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Policy Number: 038.011

Title: Coverage Determination Policy for Ophthalmologic Agents:

- **Eylea (Aflibercept); Eylea HD (Aflibercept); Lucentis (Ranibizumab); Visudyne (Verteporfin); Beovu (Brolucizumab-DBLL); Vabysmo (Faricimab-svoa); Susvimo (Ranibizumab); Byooviz (Ranibizumab-nuna); Cimerli (Ranibizumab-eqrn)**

Regions: ☒ **Texas** ☒ **New Mexico**

Impacted Areas:

☒ Network Management/Provider Services	☒ Utilization Management
☐ Member services	☐ Case management
☐ Quality Management	☐ Disease management
☐ Credentialing	☒ Claims
☐ IT	☐ Human resources
☐ Administration	☐ Finance
☐ Compliance/delegation	☒ Pharmacy
	☐ ALL

Available LCD/NCD/LCA: None

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Coverage Policy Number: 038.011

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Step Therapy Criteria

(Applies to *Intravitreal Vascular Endothelial Growth Factor (VEGF) Inhibitors)*

This policy supplements the Medicare guidelines such as NCDs, LCDs, and other Medicare manuals for the purposes of determining coverage under the Part B medical benefits. This Step Therapy Policy is implemented to enforce a step therapy requirement for new starts only. This policy is not applicable to members continuing therapy within the past 365 days. Coverage is granted if Medicare Coverage requirements PLUS these step criteria are met.

For Age Related Macular Degeneration:

Non-preferred drug(s): Lucentis, Beovu, Byooviz, Susvimo, Vabysmo, Cimerli

Preferred drug(s): Compounded Avastin (bevacizumab), then Eylea

Step Therapy Criteria

1. Coverage of **Eylea** when prescribed for **Age Related Macular Degeneration** is medically necessary when **ANY** of the criteria listed below are met:
   A. History of a trial of at least 3 doses, resulting in minimal clinical response to compounded Avastin (bevacizumab);
   B. History of contraindication or adverse event(s) to compounded Avastin (bevacizumab);
   C. Continuation of prior therapy within the past 365 days.
2. Coverage of **Lucentis, Byooviz, Susvimo, Vabysmo, Cimerli or Beovu** when prescribed for **Age Related Macular Degeneration** is medically necessary when **ANY** of the criteria listed below are met:
   A. **BOTH** of the following:
      I. Trial of at least 3 doses, resulting in minimal clinical response to compounded Avastin (bevacizumab); and
      II. History of use of Eylea, resulting in minimal clinical response to therapy;
   B. History of contraindication, intolerance, or adverse event(s) to compounded Avastin (bevacizumab) **and** Eylea
   C. Continuation of prior therapy within the past 365 days.

For all other Retinal Conditions:

Non-preferred drug(s): Lucentis, Beovu, Byooviz, Susvimo, Vabysmo, Cimerli

Preferred drug(s): Eylea

Non-Preferred Product Step Therapy Criteria

Coverage of Beovu, Byooviz, Lucentis, Susvimo, Cimerli or Vabysmo when prescribed for **ALL other retinal conditions** is medically necessary when **ANY** of the criteria listed below are met:

A. History of use of Eylea, resulting in minimal clinical response to therapy
B. History of contraindication or adverse event(s) to Eylea
C. Continuation of prior therapy within the past 365 days.

Initial/New Requests

For **initial therapy**, **ALL** of the following for each of the following agents:
Beovu (brolucizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Beovu (brolucizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic Macular Edema (DME**)
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Byooviz (ranibizumab-nuna) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Byooviz (ranibizumab-nuna) is proven and medically necessary for the treatment of:

- Diagnosis of **Macular Edema Following Retinal Vein Occlusion (RVO)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Byooviz (ranibizumab-nuna) is proven and medically necessary for the treatment of:

- Diagnosis of **Myopic Choroidal Neovascularization (mCNV)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Cimerli (ranibizumab-eqrn) is proven and medically necessary for the treatment of:

- Diagnosis of **Myopic Choroidal Neovascularization (mCNV)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Cimerli (ranibizumab-eqrn) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic macular edema (DME)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Cimerli (ranibizumab-eqrn) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic retinopathy (DR)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Cimerli (ranibizumab-eqrn) is proven and medically necessary for the treatment of:

- Diagnosis of **Macular edema following Retinal Vein Occlusion (RVO)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Cimerli (ranibizumab-eqrn) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic macular edema (DME)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic retinopathy (DR)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO**)
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea HD (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic macular edema (DME)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea HD (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic retinopathy (DR)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Eylea HD (aflibercept) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Lucentis (ranibizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Choroidal neovascularization secondary to pathologic myopia, angioid streaks/pseudoxanthoma elasticum, or ocular histoplasmosis syndrome (OHS)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Lucentis (ranibizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic macular edema (DME)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Lucentis (ranibizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic retinopathy (DR)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Lucentis (ranibizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO**)
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Lucentis (ranibizumab) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Susvimo (ranibizumab injection) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
    - Previously responded to at least TWO intravitreal injections of a VEGF inhibitor
- Dosed in accordance with FDA approved labeling for this indication

Vabysmo (faricimab-svoa) is proven and medically necessary for the treatment of:

- Diagnosis of **Neovascular age-related macular degeneration (nAMD)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Vabysmo (faricimab-svoa) is proven and medically necessary for the treatment of:

- Diagnosis of **Diabetic macular edema (DME)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Vabysmo (faricimab-svoa) is proven and medically necessary for the treatment of:

