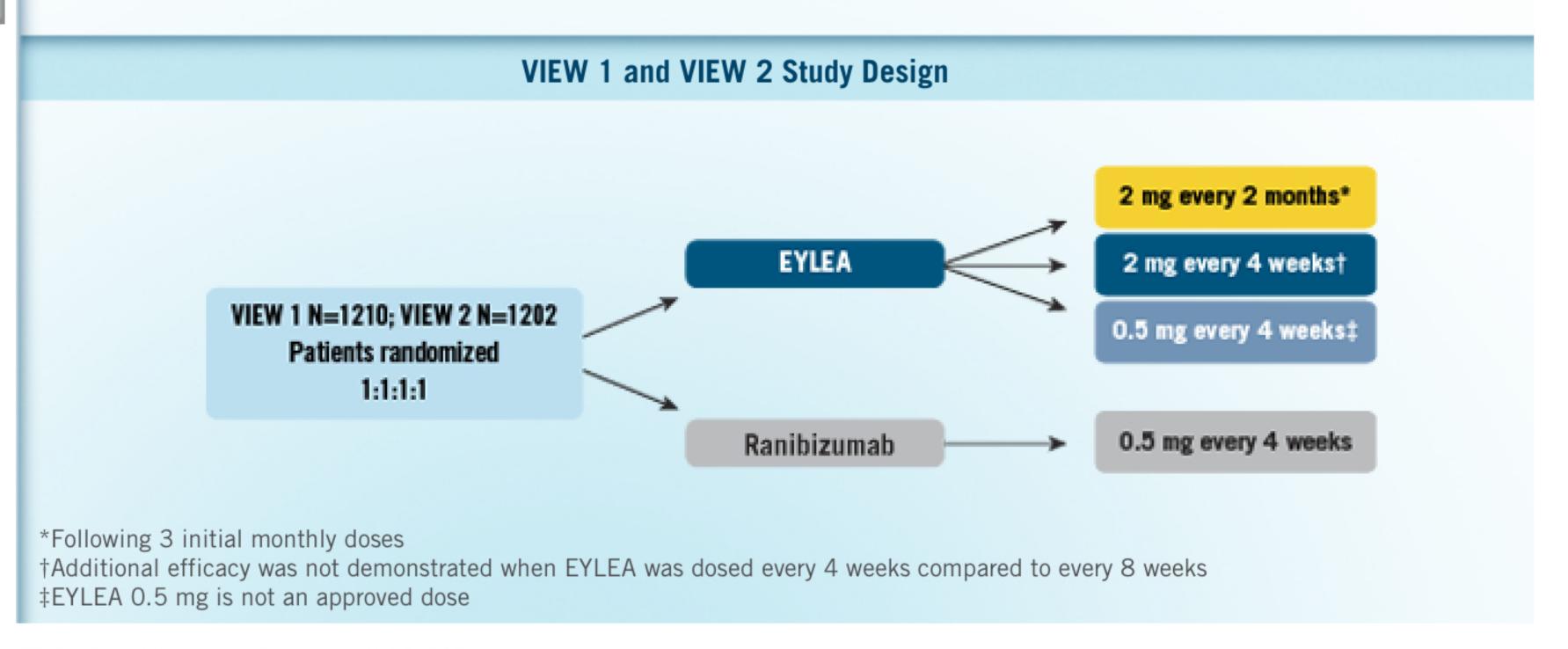
# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

Safety and efficacy were assessed in two randomized, multicenter, double-masked, active-controlled (ranibizumab) studies (VIEW 1 and VIEW 2)

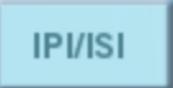


### Clinical Endpoints at 52 Weeks

- Primary Endpoint:
  - Proportion of patients who maintained visual acuity (%) (losing <15 letters of Best-Corrected Visual Acuity [BCVA])
- Key Secondary Endpoints:
  - Mean change in BCVA as measured by Early Treatment Diabetic Retinopathy Study (ETDRS)
    letter score from baseline
  - Number of patients who gained at least 15 letters of vision from baseline

### Important Safety Information from the EYLEA Prescribing Information

EYLEA® (aflibercept) Injection is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA





## IMPORTANT PRESCRIBING INFORMATION

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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.

