td>EYLEA 2 mg Q4 weeks</td>
</tr>
</tbody>
</table>

**Full Analysis Set**
- N=301
- N=304
- N=306
- N=309
- N=291

**Efficacy Outcomes**
- Proportion of patients who maintained visual acuity (%)<15 letters of BCVA loss)
  - View1: 94%, 95%, 94%, 95%, 95%, 95%
  - View2: 94%, 95%, 94%, 95%, 95%
- Difference (%) (95.1% CI)
  - View1: 0.6% (-3.2, 4.4)
  - View2: 1.3% (-2.4, 5.0)
- Mean change in BCVA as measured by ETDRS letter score from Baseline
  - View1: 7.9
  - View2: 8.1
- Difference in LS mean (%) (95.1% CI)
  - View1: 0.3% (-2.0, 2.5)
  - View2: 3.2% (0.9, 5.4)
- Number of patients who gained at least 15 letters of vision from Baseline (%)
  - View1: 92 (31%)
  - View2: 94 (31%)
- Difference (%) (95.1% CI)
  - View1: -0.4% (-7.7, 7.0)
  - View2: -2.6% (-10.2, 4.9)

BCVA = Best Corrected Visual Acuity; CI = Confidence Interval; ETDRS = Early Treatment Diabetic Retinopathy Study; LOCF = Last Observation Carried Forward; baseline values are not carried forward; 95.1% confidence intervals were presented to adjust for safety assessment conducted during the study.

### Table 5: Efficacy Outcomes at Week 24 (Full Analysis Set with LOCF) in COPERNICUS and GALILEO Studies

<table>
<thead>
<tr>
<th>COPERNICUS</th>
<th>GALILEO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>EYLEA 2 mg Q4 weeks</td>
</tr>
<tr>
<td>N=73</td>
<td>N=114</td>
</tr>
</tbody>
</table>

**Efficacy Outcomes**
- Proportion of patients who gained at least 15 letters in BCVA from Baseline (%)
  - COPERNICUS: 12%
  - GALILEO: 56%
  - COPERNICUS: 22%
  - GALILEO: 60%
  - Difference in LS mean (%) (95.1% CI)
  - COPERNICUS: -4.0% (18.0)
  - GALILEO: 7.3% (12.8)
  - Difference in LS mean (%) (95.1% CI)
  - COPERNICUS: 21.7% (17.3, 26.1)
  - GALILEO: 14.7% (10.7, 18.7)

- Difference is EYLEA 2 mg Q4 weeks minus Control
- Difference and CI are calculated using Cochran-Mantel-Haenszel (CMH) test adjusted for baseline factors; 95.1% confidence intervals were presented to adjust for the multiple assessments conducted during the study.
- p<0.01 compared with Control
- LS mean and CI based on an ANCOVA model
Treatment effects in evaluable subgroups (e.g., age, gender, race, baseline visual acuity, retinal perfusion status, and CRVO duration) in each study and in the combined analysis were in general consistent with the results in the overall populations.

### 14.3 Macular Edema Following Branch Retinal Vein Occlusion (BRVO)

The safety and efficacy of EYLEA were assessed in a 24-week, randomized, multi-center, double-masked, controlled study in patients with macular edema following BRVO. A total of 181 patients were treated and evaluable for efficacy (91 with EYLEA) in the VIBRANT study. In the study, patients were randomly assigned in a 1:1 ratio to either 2 mg EYLEA administered every 4 weeks (2Q4) or laser photocoagulation administered at baseline and subsequently as needed (control group). Patient ages ranged from 42 to 94 years with a mean of 65 years.

In the VIBRANT study, the primary efficacy endpoint was the proportion of patients who gained at least 15 letters in BCVA at week 24 compared to baseline. At week 24, the EYLEA 2 mg Q4 group was superior to the control group for the primary endpoint.

Detailed results from the analysis of the VIBRANT study are shown in Table 6 and Figure 10 below.

