

<b>Subject:</b>	Selective Vascular Endothelial Growth Factor (VEGF) Antagonists		
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## Overview

This document addresses the use of intravitreal vascular endothelial growth factor (VEGF) antagonists. Overexpression of VEGF is thought to contribute to diabetic retinopathy, and other retinal disorders associated with neovascularization. Avastin (bevacizumab) is humanized anti-VEGF antibody which blocks all VEGF isoforms. Lucentis (ranibizumab) is a truncated form of bevacizumab. Beovu (brolucizumab) is a humanized single-chain antibody fragment that blocks all VEGF-A isoforms. Eylea (aflibercept) is a recombinant fusion protein that binds to VEGF-A as well as Placental Growth Factor (PlGF). Macugen is an RNA aptamer that binds and neutralizes VEGF.

Avastin is most often used intravenously as an anti-cancer agent. While it is not FDA approved to be used intravitreally or for any ocular conditions; it is widely used in ophthalmology. Compounding pharmacies often repackage Avastin into single-use units for use by ophthalmologists. FDA and the American Academy of Ophthalmology (AAO) have issued warnings regarding the importance of obtaining repackaged Avastin from compounding pharmacies accredited by National Boards of Pharmacy to avoid the potential for contaminated products.

**Age-related macular degeneration (AMD):** AMD is an eye disease characterized by progressive degeneration of the macula and is the leading cause of vision loss in older adults. When AMD results in the development of abnormal blood vessels behind the retina, the condition is commonly referred to as “wet” or neovascular AMD. These new blood vessels tend to be fragile and loss of central vision can occur quickly over the course of weeks to months. Although most patients with advanced AMD do not become completely blind, significant visual loss can lead to disability. The AAO Preferred Practice Pattern (PPP) on AMD states, “Intravitreal injection therapy using anti-VEGF agents (e.g. aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.” Beovu is also approved for the treatment of neovascular age-related macular degeneration and is recommended in the AAO PPP. However, post marketing safety reports and new warnings about retinal vasculitis and/or retinal vascular occlusion have prompted concerns around its relative safety profile. Although Macugen is FDA-approved for AMD, it does not improve visual acuity in patients with new-onset neovascular AMD and is rarely used in current clinical practice.

**Retinal vein occlusion:** A blockage of the blood supply from the retina causes retinal vein occlusion. This condition most often affects older individuals and can be caused by a blood clot, diabetes, glaucoma, atherosclerosis or hypertension. Retinal vein occlusion is the second most common type of retinal vascular disease and is estimated to involve 180,000 eyes per year. The AAO PPP for retinal vein occlusion states, “Macular edema may complicate both central retinal vein occlusions (CRVOs) and branch retinal vein occlusions (BRVOs). The first line of treatment for the associated macular edema is anti-VEGFs.”

**Diabetic retinopathy (DR) and diabetic macular edema (DME):** Diabetic retinopathy is one of the leading causes of blindness in working-age Americans. Approximately 28% of adults with diabetes over the age of 40 develop DR. DR and DME are caused by chronically high blood sugar which disrupts blood flow and causes damage to the tiny blood vessels in the retina. In its most advanced stage, DR can cause new abnormal blood vessels to grow on the surface of the retina, which can lead to scarring and visual disturbance. This severe form is called proliferative diabetic retinopathy (PDR). Sometimes, fluid can leak into the center of the macula, causing the macula to swell, resulting in blurred vision. This is known as diabetic macular edema. Macular edema can occur at any stage of diabetic retinopathy. Intravitreal VEGF injections have shown efficacy in treating DME and in preventing progression of diabetic retinopathy.

**Rare ocular conditions:** Conditions such as neovascular glaucoma, non-myopic causes of choroidal neovascularization, radiation retinopathy, and retinopathy of prematurity have historically been treated with bevacizumab. These conditions represent an unmet medical need as there are limited or no approved therapies. Given the rarity of the conditions, high-quality evidence may not be feasible in these conditions.