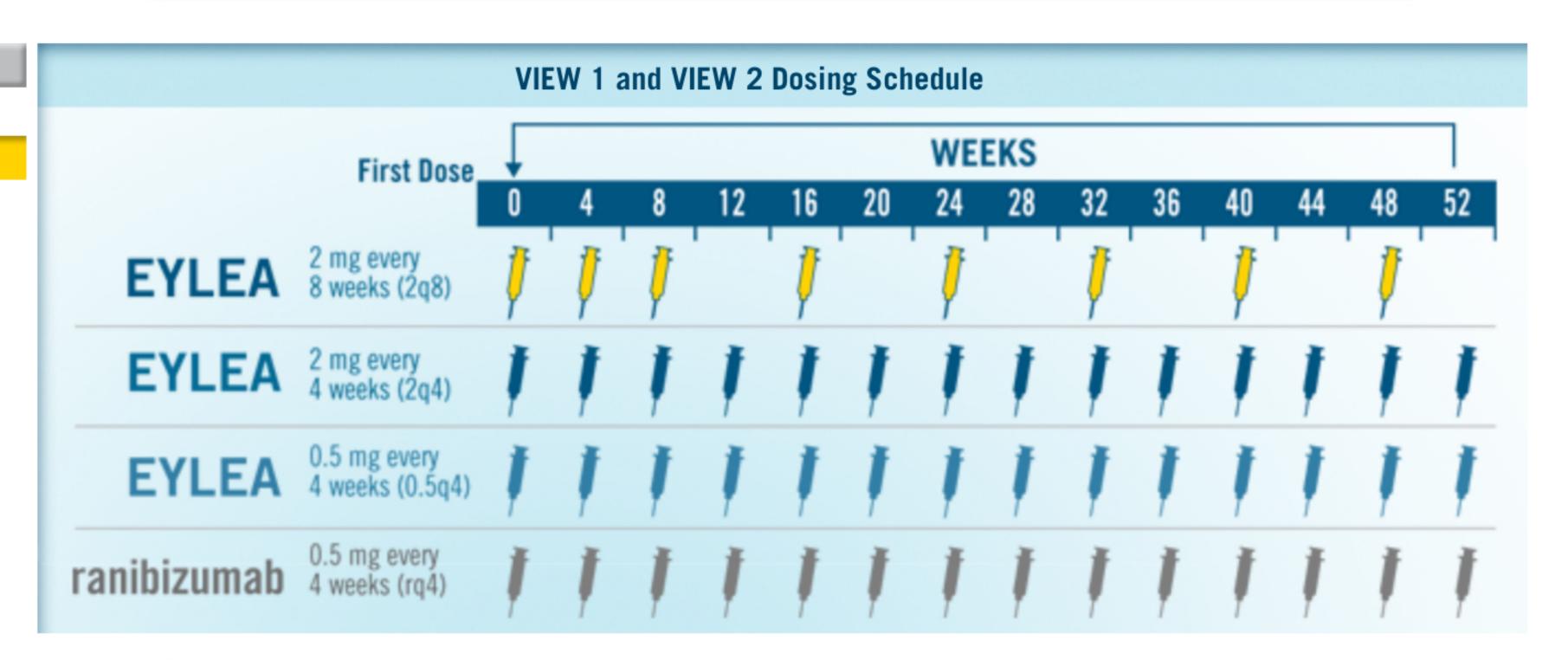
EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly).

#### IMPORTANT SAFETY INFORMATION

EYLEA® (aflibercept) Injection is contraindicated in patients with ocular



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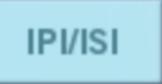


### **Patient Demographics**

- 2412 patients with predominantly classic, minimally classic, or occult neovascular Age-related Macular Degeneration were treated and evaluated<sup>3</sup>
- All patients had a baseline ETDRS BCVA score of 73 to 25 letters (Snellen equivalent of 20/40 to 20/320 vision)<sup>3</sup>
- Patient ages ranged from 49 to 99 years with a mean of 76 years

### **Important Prescribing Information for EYLEA**

- The recommended dose for EYLEA for the treatment of wet AMD is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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





## IMPORTANT PRESCRIBING INFORMATION

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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.

EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly).

#### IMPORTANT SAFETY INFORMATION

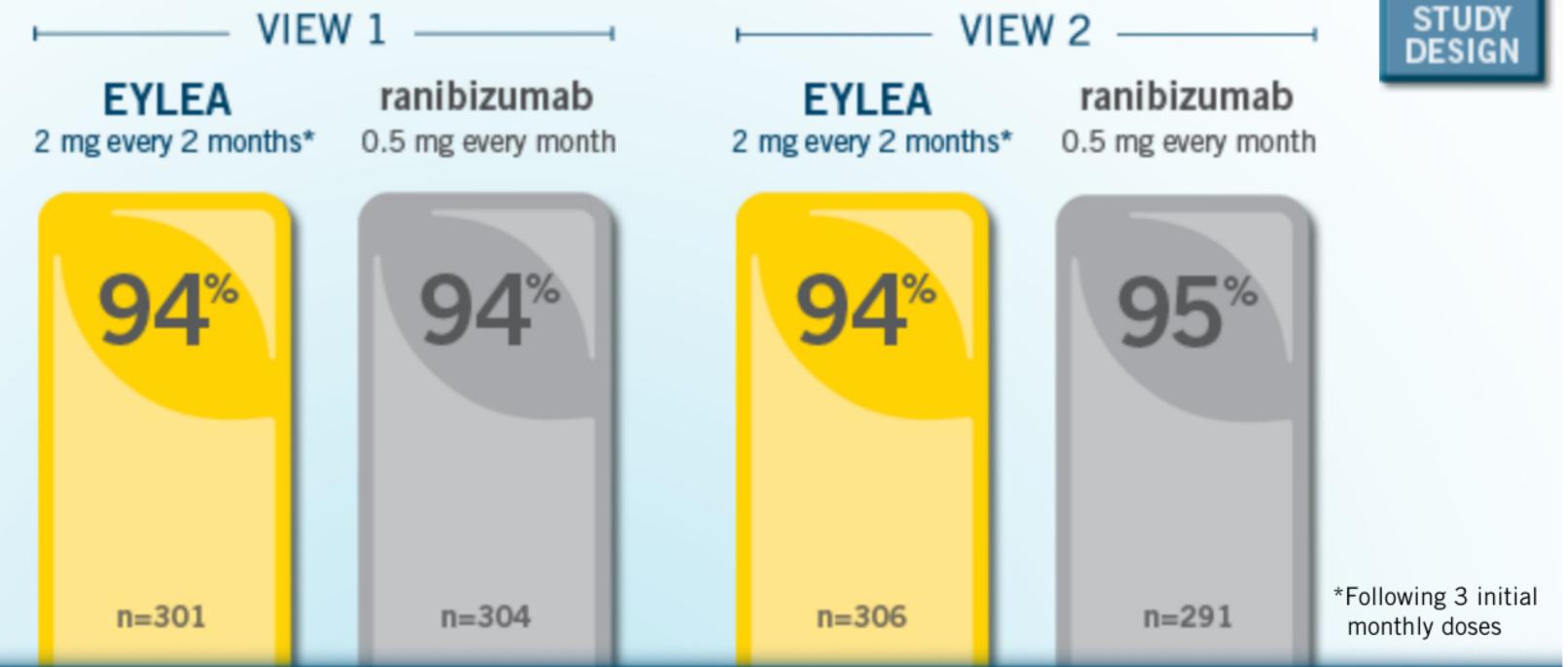
EYLEA® (aflibercept) Injection is contraindicated in patients with ocular



# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

EYLEA 2 mg every 2 months (following 3 initial monthly doses) demonstrated clinically equivalent efficacy to monthly ranibizumab in the proportion of patients who maintained vision at week 52<sup>3</sup>

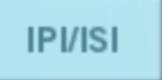
Primary Endpoint: Maintenance of Vision (<15 Letters Lost) Based on BCVA as Measured by ETDRS at 52 Weeks vs Baseline



- The proportion of patients dosed with EYLEA, 2 mg once every 4 weeks (monthly), losing fewer than 15 letters of vision at 52 weeks was 95% in VIEW 1 and 95% in VIEW 2
- The recommended dose for EYLEA for the treatment of Wet AMD is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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

### Important Safety Information from the EYLEA Prescribing Information

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





## IMPORTANT PRESCRIBING INFORMATION

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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.