- Diagnosis of **Macular Edema Following Retinal Vein Occlusion (RVO)**
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis
- Dosed in accordance with FDA approved labeling for this indication

Visudyne (verteporfin for injection) is proven and medically necessary for the treatment of:

- Diagnosis of predominantly **classic subfoveal choroidal neovascularization** due to one of the following:
    - Age-related macular degeneration
    - Pathologic myopia
    - Presumed ocular histoplasmosis
- Dosed in accordance with FDA approved labeling for this indication

Renewal/Continuation of Therapy Requests

WellMed Medical Management **will cover** renewal or continuation of therapy requests for, Beovu, Byooviz, Cimerli, Eylea, Eylea HD, Lucentis, Susvimo, Vabysmo and Visudyne if **ALL** of following criteria are met:

- Documentation of positive clinical response to anti-VEGF therapy
- Intravitreal VEGF or dual VEGF/Ang-2 inhibitor administration is no more than 12 doses per year per eye, regardless of diagnosis.

For Visudyne:
Documentation of positive clinical response as evidenced by at least **ONE** of the following:

A. Detained neovascularization; or
B. Improvement in visual acuity; or
C. Maintenance of corrected visual acuity from prior treatment; or
D. Supportive findings from optical coherence tomography or fluorescein angiography

FDA Approved Dose and Indication

Drug	FDA approved Indication	Approved Dosing
Beovu (brolucizumab)	Neovascular age-related macular degeneration (nAMD)	The recommended dose is 6 mg (0.05 mL) into affected eye(s) once monthly (approximately every 25 to 31 days) for the first 3 doses, then 6 mg every 8 to 12 weeks thereafter. Maximum of 12 doses per year per eye.
	Diabetic macular edema (DME)	The recommended dose is 6 mg (0.05 mL) into affected eye(s) every six weeks (approximately every 39 to 45 days) for the first 5 doses, then 6 mg every 8 to 12 weeks thereafter. Maximum of 12 doses per year per eye.
Byooviz (ranibizumab-nuna)	Neovascular age-related macular degeneration (nAMD)	The recommended dose is 0.5 mg (0.05 ML) administered by intravitreal injection once a month (approximately 28 days). Patients may be treated with 3 monthly doses followed by less frequent dosing. Patients may also be treated with one dose every 3 months after 4 monthly doses. Maximum of 12 doses per year per eye.
	Macular Edema Following Retinal Vein Occlusion (RVO)	The recommended dose is 0.5 mg (0.05 ML) administered by intravitreal injection once a month (approximately 28 days). Maximum of 12 doses per year per eye.
	Myopic Choroidal Neovascularization (mCNV)	The recommended dose is 0.5 mg (0.05 ML) administered by intravitreal injection once a month (approximately 28 days)

		for up to 3 months. May be retreated if necessary. Maximum of 12 doses per year per eye.
Cimerli (ranibizumab- eqrn)	Myopic choroidal neovascularization (mCNV)	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days) for up to 3 months. May be retreated if necessary. Maximum of 12 doses per year per eye.
	Diabetic macular edema (DME)	The recommended dose is 0.3 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Maximum of 12 doses per year per eye.
	Diabetic retinopathy	
	Macular edema following retinal vein occlusion (RVO)	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Maximum of 12 doses per year per eye.
	Neovascular (wet) age-related macular degeneration (nAMD)	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Treatment may be reduced to 3 once monthly doses, followed by an average of 4 to 5 injections over the subsequent 9 months. Maximum of 12 doses per year per eye.
Eylea (aflibercept)	Diabetic macular edema (DME) Diabetic retinopathy (DR)	The recommended dose is 2 mg (0.05 mL) into affected eye(s) every 4 weeks (approximately every 28 days, monthly) for the first 20 weeks (5 months), then 2 mg every 8 weeks (2 months). Maximum of 12 doses per year per eye.

	Macular edema secondary to BRVO or CRVO	The recommended dose is 2 mg (0.05 mL) once every 4 weeks. Maximum of 12 doses per year per eye.
	Neovascular age-related macular degeneration (nAMD)	The recommended dose is 2 mg (0.05 mL) into affected eye(s) every 4 weeks (approximately every 28 days, monthly) for the first 12 weeks (3 months), followed by 2 mg once every 8 weeks (2 months). Maximum of 12 doses per year per eye.
Eylea HD (aflibercept)	Neovascular (Wet)Age-Related Macular Degeneration (nAMD)	The recommended dose is 8 mg (0.07 mL) into affected eye(s) every 4 weeks (approximately every 28 days +/- 7 days) for the first 3 doses, then 8 mg every 8 to 16 weeks +/- 1 week. Maximum of 12 doses per year per eye.
	Diabetic Macular Edema (DME)	
	Diabetic Retinopathy (DR)	The recommended dose is 8 mg (0.7 mL) into affected eye(s) every 4 weeks (approximately every 28 days +/- 7 days) for the first 3 doses, followed by 8 mg once every 8 to 12 weeks +/- 1 week. Maximum of 12 doses per year per eye.
Lucentis (ranibizumab)	Choroidal neovascularization secondary to pathologic myopia, angioid streaks/pseudoxanthoma elasticum, or ocular histoplasmosis syndrome	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days) for up to 3 months. May be retreated if necessary. Maximum of 12 doses per year per eye.
	Diabetic macular edema (DME) Diabetic retinopathy (DR)	The recommended dose is 0.3 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Maximum of 12 doses per year per eye.