Intraocular injections pose a risk for infection, retinal detachment and traumatic lens injury. These injections require the treating physician to adhere to appropriate aseptic technique, educate individuals regarding worrisome symptoms and monitor individuals after each injection as increases in intraocular pressure have been seen.

**Biosimilar Agents:** Biosimilar products must be highly similar to the reference product and there must be no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Biosimilars must utilize the same mechanism of action (MOA), route of administration, dosage form and strength as the reference product; and the indications proposed must have been previously approved for the reference product. The potential exists for a biosimilar product to be approved for one or more indications for which the reference product is licensed based on extrapolation of data intended to demonstrate biosimilarity in one indication. Sufficient scientific justification for extrapolating data is necessary for FDA approval. Factors and issues that should be considered for extrapolation include the MOA for each indication, the pharmacokinetics, bio-distribution, and immunogenicity of the product in different patient populations, and differences in expected toxicities in each indication and patient population. Mvasi (bevacizumab-awwb) and Zirabev (bevacizumab-bvzr) are FDA approved biosimilar agents to Avastin. They share the same FDA approved uses as Avastin, with the exception of Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. These indications remain under orphan drug exclusivity. Neither Mvasi nor Zirabev have been studied in ophthalmic indications. However, since both Mvasi and Zirabev have demonstrated biosimilarity to Avastin for FDA indications, it is reasonable that biosimilarity can be extrapolated to other FDA indications and off-label indications, as well. Byooviz (ranibizumab-nuna) is an FDA approved biosimilar to Lucentis and carries indications for AMD, retinal vein occlusion, and myopic choroidal neovascularization. The FDA approval of Byooviz was based on the totality of evidence demonstrating biosimilarity, including a randomized, double-masked, parallel group, multicenter phase 3 study in 705 patients with wet AMD. Results showed that after 24 weeks of monthly treatment with either Lucentis or Byooviz, the least square mean change in best corrected visual acuity (BCVA) from baseline to week 8 were 6.2 and 7.2 letters, respectively. The adjusted treatment difference between groups was -0.8 letters (90% CI, -1.8 to 0.2 letter), which was within the predefined equivalence limits of -3 to 3 letters. While Byooviz is not FDA approved for diabetic macular edema or diabetic retinopathy, efficacy may be extrapolated based on biosimilarity.

Macugen (pegaptanib) was discontinued by the manufacturer. Criteria will remain active until September 2022 as claims can adjudicate several years after agent discontinuation.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

### Macugen (pegaptanib)

Requests for Macugen (pegaptanib) may be approved if the following criteria are met:

- I. Individual has a diagnosis of established neovascular "wet" age-related macular degeneration.

Requests for Macugen (pegaptanib) may not be approved for the following:

- I. All other indications not included above; **OR**
- II. Diabetic eye disease; **OR**
- III. As a treatment of other forms of age-related macular degeneration to prevent progression to neovascular "wet" age-related macular degeneration.

### Avastin (bevacizumab); Mvasi (bevacizumab-awwb); Zirabev (bevacizumab-bvzr)

Requests for Avastin (bevacizumab), Mvasi (bevacizumab-awwb), or Zirabev (bevacizumab-bvzr) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
  - A. Diabetic macular edema (including individuals with non-proliferative diabetic retinopathy and macular edema) (AAO 2019); **OR**
  - B. Proliferative or moderate to severe non-proliferative diabetic retinopathy with or without diabetic macular edema (AAO2019, DP B IIa); **OR**
  - C. Established neovascular "wet" age-related macular degeneration (AHFS); **OR**
  - D. Macular edema from branch retinal vein occlusion (AAO 2019); **OR**

- E. Macular edema from central retinal vein occlusion (AAO 2019); **OR**
  - F. Neovascular glaucoma (Costagliola 2008, DP B IIb); **OR**
  - G. Choroidal neovascularization associated with myopic degeneration (AAO Consensus 2017, DP B IIb); **OR**
  - H. Other rare causes of choroidal neovascularization for **one or more** of the following conditions (Weber 2016):
    - 1. angioid streaks; **OR**
    - 2. choroiditis (including, but not limited to histoplasmosis induced choroiditis); **OR**
    - 3. retinal dystrophies; **OR**
    - 4. trauma; **OR**
    - 5. pseudoxanthoma elasticum;
- OR**
- I. Radiation retinopathy (Finger 2016); **OR**
  - J. Retinopathy of prematurity (Sankar 2018, DP B IIb).