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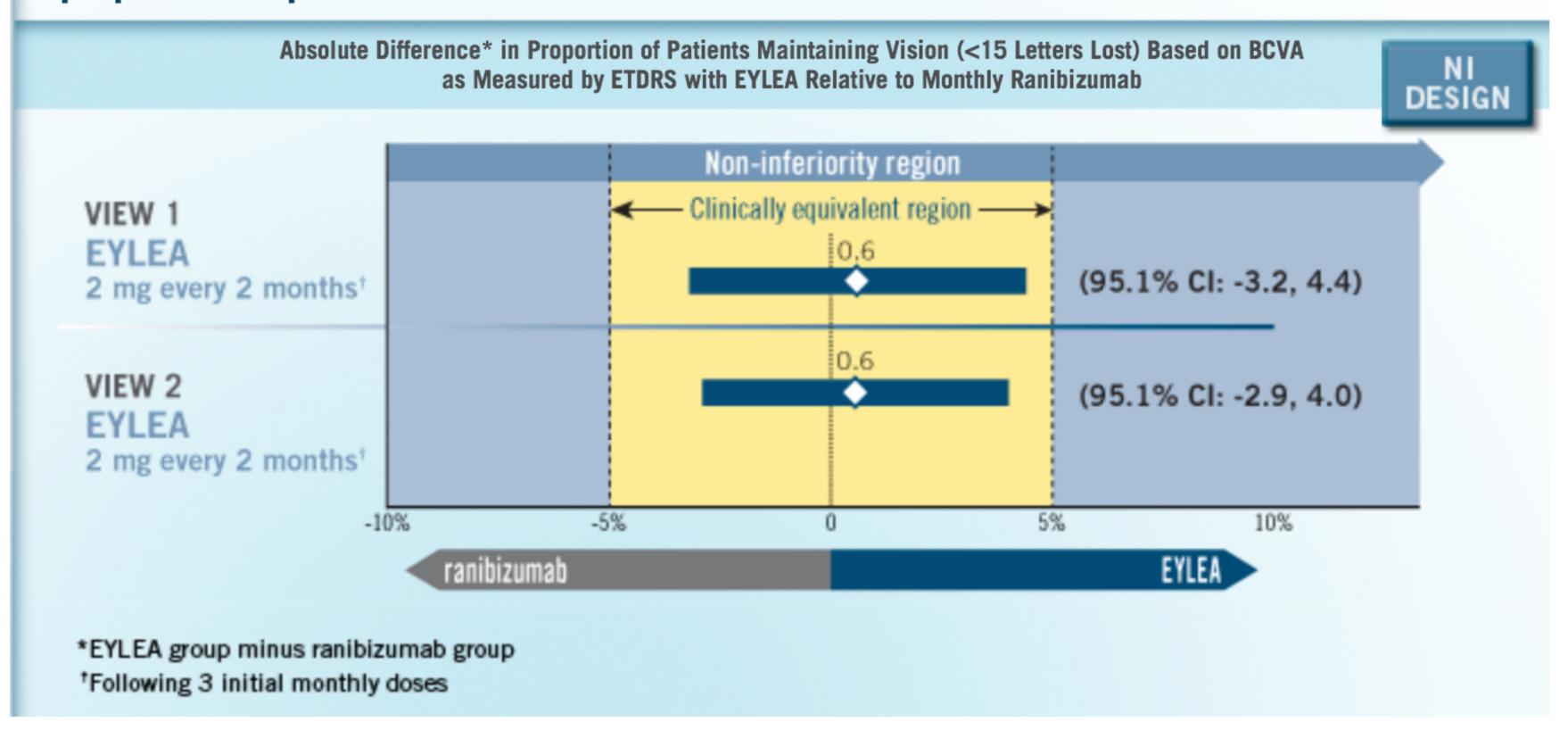
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# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