	Macular edema secondary to BRVO or CRVO	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Maximum of 12 doses per year per eye.
	Neovascular age-related macular degeneration (nAMD)	The recommended dose is 0.5 mg (0.05 mL) to affected eye(s) once a month (approximately every 28 days). Treatment may be reduced to 3 once monthly doses, followed by an average of 4 to 5 injections over the subsequent 9 months. Maximum of 12 doses per year per eye.
Vabysmo (faricimab)	Diabetic macular edema (DME)	The recommended dose is one of the following regimens: 1) 6 mg (0.05 mL) administered by intravitreal injection every 4 weeks for at least 4 doses, followed by extensions of up to 4-week interval increments or reductions of up to 8-week interval increments based on response; or 2) 6 mg (0.05 mL) administered every 4 weeks for the first 6 doses, followed by 6 mg dose via intravitreal injections at intervals of every 8 weeks over the next 28 weeks. Although most patients require dosing every 8 weeks, some patients may need dosing every 4 weeks. Maximum of 12 doses per year per eye.
	Neovascular age-related macular degeneration (nAMD)	The recommended dose is 6 mg (0.05 mL) by intravitreal injection every 4 weeks for the first 4 doses, followed by one of the following three regimens: 1) Weeks 28 and 44; 2) Weeks 24, 36, and 48; or 3) Weeks 20, 28,

		36 and 44. Although most patients require dosing every 8 weeks, some patients may need dosing every 4 weeks. Maximum of 12 doses per year per eye.
	Macular Edema Following Retinal Vein Occlusion (RVO)	The recommended dose for is 6 mg (0.05 mL of 120 mg/mL) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for 6 months
Susvimo (ranibizumab injection)	Neovascular Age-related Macular Degeneration	The recommended dose of is 2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the implant with refills every 24 weeks (approximately 6 months).
Visudyne (verteporfin for injection)	Classic subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration (AMD), pathologic myopia or presumed ocular histoplasmosis	The recommended dose is 6 mg/m2 body surface area.

General Background

Age-related macular degeneration (AMD) and diabetic macular edema or retinopathy is among the leading causes of severe vision loss in people over the age of 65 years in the United States[2.] In the United States, an estimated 11 million Americans suffer from AMD, a disease that causes deterioration of the central vision, which is necessary for day to day activities. According to the American Academy of Ophthalmology Neovascular AMD is considered the most advanced form of AMD and leads to faster vision loss. It is responsible for approximately 90 percent of all cases
of AMD. The prevalence of diabetic macular edema increases with the duration of diabetes and it is the most common cause of visual impairment in diabetic patients.
Avastin® (bevacizumab), Lucentis®(ranibizumab) and Eylea® (Aflibercept) are vascular endothelial growth factor receptor (VEGF) inhibitors that have been shown to be effective in treating neovascular age-related macular edema (AMD), macular edema due to diabetes (i.e. proliferative diabetic retinopathy) and macular edema due to retinal vein occlusion. Intravitreal injection of these drugs can limit the progression of neovascular AMD and stabilize, or reverse visual loss as well as improve vascular function. Bevacizumab and ranibizumab are closely-related antibodies. Ranibizumab is an antibody fragment (Fab fragment) of bevacizumab with some modifications to the amino acid sequence that increase its binding of VEGF. Aflibercept is a recombinant fusion protein consisting of portions of human VEGF receptors 1 and 2 domains fused to the Fc portion of human IgG1.

Visudyne® (verteporfin) is a light-activated reconstituted drug for intravenous administration. Visudyne® therapy is a two-stage process requiring administration of both verteporfin for injection and non-thermal red lights. Verteporfin therapy is used to reduce or delay the loss of vision caused by leakage of the abnormal blood vessels. This drug was first approved by the FDA on April 12, 2000, and approved for inclusion in the United States Pharmacopoeia on July 18, 2000, meeting Medicare's definition of a drug when used in conjunction with Ocular photodynamic therapy, and furnished intravenously incident to a physician's service.
Beovu® (Brolucizumab-DBLL) is a human vascular endothelial growth factor (VEGF) inhibitor that binds to 3 major isoforms of VEGF-A [VEGF (110), VEGF (121), and VEGF (165)]. Prevented interaction of VEGF-A with VEGFR-1 and VEGFR-2 results in suppression of endothelial cell proliferation, neovascularization, and vascular permeability.
Beovu is contraindicated for use in patients with Ocular or periocular infections and those with Active intraocular inflammation.
Vabysmo (faricimab-svoa) is a bispecific antibody that blocks both vascular endothelial growth factor-A (VEGF-A) as well as angiopoietin-2 (Ang-2). By inhibiting VEGF-A, faricimab suppresses endothelial cell proliferation, neovascularization, and vascular permeability. By inhibiting Ang-2, faricimab is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A. Ang-2 levels are increased in some patients with nAMD and DME.
Susvimo is Ranibizumab intravitreal implant. The Susvimo implant provides a continuous release of ranibizumab where the release of ranibizumab into the vitreous decreases over time as the concentration in the implant decreases with a half-life of approximately 25 weeks. The ranibizumab serum concentrations with a SUSVIMO 24-week treatment interval are maintained below the maximum and above the minimum concentrations experienced with monthly 0.5 mg intravitreal ranibizumab.
The Susvimo Intraocular implant has a Black Box Warning- It has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab. In clinical trials, 2.0% of patients receiving an implant experienced an episode of endophthalmitis.

Clinical Evidence

The American Academy of Ophthalmology (AAO) supports the use of intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.
In their Diabetic Retinopathy Preferred Practice Pattern, the AAO states that intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents have been shown to be an effective treatment for center-involving diabetic macular edema and also as an alternative therapy for proliferative diabetic retinopathy.