### Lucentis (ranibizumab); Byooviz (ranibizumab-nuna)

Requests for Lucentis (ranibizumab) or Byooviz (ranibizumab-nuna) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
  - A. Choroidal neovascularization associated with myopic degeneration; **OR**
  - B. Diabetic macular edema (including individuals with non-proliferative diabetic retinopathy and macular edema); **OR**
  - C. Proliferative or moderate to severe non-proliferative diabetic retinopathy with or without diabetic macular edema ; **OR**
  - D. Established neovascular “wet” age-related macular degeneration; **OR**
  - E. Macular edema from branch retinal vein occlusion; **OR**
  - F. Macular edema from central retinal vein occlusion; **OR**
  - G. Radiation retinopathy (Finger 2016).

### Eylea (aflibercept)

Requests for Eylea (aflibercept) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
  - A. Diabetic macular edema (including individuals with non-proliferative diabetic retinopathy and macular edema); **OR**
  - B. Proliferative or moderate to severe non-proliferative diabetic retinopathy with or without diabetic macular edema ; **OR**
  - C. Established neovascular “wet” age-related macular degeneration; **OR**
  - D. Macular edema from branch retinal vein occlusion; **OR**
  - E. Macular edema from central retinal vein occlusion.

### Beovu (brolucizumab-dblI)

Requests for Beovu (brolucizumab-dblI) may be approved if the following criteria are met:

- I. Individual has a diagnosis of established neovascular “wet” age-related macular degeneration.

Requests for intravitreal injections of Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), Eylea (aflibercept), or Beovu (brolucizumab-dblI) may not be approved when the above criteria are not met and for all other indications.

## Step Therapy

**Note:** When an intravitreal VEGF antagonist is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred<sup>1</sup> agent or agents.

A list of the preferred intravitreal VEGF antagonist(s) are available [here](#).

### Non-preferred Intravitreal VEGF Antagonists Step Therapy

Requests for a non-preferred intravitreal VEGF antagonist may be approved when the following criteria are met:

- I. Individual has been on the requested agent;

OR

II. Individual has had a trial and inadequate response or intolerance to one preferred agent:

OR

III. The preferred agents are not FDA-approved and do not have an accepted off-label use per the off-label use policy for the prescribed indication and the requested non-preferred agent does;

OR

IV. If a bevacizumab product (Avastin, Mvasi, Zirabev) is the sole preferred agent approvable for the diagnosis and individual is requesting for a diagnosis other than age-related macular degeneration.

<sup>1</sup>Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

## Quantity Limits

### Vascular Endothelial Growth Factor (VEGF) Antagonists Quantity Limit

Drug	Limit
Eylea (aflibercept) 2 mg vial	2 mg per eye; each eye may be treated as frequently as every 4 weeks
Lucentis (ranibizumab) 0.3 mg, 0.5 mg vial & syringe	<b>Diabetic macular edema and diabetic retinopathy:</b> 0.3 mg per eye; each eye may be treated as frequently as every 4 weeks <b>Age related macular degeneration, branch or central retinal vein occlusion, myopic choroidal neovascularization, and radiation retinopathy:</b> 0.5 mg per eye; each eye may be treated as frequently as every 4 weeks
Byooviz (ranibizumab-nuna) 0.5 mg vial	0.5 mg per eye; each eye may be treated as frequently as every 4 weeks
Macugen (pegaptanib sodium) 0.3 mg prefilled syringe	One syringe (0.3 mg) per eye; each eye may be treated as frequently as every 6 weeks
Avastin (bevacizumab) 100 mg, 400 mg vial; Mvasi (bevacizumab-awwb) 100 mg, 400 mg vial; Zirabev (bevacizumab-bvzr) 100 mg, 400 mg vial (when used for ophthalmologic indications)	1.25 mg per eye; each eye may be treated as frequently as every 4 weeks
Beovu (brolucizumab-dbli) 6 mg vial	6 mg per eye; each eye may be treated as frequently as every 8 weeks**
Override Criteria	
**For Beovu, may approve up to 1 (one) additional single-use vial (6 mg/vial) per eye in the first 8 weeks of treatment.	