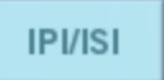
EYLEA 2 mg every 2 months (following 3 initial monthly doses) demonstrated non-inferior and clinically equivalent efficacy to monthly ranibizumab in the proportion of patients who maintained vision at week 52



- The specified requirement for non-inferiority was that the upper limit of the 95.1% confidence interval (CI) of the difference between EYLEA and ranibizumab be above -10%<sup>3</sup>
- Actual upper limits in the per protocol set for all EYLEA doses compared to ranibizumab 0.5 mg monthly were above -10% (non-inferiority) and within ±5% (clinically equivalent) for the primary endpoint<sup>3</sup>

### Important Safety Information from the EYLEA Prescribing Information

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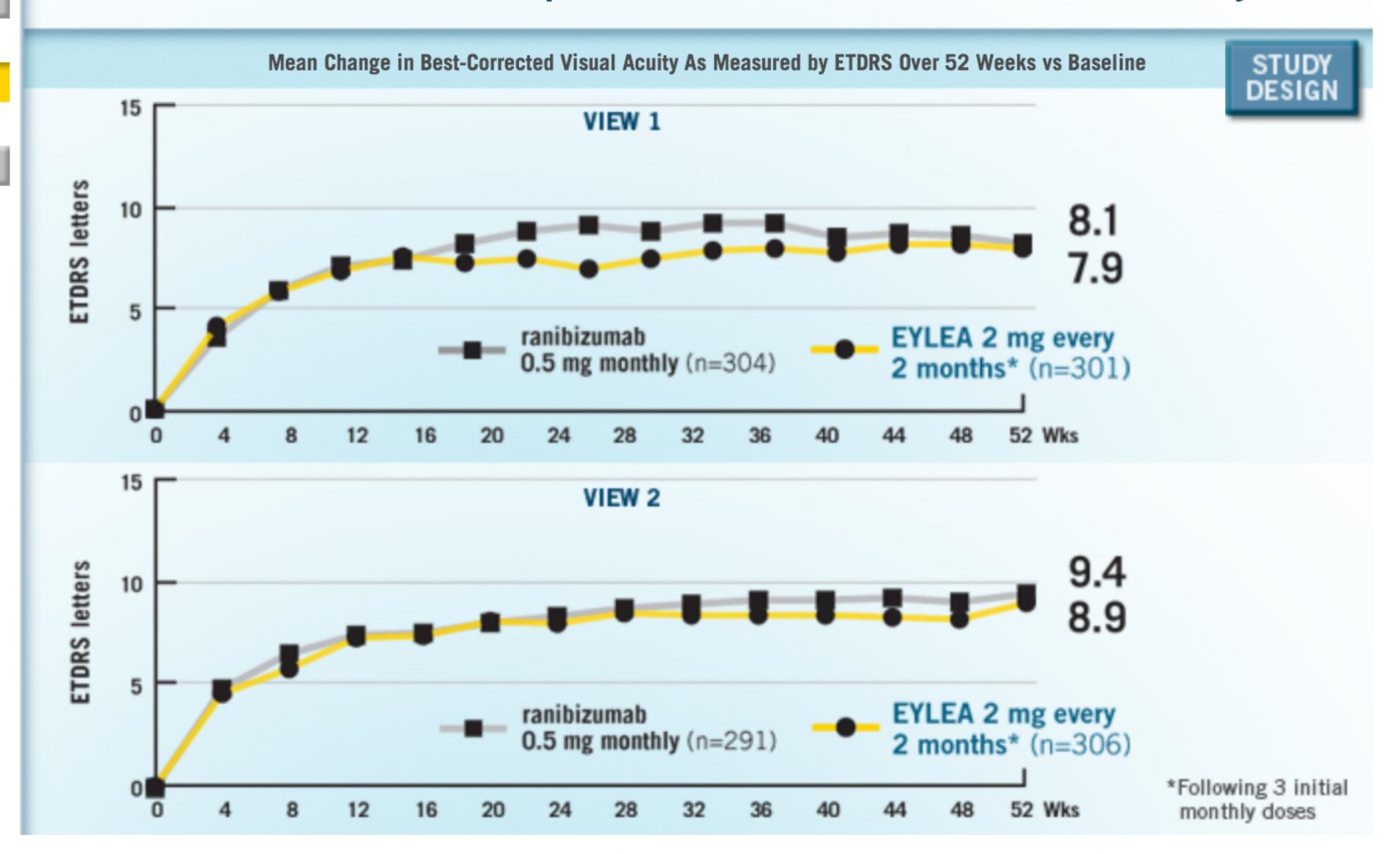
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# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