In their Retinal Vein Occlusions Preferred Practice Pattern, the AAO states that Macular edema may complicate both CRVOs and BRVOs. The safest treatment for the associated macular edema is the use of antivascular endothelial growth factors (anti-VEGFs). Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation in BRVO has a potential role in treatment.

Diabetic Macular Edema
Aflibercept, brolucizumab-dbll, faricimab, ranibizumab and ranibizumab-eqrn are indicated for the treatment of diabetic macular edema (DME).
Virgili et al. evaluated the effects in preserving and improving vision and acceptability, including the safety, compliance with therapy and quality of life, of antiangiogenic therapy with anti-VEGF modalities for the treatment of diabetic macular oedema (DMO). A database search was conducted which included randomized controlled trials (RCTs) comparing any antiangiogenic drugs with an anti-VEGF mechanism of action versus another treatment, sham treatment or no treatment in people with DMO. The primary outcome measured was the proportion of people improving or losing vision by three or more lines. Eighteen studies were included in this review. Approximately one in five people gained 3 lines of vision, using antiangiogenic therapy compared with laser, using seven to nine intraocular injections in the first year, and three or four injections in the second year. Benefits were also detected when the drug was compared to no treatment and when it was added to photocoagulation and compared to photocoagulation alone. Antiangiogenic treatment was well tolerated in these studies, with few reported injection-related adverse events and no increase in the number of reported overall and cardiovascular adverse events. Researchers concluded that the evidence utilized in the review was of high quality regarding efficacy compared to laser photocoagulation, the standard treatment, because the effects were large and consistent between studies. The evidence was also of moderate quality regarding safety, since safety had to be confirmed in patients with higher morbidity, particularly regarding cardiovascular risk.

Two randomized, multi-center, double-masked, active comparator-controlled 2-year studies (YOSEMITE – NCT03622580 and RHINE – NCT03622593) assessed the safety and efficacy of **faricimab (Vabysmo**) in patients with DME. Patients (n = 1,891) with diabetes were enrolled in the two studies with a total of 1,262 patients treated with at least one dose of faricimab. Patient ages ranged from 24 to 91 years old (mean = 62.2 years). The overall population included both anti-VEGF naïve patients (78%) and patients who had been previously treated with a VEGF inhibitor prior to study participation (22%). The studies were identically designed, 2 year studies. Patients were randomized in a 1:1:1 ratio to one of three treatment regimens: 1) aflibercept Q8W, patients received fixed aflibercept 2 mg administered every 8 weeks (Q8W) after the first five monthly doses; 2) faricimab Q8W, patients received fixed faricimab 6 mg administered Q8W after the first six monthly doses; and 3) faricimab variable, patients received faricimab 6 mg administered every 4 weeks for at least four doses and until the central subfield thickness (CST) of the macula measured by optical coherence tomography was less than approximately 325 microns, then

the interval of dosing was modified by up to 4 week interval extensions or reductions in up to 8 week interval increments based on CST and visual acuity disease activity criteria at study drug dosing visits. After 4 initial monthly doses, the patients in the faricimab variable arm could have received between the minimum of three and the maximum of eleven total injections through Week 56 inclusive. At Week 56, 32% of patients had completed at least one Q12W interval followed by one full Q16W interval. Seventeen percent (17%) of patients were treated on Q8W and/or Q4W dosing intervals through Week 56 (7% only on Q4W). These percentages are reflective of what happened within the conduct of these trials, but the percentages are not generalizable to a broader DME population due to the inclusion/exclusion criteria limited enrollment to a select subset of DME patients and that there is no empirical data that a similar magnitude would be observed if eligibility criteria allowed for broader enrollment. Both studies demonstrated non-inferiority to the comparator control (aflibercept) at the primary endpoint, defined as the mean change from baseline in BCVA at year 1 (average of the week 48, 52, and 56 visits), measured by the ETDRS Letter Score. The primary endpoint analysis was a non-inferiority comparison for the mean change in BCVA between the aflibercept and faricimab groups. In both studies, faricimab Q8W and faricimab variable treated patients had a mean change from baseline in BCVA that was noninferior to the patients treated with aflibercept Q8W. Clinical efficacy for the second year study has not been reviewed.79

The safety and efficacy of **Beovu** were assessed in two randomized, multi-center, double-masked, active controlled studies (KESTREL – NCT03481634 and KITE - NCT03481660) in patients with DME. A total of 926 patients were treated in these studies for 1 year (558 on brolucizumab and 368 on aflibercept 2 mg). Patient ages ranged from 23 to 87 years with a mean of 63 years. In KESTREL, patients were randomized in a 1:1:1 ratio to the following dosing regimens: 1) brolucizumab 6 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 6 mg every 8 or 12 weeks, 2) brolucizumab 3 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 3 mg every 8 or 12 weeks, and 3) aflibercept 2 mg administered once every 4 weeks for first 5 doses, followed by aflibercept 2 mg every 8 weeks. In KITE, patients were randomized in a 1:1 ratio to the following dosing regimens: 1) brolucizumab 6 mg administered once every 6 weeks for first 5 doses, followed by brolucizumab 6 mg every 8 or 12 weeks and 2) aflibercept 2 mg administered once every 4 weeks for first 5 doses, followed by aflibercept 2 mg every 8 weeks. In both studies, after the first five doses (Weeks 0, 6, 12, 18 and 24), brolucizumab patients were treated every 12 weeks, with the option of adjusting to an every 8 week dosing interval based on disease activity. Disease activity was assessed by changes in visual acuity and/or anatomical parameters, including central subfield thickness CST and/or presence of IRF/SRF although the utility of the specific action parameters used has not been established. Disease activity was assessed by a physician during the first 12 week interval (at Weeks 32 and 36) and at each subsequent scheduled 12 week treatment visit. Patients who showed disease activity at any of these visits were adjusted to an every 8 week treatment interval. The comparator aflibercept was administered every 8 weeks after the first 5 monthly doses. The primary efficacy endpoint for both studies was the change from baseline to Week 52 in Best Corrected Visual Acuity (BCVA) as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score with the primary objective being to demonstrate non-inferiority of Beovu vs. aflibercept 2 mg. In both studies, Beovu was non-inferior to aflibercept 2 mg for the change in BCVA from baseline to Week 52 and the change from baseline over the period Week 40 through Week 52. After 5 initial q6w loading doses, the patients in the Beovu arm could have received between the minimum of 2 and maximum of 3 additional injections through Week 52. At Week 52, the median number of injections given over 12 months was 7 in patients treated with Beovu. Through Week 52, 55% (KESTREL) and 50% (KITE) of patients remained on Beovu every 12 weeks. The probability of remaining on every 12-week dosing from Week 36 to Week 52 was 88% and 95% in KESTREL and KITE, respectively. Treatment effects in evaluable subgroups (i.e. age, gender, baseline HbA1c, baseline visual acuity, baseline central subfield thickness, DME lesion type, duration of DME since diagnosis, retinal fluid status) in each study were