#### Table 6: Efficacy Outcomes at Week 24 (Full Analysis Set with LOCF) in VIBRANT Study

<table>
<thead>
<tr>
<th>VIBRANT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>EYLEA 2 mg Q4 weeks</td>
</tr>
<tr>
<td>N</td>
<td>90</td>
<td>91</td>
</tr>
</tbody>
</table>

**Efficacy Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Control (%)</th>
<th>EYLEA 2 mg Q4 weeks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of patients who gained at least 15 letters in BCVA from Baseline (%)</td>
<td>26.7%</td>
<td>52.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>(95% CI)</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weighted Difference a,b (%)</td>
<td>26.6%c</td>
<td>(13.0, 40.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>(SD)</th>
<th>(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in BCVA as measured by ETDRS letter score from Baseline</td>
<td>6.9 (12.9)</td>
<td>17.0 (11.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>(95% CI)</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference in LS mean a,d</td>
<td>10.5%c</td>
<td>(7.1, 14.0)</td>
</tr>
</tbody>
</table>

---

a Difference is EYLEA 2 mg Q4 weeks minus Control
b Difference and CI are calculated using Mantel-Haenszel weighting scheme adjusted for region (North America vs. Japan) and baseline BCVA category (> 20/200 and ≤ 20/200)

c p<0.01 compared with Control
d LS mean and CI based on an ANCOVA model
Results from the analysis of the VIVID and VISTA studies are shown in Table 7 and Figure 11 below.

### Table 7: Efficacy Outcomes at Weeks 52 and 100 (Full Analysis Set with LOCF) in VIVID and VISTA Studies

<table>
<thead>
<tr>
<th></th>
<th>VIVID</th>
<th>VISTA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EYLEA 2 mg Q8 weeks</td>
<td>EYLEA 2 mg Q4 weeks</td>
</tr>
<tr>
<td>Full Analysis Set</td>
<td>N=135</td>
<td>N=136</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Control</td>
</tr>
</tbody>
</table>

#### Efficacy Outcomes at Week 52

<table>
<thead>
<tr>
<th></th>
<th>VIVID</th>
<th>VISTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in BCVA as measured by ETDRS letter score from Baseline (SD)</td>
<td>9.7 (9.3)</td>
<td>10.5 (9.6)</td>
</tr>
<tr>
<td>Difference&lt;sup&gt;a&lt;/sup&gt; in LS mean (97.5% CI)</td>
<td>9.1&lt;sup&gt;d&lt;/sup&gt; (6.3, 11.8)</td>
<td>9.3&lt;sup&gt;d&lt;/sup&gt; (6.5, 12.0)</td>
</tr>
<tr>
<td>Proportion of patients who gained at least 15 letters in BCVA from Baseline (%)</td>
<td>33.3%</td>
<td>32.4%</td>
</tr>
<tr>
<td>Adjusted Difference&lt;sup&gt;c,e&lt;/sup&gt; (%) (97.5% CI)</td>
<td>24.2&lt;sup&gt;d&lt;/sup&gt; (13.5, 34.9)</td>
<td>23.3&lt;sup&gt;d&lt;/sup&gt; (12.6, 33.9)</td>
</tr>
</tbody>
</table>

#### Efficacy Outcomes at Week 100

<table>
<thead>
<tr>
<th></th>
<th>VIVID</th>
<th>VISTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in BCVA as measured by ETDRS letter score from Baseline (SD)</td>
<td>9.4 (10.5)</td>
<td>11.4 (11.2)</td>
</tr>
<tr>
<td>Difference&lt;sup&gt;a&lt;/sup&gt; in LS mean (97.5% CI)</td>
<td>8.2&lt;sup&gt;d&lt;/sup&gt; (5.2, 11.3)</td>
<td>10.7&lt;sup&gt;d&lt;/sup&gt; (7.6, 13.8)</td>
</tr>
<tr>
<td>Proportion of patients who gained at least 15 letters in BCVA from Baseline (%)</td>
<td>31.1%</td>
<td>38.2%</td>
</tr>
<tr>
<td>Adjusted Difference&lt;sup&gt;c,e&lt;/sup&gt; (%) (97.5% CI)</td>
<td>19%&lt;sup&gt;d&lt;/sup&gt; (8.0, 29.9)</td>
<td>26.1%&lt;sup&gt;d&lt;/sup&gt; (14.8, 37.5)</td>
</tr>
</tbody>
</table>

<sup>a</sup> After treatment initiation with 5 monthly injections
<sup>b</sup> LS mean and CI based on an ANCOVA model with baseline BCVA measurement as a covariate and a factor for treatment group. Additionally, protocol specified stratification factors were included in the model.
<sup>c</sup> Difference is EYLEA group minus Control group
<sup>d</sup> p<0.01 compared with Control
<sup>e</sup> Difference with confidence interval (CI) and statistical test is calculated using Mantel-Haenszel weighting scheme adjusted by protocol specified stratification factors.