# EYLEA 2 mg every 2 months (following 3 initial monthly doses) and monthly ranibizumab achieved similar improvements in and maintenance of visual acuity<sup>3</sup>



The mean change in BCVA versus baseline for patients dosed with EYLEA 2 mg once every 4 weeks (month) was 10.9 and 7.6 in VIEW 1 and VIEW 2, respectively

### Important Safety Information from the EYLEA Prescribing Information

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors





## IMPORTANT PRESCRIBING INFORMATION

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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.

EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly).

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EYLEA® (aflibercept) Injection is contraindicated in patients with ocular



# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

EYLEA 2 mg every 2 months (following 3 initial monthly doses) and monthly ranibizumab achieved similar proportions of patients who gained at least 15 letters of vision at 52 weeks<sup>3</sup>

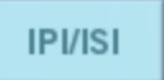
STUDY Proportion of Patients Gaining 15 Letters of Best-Corrected Visual Acuity as Measured by ETDRS at 52 Weeks vs Baseline DESIGN VIEW 1 VIEW 2 ranibizumab ranibizumab EYLEA EYLEA 2 mg every 2 months\* 2 mg every 2 months\* 0.5 mg every month 0.5 mg every month 31% 31% n=291 n=301 n=304 n=306

Last Observation Carried Forward (LOCF): full analysis set \*Following 3 initial monthly doses

- Among patients dosed with EYLEA 2 mg once every 4 weeks (monthly), 38% and 29% gained ≥15 letters versus baseline in VIEW 1 and VIEW 2, respectively
- Anatomic measures of disease activity improved similarly in all treatment groups from baseline to week 52. Anatomic data were not used to influence treatment decisions

### Warnings and Precautions from the EYLEA Prescribing Information

■ There is a potential risk of arterial thromboembolic events (ATEs) following use of intravitreal VEGF inhibitors, including EYLEA, defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of ATEs in the VIEW 1 and VIEW 2 wet AMD studies in patients treated with EYLEA was 1.8% during the first year. The incidence of ATEs in the COPERNICUS and GALILEO CRVO studies was 0% in patients treated with EYLEA compared with 1.4% in patients receiving sham control during the first six months





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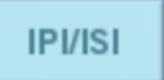
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### Most Common Adverse Reactions (≥1%) in Phase 3 Studies\*

STU	DY
DESI	GN

Adverse reactions	EYLEA (N=1824)	ranibizumab (N=595)
Conjunctival hemorrhage	25%	28%
Eye pain	9%	9%
Cataract	7%	7%
Vitreous detachment	6%	6%
Vitreous floaters	6%	7%
Intraocular pressure increased	5%	7%
Conjunctival hyperemia	4%	8%
Corneal erosion	4%	5%
Detachment of the retinal pigment epitheliu	m 3%	3%
Injection site pain	3%	3%
Foreign body sensation in eyes	3%	4%
Lacrimation increased	3%	1%
Vision blurred	2%	2%
Intraocular inflammation	2%	3%
Retinal pigment epithelium tear	2%	1%
Injection site hemorrhage	1%	2%
Eyelid edema	1%	2%
Corneal edema	1%	1%

Less common serious adverse reactions reported in less than 1% of the patients treated with EYLEA were retinal detachment, retinal tear, and endophthalmitis. Hypersensitivity has also been reported in less than 1% of patients treated with EYLEA





## IMPORTANT PRESCRIBING INFORMATION

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EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly).