generally consistent with the results in the overall population. In both studies, Beovu demonstrated a significant reduction from baseline in CST starting at Week 4 and continuing up to Week 52.

Neovascular Age-Related Macular Degeneration (AMD)
Aflibercept, pegaptanib, ranibizumab, and brolucizumab-DBLL are indicated for the treatment of neovascular age-related macular degeneration.

Solomon et al evaluated the ocular and systemic effects of, and quality of life associated with, intravitreally injected anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) for the treatment of neovascular AMD compared with no anti-VEGF treatment; and the relative effects of one anti-VEGF agent compared with another when administered in comparable dosages and regimens.21 A database search identified 12 randomized controlled trials which included 5496
patients with neovascular AMD. Patients treated with any of the three anti-VEGF agents more often experienced improved vision, less often lost vision, and were less likely to be legally blind than patients treated with control interventions after one year of treatment. Additionally, these patients also showed improvements in structural areas of the eye that doctors use to monitor disease progression and treatment response compared with untreated patients. Compared with control treatments, treatment with ranibizumab or bevacizumab yielded larger improvements than pegaptanib. No trial compared pegaptanib directly with other anti-VEGF agents. When bevacizumab and ranibizumab were compared with each other, there were no major differences with respect to vision-related outcomes; there was, however, a large difference in cost between the two agents. Inflammation and increased pressure in the eye were the most common vision-related adverse events with anti-VEGF agents. Endophthalmitis was reported in < 1% of anti- VEGF-treated patients and no cases were reported in control groups. The occurrence of serious adverse health effects, such as high blood pressure and internal bleeding, was comparable across anti-VEGF-treated groups and control groups; however, the number of events was small relative to the number of people in the studies making it difficult to detect any meaningful differences between groups. Few data were available for visual function (e.g., reading speed and critical print size), quality of life, and economic outcomes. The overall quality of the evidence was very good, with most trials having an overall low risk of bias. The results of the review indicated the effectiveness of anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) in terms of maintaining visual acuity; ranibizumab and bevacizumab were also shown to improve visual acuity. The information available on the adverse effects of each medication do not suggest a higher incidence of potentially vision-threatening complications with intravitreal injection compared with control interventions; however, clinical trial sample sizes may not have been sufficient to detect rare safety outcomes.

Mean best-corrected visual acuity change from baseline to week 48 was noninferior with brolucizumab-dbll 6 mg compared with aflibercept 2 mg in the 2-year randomized HAWK and HARRIER studies. After the loading phase, patients without disease activity received brolucizumab-dbll maintenance treatments every 12 weeks. Overall safety was similar between brolucizumab-dbll and aflibercept.

Two identically designed, randomized, multi-center, double-masked, active comparator-controlled, 2-year studies (TENAYA – NCT03823287 and LUCERNE – NCT03823300) assessed the safety and efficacy of faricimab in patients with nAMD. Patients (N=1329) were newly diagnosed and treatment-naïve with ages ranging from 50 to 99 (meaN = 75.9 years). Patients were randomized in a 1:1 ratio to one of two treatment arms: 1) aflibercept 2 mg administered fixed every 8 weeks after three initial monthly doses; and faricimab 6 mg administered by intravitreal injection every 4 weeks for the first 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to determine whether to give a 6 mg dose via intravitreal injection on one of the following three regimens: 1) Weeks 28 and 44 (Q16W dosing); 2) Weeks 24, 36, and 48 (Q12W dosing); or 3) Weeks 20, 28, 36, and 44 (Q8W dosing). At week 48, after 4 initial monthly doses in the faricimab arm, 45% of patients received Q16W dosing, 33%

of patients received Q12W dosing, and the remaining 22% of patients received Q8W dosing. Both studies demonstrated non-inferiority to the comparator control (aflibercept) at the primary endpoint, defined as the mean change from baseline in Best Corrected Visual Acuity (BCVA) when averaged over the week 40, 44, and 48 visits and measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter chart. The primary endpoint analysis was a non-inferiority comparison for the mean change in BCVA between the aflibercept and the faricimab arm.
In both studies, faricimab-treated patients had a non-inferior mean change from baseline in BCVA compared to patients treated with aflibercept. The clinical efficacy for the second year of the study has not been reviewed.