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Treatment effects in the subgroup of patients who had previously been treated with a VEGF inhibitor prior to study participation were similar to those seen in patients who were VEGF inhibitor naive prior to study participation.

Treatment effects in evaluable subgroups (e.g., age, gender, race, baseline HbA1c, baseline visual acuity, prior anti-VEGF therapy) in each study were in general consistent with the results in the overall populations.

### 14.5 Diabetic Retinopathy (DR) in Patients with DME

In the VIVID and VISTA studies, an efficacy outcome was the change in the Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (ETDRS-DRSS). The ETDRS-DRSS score was assessed at baseline and approximately every 6 months thereafter for the duration of the studies [see Clinical Studies (14.4)].

All enrolled patients had DR and DME at baseline. The majority of patients enrolled in these studies (77%) had moderate-to-severe nonproliferative diabetic retinopathy (NPDR) based on the ETDRS-DRSS. At week 100, the proportion of patients improving by at least 2 steps on the ETDRS-DRSS was significantly greater in both EYLEA treatment groups (2Q4 and 2Q8) when compared to the control group.
Results from the analysis of ETDRS-DRSS at week 100 in the VIVID and VISTA studies are shown in Table 8 below.

**Table 8: Proportion of Patients who Achieved a ≥2-Step Improvement from Baseline in the ETDRS-DRSS Score at Week 100 (LOCF) in VIVID and VISTA Studies**

<table>
<thead>
<tr>
<th>VIVID</th>
<th>VISTA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EYLEA 2 mg Q8 weeks</strong></td>
<td><strong>EYLEA 2 mg Q4 weeks</strong></td>
</tr>
<tr>
<td>Evaluable Patients</td>
<td>N=101</td>
</tr>
<tr>
<td>Number of patients with a ≥2-step improvement on ETDRS-DRSS from Baseline (%)</td>
<td>32 (32%)</td>
</tr>
<tr>
<td>Difference in (%) (97.5% CI)</td>
<td>24% (12, 36)</td>
</tr>
</tbody>
</table>

*a* Non-gradable post-baseline ETDRS-DRSS values were treated as missing and were imputed using the last gradable ETDRS-DRSS values (including baseline values if all post-baseline values were missing or non-gradable)

*b* After treatment initiation with 5 monthly injections

*c* The number of evaluable patients included all patients who had valid ETDRS-DRSS data at baseline.

*d* Difference with confidence interval (CI) was calculated using Mantel-Haenszel weighting scheme adjusted by protocol specified stratification factors

*e* Difference is EYLEA minus Control group

*f* p<0.01 compared with Control

Results of the evaluable subgroups (e.g., age, gender, race, baseline HbA1c, baseline visual acuity) on the proportion of patients who achieved a ≥2-step improvement on the ETDRS-DRSS from baseline to week 100 were, in general, consistent with those in the overall population.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

Each Vial is for single eye use only. EYLEA is supplied in the following presentation [see Dosage and Administration (2.6) and (2.7)].

<table>
<thead>
<tr>
<th>NDC NUMBER</th>
<th>CARTON TYPE</th>
<th>CARTON CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>61755-005-02</td>
<td>Vial</td>
<td>one single-use, sterile, 3-mL, glass vial designed to deliver 0.05 mL of 40 mg/mL EYLEA, one 19-gauge x 1½-inch, 5-micron, filter needle for withdrawal of the vial contents, one 30-gauge x ½-inch injection needle for intravitreal injection, one 1-mL syringe for administration, one package insert</td>
</tr>
</tbody>
</table>

**STORAGE**

EYLEA should be refrigerated at 2°C to 8°C (36°F to 46°F). Do Not Freeze. Do not use beyond the date stamped on the carton and container label. Protect from light. Store in the original carton until time of use.

### 17 PATIENT COUNSELING INFORMATION

In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist [see Warnings and Precautions (5.1)].

Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations [see Adverse Reactions (6)]. Advise patients not to drive or use machinery until visual function has recovered sufficiently.