#### **IMPORTANT SAFETY INFORMATION**

EYLEA® (aflibercept) Injection is contraindicated in patients with ocular



## IMPORTANT PRESCRIBING INFORMATION FOR EYLEA® (aflibercept) INJECTION

- EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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
- EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO).
  The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly)

## IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

- EYLEA® (aflibercept) Injection is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA
- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. 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. Intraocular inflammation has been reported with the use of EYLEA
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately
- There is a potential risk of arterial thromboembolic events (ATEs) following use of intravitreal VEGF inhibitors, including EYLEA, defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of ATEs in the VIEW 1 and VIEW 2 wet AMD studies in patients treated with EYLEA was 1.8% during the first year. The incidence of ATEs in the COPERNICUS and GALILEO CRVO studies was 0% in patients treated with EYLEA compared with 1.4% in patients receiving sham control during the first six months
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and increased intraocular pressure
- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis, traumatic cataract, increased intraocular pressure, and vitreous detachment
- Please see the full Prescribing Information for EYLEA

# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

### **General Dosing Information**

- EYLEA (aflibercept) Injection is indicated for the treatment of patients with neovascular (wet)
   Age-related Macular Degeneration (AMD)
- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA
- EYLEA IS FOR OPHTHALMIC INTRAVITREAL INJECTION ONLY
- The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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
- No special dosage modification is required for any of the populations that have been studied (eg, gender, elderly, renally impaired)







## IMPORTANT PRESCRIBING INFORMATION

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#### EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses<sup>1,2</sup>

#### **How Supplied**

- One single-use glass vial 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



#### **Important Administration Considerations**

- 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 (eg, eye pain, redness of the eye, photophobia,
  blurring of vision) without delay





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# Serious Non-ocular (Systemic) Adverse Reactions Over First 52 Weeks That Occurred in at Least 1% of Patients in Either Group 14



Disorder	EYLEA (N=1824)	ranibizumab (N=595)
Any serious non-ocular adverse event	14%	14%
Infections/infestations	2%	3.5%
Cardiac	3%	3%
Neoplasms	2.5%	2%
Vascular disorders	1%	1%
Injury/poisoning/procedural complications	2%	1%
Musculoskeletal/connective tissue	0.5%	1%
Gastrointestinal	1.5%	1%
Respiratory/thoracic/mediastinal	1%	1%
General/administration site	1%	1%
Nervous system	2%	0.5%

- There was a similar overall incidence for EYLEA® (aflibercept) Injection 2 mg every 8 weeks or monthly and 0.5 ranibizumab monthly of systemic (nonocular) adverse events, serious systemic adverse events (including ATEs) and deaths
- Among the EYLEA treatment groups, there was no evidence of a dose response for adverse events

### Important Safety Information from the EYLEA Prescribing Information

- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and increased intraocular pressure
- There is a potential risk of arterial thromboembolic events (ATEs) following use of intravitreal VEGF inhibitors, including EYLEA, defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of ATEs in the VIEW 1 and VIEW 2 wet AMD studies in patients treated with EYLEA was 1.8% during the first year. The incidence of ATEs in the COPERNICUS and GALILEO CRVO studies was 0% in patients treated with EYLEA compared with 1.4% in patients receiving sham control during the first six months