Woo et al. evaluated the equivalence of efficacy, similar safety, and similar immunogenicity of a ranibizumab biosimilar product (SB11) compared with the reference ranibizumab with neovascular age-related macular degeneration in a randomized, doublemasked, parallel-group phase 3 equivalence study. The study was conducted in 75 centers in 9 countries from March 14, 2018 to December 9, 2019, among 705 participants 50 years or older with neovascular age-related macular degeneration with active subfoveal choroidal neovascularization lesions. Patients were randomized in a 1:1 ratio to receive intravitreous injection of either SB11 or ranibizumab, 0.5 mg, every 4 weeks through week 48. Preplanned interim analysis after all participants completed the week 24 assessment of primary efficacy end points at week 8 for change from baseline in best-corrected visual acuity (BCVA) and week 4 for central subfield thickness (CST), with predefined equivalence margins for adjusted treatment differences of −3 letters to 3 letters for BCVA and −36 µm to 36 µm for CST. Least-squares mean (SE) changes in BCVA from baseline at week 8 were 6.2 (0.5) letters in the SB11 group vs 7.0 (0.5) letters in the ranibizumab group. Least-squares mean (SE) changes in CST from baseline at week 4 were −108 (5) µm in the SB11 group vs −100 (5)µm in the ranibizumab group. Incidences of treatment-emergent adverse events (231 of 350 [66.0%] vs 237 of 354 [66.9%]), including serious treatment emergent adverse events (44 of 350 [12.6%] vs 44 of 354 [12.4%]) and treatment-emergent adverse events leading to study drug discontinuation (8 of 350 [2.3%] vs 5 of 354 [1.4%]), were similar in the SB11 and ranibizumab groups. Immunogenicity was low, with a cumulative incidence of antidrug antibodies up to week 24 of 3.0% (10 of 330) in the SB11 group and 3.1% (10 of 327) in the ranibizumab group. These findings of equivalent efficacy and similar safety and immunogenicity profiles compared with ranibizumab support the use of SB11 for patients with neovascular age-related macular degeneration.

Macular Edema Secondary to BRVO/CRVO

Afilbercept and ranibizumab are indicated for the treatment of macular edema following retinal vein occlusion (RVO).6,7 The efficacy and safety of intravitreal bevacizumab injections into eyes with macular edema secondary to central retinal vein occlusion (CRVO) was evaluated in a prospective clinical trial (n=45 eyes) by Zhang et al.20 Study subjects were treated with 3 initial intravitreal bevacizumab injections of 1.25 mg at monthly intervals. Retreatment was based on central retinal thickness (CRT) measured by optical coherence tomography (OCT) performed monthly, while fluorescein angiography was performed every 3 months. Main outcome parameters were visual acuity (VA, using the Early Treatment of Diabetic Retinopathy Study protocol) and CRT in an 18-month follow-up period. Mean VA increased from 40.9 letters at baseline to 61.9 letters (+21 letters; $p<0.001$) at month 18; CRT decreased from 572.3 µm at baseline to 273.2 µm at month 18 (-299.1 µm; $p<0.001$). Neither age, duration of CRVO, baseline VA, nor baseline CRT was correlated with the change in VA. No drug-related systemic or ocular side effects were observed following intravitreal bevacizumab treatment.

Choroidal Neovascularization Secondary to Pathologic Myopia

Ranibizumab, ranibizumab-eqrn, and ranibizumab-nuna are indicated for the treatment of choroidal neovascularization secondary to pathologic myopia.

Cha DM et al compared the long-term efficacy of versus bevacizumab for myopic choroidal neovascularization (CNV) in retrospective, multicenter, comparative, non-randomized study in 64 consecutive patients [ranibizumab (N = 22) or bevacizumab (N = 42 patients)].9 Best-corrected visual acuity (BCVA) and central foveal thickness (CFT) on optical coherence tomography were evaluated before and after treatment. All the patients were followed for at least 12 months. BCVA (logarithm of the minimal angle of resolution) improved from 0.63 ±0.30 to 0.43 ±0.27, 0.41 ±0.37, 0.40 ±0.39, 0.39 ±0.43, and 0.39 ±0.42 at 1, 2, 3, 6, and 12 months after treatment in the ranibizumab group, and from 0.67 ±0.28 to 0.52 ±0.31, 0.49 ±0.31, 0.4 7±0.31, 0.42 ±0.32, and 0.46 ±0.43 in the bevacizumab group (all $P < 0.05$ compared with baseline BCVA in each group). CFT decreased by 20.21%, 19.58%, and 22.43% from the baseline 304 ±76 µm at 3, 6, and 12 months after treatment in the former group, and by 15.20%, 15.67%, and 15.56% from the baseline 297 ±62 µm in the latter group (all $P < 0.05$ compared with baseline CFT in each group). BCVA improvement and CFT reduction did not statistically differ when compared at the same periods from treatment between 2 groups. Neither ocular nor systemic safety problems appeared during follow up. Researchers concluded that the outcomes of the study showed a similar functional and anatomical improvement after treatment for ranibizumab and bevacizumab in patients with myopic CNV over a 12-month follow-up period.

In a phase III, 12-month, randomized, double-masked, multicenter, active-controlled study, researchers evaluated the efficacy and safety of ranibizumab 0.5 mg, guided by visual acuity (VA) stabilization or disease activity criteria, versus verteporfin photodynamic therapy (vPDT) in patients (N = 277) with visual impairment due to myopic choroidal neovascularization (CNV).11 Patients were randomized to receive ranibizumab on day 1, month 1, and thereafter as needed guided by VA stabilization criteria (group I, N = 106); ranibizumab on day 1 and thereafter as needed guided by disease activity criteria (group II, N = 116); or vPDT on day 1 and disease activity treated with ranibizumab or vPDT at investigators' discretion from month 3 (group III, N = 55). Primary outcomes measured included average best-corrected visual acuity (BCVA) change from baseline to month 1 through months 3 (primary) and 6, mean BCVA change and safety over 12 months. Ranibizumab treatment in groups I and II was superior to vPDT based on mean average BCVA change from baseline to month 1 through month 3 (group I: + 10.5, group II: + 10.6 vs. group III: + 2.2 Early Treatment Diabetic Retinopathy Study [ETDRS] letters; both $P < 0.0001$). Ranibizumab treatment guided by disease activity was noninferior to VA stabilization-guided retreatment based on mean average BCVA change from baseline to month 1 through month 6 (group II: + 11.7 vs. group I: + 11.9 ETDRS letters;

P < 0.00001). Mean BCVA change from baseline to month 12 was + 13.8 (group I), + 14.4 (group II), and + 9.3 ETDRS letters (group III). At month 12, 63.8% to 65.7% of patients showed resolution of myopic CNV leakage. Patients received a median of 4.0 (group I) and 2.0 (groups II and III) ranibizumab injections over 12 months. No deaths or cases of endophthalmitis and myocardial infarction occurred. CONCLUSIONS: Ranibizumab treatment, irrespective of retreatment criteria, provided superior BCVA gains versus vPDT up to month 3. Ranibizumab treatment guided by disease activity criteria was noninferior to VA stabilization criteria up to month 6. Over 12 months, individualized ranibizumab treatment was effective in improving and sustaining BCVA and was generally well tolerated in patients with myopic CNV.

Yoon et al. compared visual outcomes after treatment with intravitreal antivascular endothelial growth factor (anti-VEGF) injection or photodynamic therapy (PDT) in patients with myopic choroidal (CNV).23 One hundred and forty-two eyes of 128 consecutive patients treated with anti-VEGF (ranibizumab or bevacizumab) and/or PDT for myopic choroidal neovascularization were retrospectively reviewed. Patients were categorized into 3 groups: PDT (51 eyes), anti-VEGF (63 eyes), and a combination group (PDT with anti-VEGF) (28 eyes). Corrected visual acuity values at baseline and 3, 6, 9, and 12 months after treatment were compared. The anti-VEGF group showed significant postoperative improvement in visual acuity compared with the PDT and combination groups (P = 0.01 and 0.04, respectively). The anti-VEGF group demonstrated visual improvement from baseline at every follow-up visit after treatment (P = 0.04, 0.02, 0.01, and 0.002, respectively). The anti-VEGF group showed visual improvement (Snellen equivalent) from 0.57 logarithm of the minimum angle of resolution (0.27) to 0.33 logarithm of the minimum angle of resolution (0.47) (P = 0.01). Furthermore, 98.4% of patients in the anti-VEGF group and 92.8% of those in the combination group lost < 15 letters from baseline visual acuity compared with 72.6% in the PDT group (P = 0.001 and 0.02, respectively). In the anti-VEGF group, 39.7% of patients improved from baseline by 15 or more letters compared with 17.7% in the PDT group (P = 0.02) and 21.4% in the combination group (P = 0.07). Based on these findings, the investigators concluded that intravitreal anti-VEGF injection is superior to PDT alone or a combination of PDT with anti-VEGF for treating myopic choroidal neovascularization.

Vadalà et al. assessed the efficacy and safety of ranibizumab in the treatment of choroidal neovascularisation (CNV) caused by pathologic myopia (PM) in a prospective, multicentre, interventional case series. Ranibizumab was an effective treatment for stabilizing and improving vision with a low number of injections in 92.5% of patients with myopic CNV in a long-term follow-up.

Proliferative Diabetic Retinopathy

Aflibercept, ranibizumab, and ranibizumab-eqrn are indicated for diabetic retinopathy [(Non Proliferative Diabetic Retinopathy (NPDR), Proliferative Diabetic Retinopathy (PDR)].5,7,84 Intravitreal bevacizumab has been studied as an adjunct to laser photocoagulation, to facilitate pars plana vitrectomy, and as a monotherapy for treatment of proliferating diabetic retinopathy (PDR).17,59-60 Ahmadieh et al. evaluated the effect of preoperative intravitreal bevacizumab (IVB) injections on the rate of early (≤ 4 weeks) post vitrectomy hemorrhage in patients (N = 68) with proliferative diabetic retinopathy.18 Subjects were randomly assigned to receive either 1.25 mg IVB (N = 35) one week prior to surgery or control (N = 33). The primary outcome measure was the incidence of early post vitrectomy hemorrhage. Secondary outcome measures included changes in best-corrected visual acuity (BCVA) and IVB-related adverse events. In the intention-to-treat analysis, the incidence of post vitrectomy hemorrhage 1 week and 1 month after surgery was significantly lower in the IVB group compared with the control group (P = 0.023 and P = 0.001, respectively). Mean BCVA improved from 1.88 logarithm of minimum angle of resolution (logMAR) units in both study groups before surgery to 0.91 logMAR units and 1.46 logMAR units 1 month after vitrectomy in the IVB and control groups, respectively (P = 0.001). Resolution of vitreous hemorrhage was observed in 9 eyes (25.7%) after IVB injection, obviating the need for vitrectomy; the corresponding figure was 2 eyes (6.1%) in the control group (P = 0.028). The

per-protocol analysis included 16 eyes in the IVB group and 18 eyes in the control group; post vitrectomy hemorrhage occurred less frequently 1 week and 1 month after surgery in the IVB group compared with the control group (P = 0.033 and P = 0.003, respectively). Mean improvement in BCVA 1 month after vitrectomy was -1.05 logMAR units in the IVB group and -0.42 logMAR units in the control group (P = 0.004). No IVB-related complication was observed in the treatment group. The investigators concluded that IVB one week before vitrectomy appears to reduce the incidence of early post vitrectomy hemorrhage in diabetic patients. The need for vitrectomy may be decreased significantly in these cases as well.