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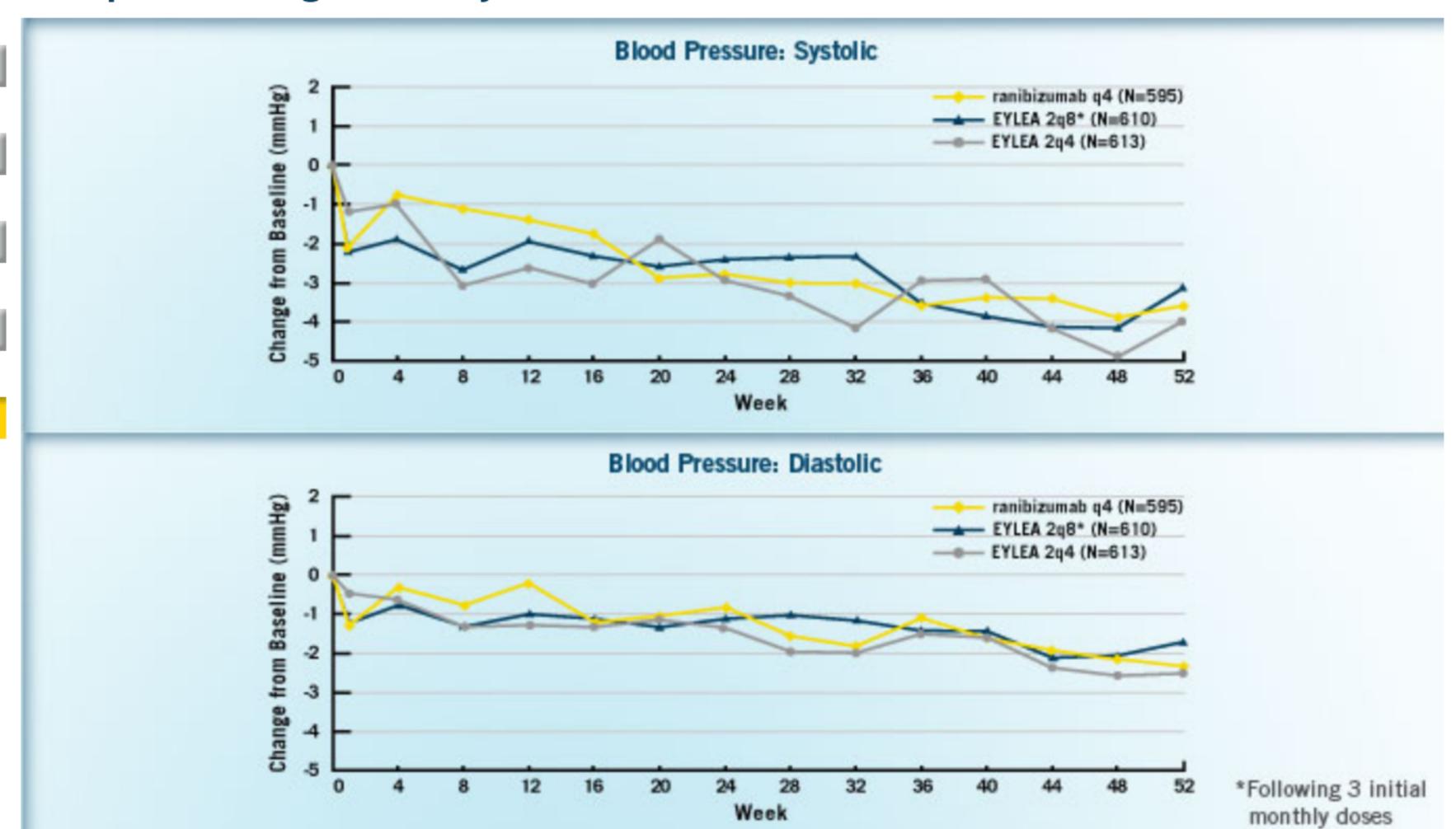
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### **Pre-Specified Integrated Analysis**<sup>14</sup>

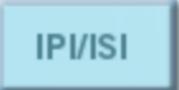


# Changes in systolic and diastolic blood pressure were similar across all EYLEA® (aflibercept) Injection and ranibizumab 0.5 mg monthly study arms over 52 weeks<sup>14</sup>

The incidence of blood pressure-related serious adverse events was 0.3% with ranibizumab 0.5 mg every 4 weeks and 0.3% across all EYLEA study arms over 52 weeks<sup>3</sup>

### Important Safety Information from the EYLEA Prescribing Information

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Comprehensive Support for You and Your Patients



EYLEA4U is a comprehensive support program designed to meet your patients' information, access, and reimbursement needs



EYLEA, EYLEA4U, and Time Between Treatments are registered trademarks of Regeneron Pharmaceuticals, Inc.





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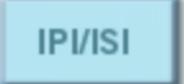


\*Neovascular (wet) Age-related Macular Degeneration (AMD)
†Recommended dose: 2 mg every 4 weeks for first 12 weeks, followed by 2 mg every 8 weeks
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# EYLEA® (aflibercept) Injection: The Only VEGF Inhibitor Approved for Every 2-Months Dosing Following 3 Initial Monthly Doses 1,2

### References

- Lucentis® (ranibizumab injection) Prescribing Information, Genentech, Inc. Revised Aug 2012.
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## IMPORTANT PRESCRIBING INFORMATION

EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg 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

EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly)

# IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

FYLFA is contraindicated in patients