In order to evaluate the safety and effectiveness of intravitreal bevacizumab (IVB) as an adjunct to vitrectomy, di Lauro et al. performed a randomized controlled trial on 72 eyes of 68 patients affected by vitreous hemorrhage (VH) and tractional retinal detachment (TRD) which occurred as a consequence of active proliferative diabetic retinopathy (PDR).19 Participants were assigned in a 1:1:1 ratio to receive a placebo injection or an intravitreal injection of 1.25 mg of bevacizumab, either 7 or 20 days before the vitrectomy. Complete ophthalmic examinations and color fundus photography were performed at baseline and 1, 6, 12, and 24 weeks after the surgery. In the placebo group, intraoperative bleeding occurred in 19 cases (79.1%), the use of endodiathermy was necessary in 13 patients (54.1%), relaxing retinotomy was performed on one patient (4.1%), and in four cases (16.6%) iatrogenic retinal breaks occurred. The surgical mean time was 84 minutes (SD 12 minutes). In subjects receiving IVB seven days prior to vitrectomy, intraoperative bleeding occurred in two cases (8.3%) and the use of endodiathermy was necessary in two patients (8.3%). No iatrogenic breaks occurred during the surgery. The surgical mean time was 65 minutes (SD 18 minutes). For those subjects receiving IVB twenty days before vitrectomy, intraoperative bleeding occurred in three cases (12.5%), the use of endodiathermy was necessary in three patients (1.5%), and an iatrogenic break occurred in one patient (4.1%) while the delamination of fibrovascular tissue was being performed. The surgical mean time was 69 minutes (SD 21 minutes). The average difference in the surgical time was statistically significant between the placebo group and the 7-day IVB group (P = 0.025), and between the placebo group and the 20-day IVB group (P = 0.031). At completion of surgery, the retina was completely attached in all eyes. The researchers concluded that best surgical results are achieved performing the IVB 7 days preoperatively.

Efficacy and safety data of Eylea HD in DR are derived from the PHOTON study. In the PHOTON study, a key efficacy outcome was the change in the ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS). The proportion of patients achieving ≥ 2step improvement on ETDRS-DRSS was similar between the Eylea HD every 12 weeks and Eylea every 8 weeks. The Eylea HD every 16-week treatment arm did not meet the non-inferiority criteria for the proportion of patients with a ≥ 2-step improvement on ETDRS-DRSS and is not considered clinically equivalent to Eylea administered every 8 weeks.

HCPCS Code

HCPCS Code	Description	Dosage Form	Route Of Admin: *IV: Intravenously IVI: Intravitreal injection*
J0178	Aflibercept injection (Eylea) 1mg	2mg/0.05 mL solution in a single-dose pre-filled syringe or in a single-dose vial	IVI
J2778	Ranibizumab injection (Lucentis) 0.1mg	10 mg/mL solution (0.5 mg) 6 mg/mL solution (0.3 mg)	IVI
J0179	Brolucizumab-dbll, injection (Beovu) 1mg	6 mg/0.05 mL solution in single dose vial or single dose pre-filled syringe	IVI
J3396	Verteporfin, injection (Visudyne) 0.1mg	15 mg of verteporfin single-dose vial for reconstitution Reconstituted solution concentration is 2 mg/mL per vial	IV
J2777	Faricimab-svoa, injection (Vabysmo) 0.1mg	120 mg/mL solution in a single-dose vial	IVI
J2779	Ranibizumab implant, (Susvimo) 0.1 mg	100 mg/mL solution in a single-dose vial	IVI
Q5124	Ranibizumab-nuna injection, (Byooviz) 0.1mg	10 mg/mL solution in single dose vial (0.05 mL)	IVI
Q5128	Ranibizumab-eqrn (Cimerli) 0.1mg	10 mg/mL solution (0.5 mg) 6 mg/mL solution (0.3 mg)	IVI
C9399	Unclassified drugs or biologics (Eylea HD)	8mg (0.07mL of 114.3mg/mL solution) in a single-dose vial	IVI
J3490	Unclassified drug (Eylea HD)	8mg (0.07mL of 114.3mg/mL solution) in a single-dose vial	IVI
J9035	Injection, bevacizumab, 10 mg (Avastin)	Compounded medication	IVI
J3590	Unclassified biologics (Eylea HD)	8mg (0.07mL of 114.3mg/mL solution) in a single-dose vial	IVI

Acronyms

AMD = Age-related macular degeneration,

anti-VEGF = anti- vascular endothelial growth factors,

CNV = Choroidal neovascularization,

NCD = National Coverage Determinations,

LCD = Local Coverage Determinations ,

FA = Fluorescein angiogram,

VMA = Vitreomacular adhesion,

RCT = Randomized controlled trial,

AAO = American Academy of Ophthalmology,

OCT = Optical coherence tomography,

CRT = Central retinal thickness,

VA = Visual acuity

BCVA = Best Corrected Visual Acuity

ETDRS = Early Treatment Diabetic Retinopathy Study

CST = Central subfield thickness

SRF/IRF = Subretinal fluid /intraretinal fluid

BRVO = Branch retinal vein occlusion

CRVO = Central retinal vein occlusion

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