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

### Intravitreal injections of pegaptanib [Macugen]

#### CPT

**67028** Intravitreal injection of a pharmacologic agent [*when billed in conjunction with intravitreal injection of pegaptanib HCPCS code listed below*]  
\*Inclusion of this code in the clinical policy is informational only and does not denote a requirement for pre or post service medical necessity review.

#### HCPCS

**J2503** Injection, pegaptanib sodium, 0.3 mg [Macugen]

#### ICD-10 Diagnosis

**H35.3210-H35.3293** Exudative age-related macular degeneration

### Intravitreal injections of bevacizumab [Avastin] [Mvasi] [Zirabev]

## HCPCS

<b>C9257</b>	Injection, bevacizumab, 0.25 mg [Avastin]
<b>J9035</b>	Injection, bevacizumab, 10 mg [when specified as Avastin intravitreal]
<b>Q5107</b>	Injection, bevacizumab-awwb, biosimilar, 10 mg [Mvasi]
<b>Q5118</b>	Injection, bevacizumab-bvzr, biosimilar, 10 mg [Zirabev]

## ICD-10 Diagnosis

<b>B39.0-B39.9</b>	Histoplasmosis
<b>E08.311-E08.3519</b>	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
<b>E08.3521-E08.3599</b>	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
<b>E09.311-E09.3519</b>	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E09.311 and ranges E09.3211-E09.3219, E09.3311-E09.3319, E09.3411-E09.3419, E09.3511-E09.3519, and E09.319 when specified as proliferative diabetic retinopathy]
<b>E09.3521-E09.3599</b>	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E10.311-E10.3519</b>	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, and E10.319 when specified as proliferative diabetic retinopathy]
<b>E10.3521-E10.3599</b>	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E11.311-E11.3519</b>	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, and E11.319 when specified as proliferative diabetic retinopathy]
<b>E11.3521-E11.3599</b>	Type 2 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E13.311-E13.3519</b>	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]
<b>E13.3521-E13.3599</b>	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>H21.1X1-H21.1X9</b>	Other vascular disorders of iris and ciliary body (neovascularization)
<b>H30.001-H30.049</b>	Focal chorioretinal inflammation
<b>H30.101-H30.149</b>	Disseminated chorioretinal inflammation
<b>H30.891-H30.899</b>	Other chorioretinal inflammations
<b>H30.90-H30.93</b>	Unspecified chorioretinal inflammation
<b>H32</b>	Chorioretinal disorders in diseases classified elsewhere
<b>H34.8110</b>	Central retinal vein occlusion, right eye, with macular edema
<b>H34.8120</b>	Central retinal vein occlusion, left eye, with macular edema
<b>H34.8130</b>	Central retinal vein occlusion, bilateral, with macular edema
<b>H34.8190</b>	Central retinal vein occlusion, unspecified eye, with macular edema
<b>H34.8310</b>	Tributary (branch) retinal vein occlusion, right eye, with macular edema
<b>H34.8320</b>	Tributary (branch) retinal vein occlusion, left eye, with macular edema
<b>H34.8330</b>	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
<b>H34.8390</b>	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
<b>H35.00-H35.09</b>	Background retinopathy and retinal vascular changes
<b>H35.101-H35.179</b>	Retinopathy of prematurity
<b>H35.3210-H35.3293</b>	Exudative age-related macular degeneration
<b>H35.33</b>	Angioid streaks of macula
<b>H35.50-H35.54</b>	Hereditary retinal dystrophy
<b>H35.9</b>	Unspecified retinal disorder [specified as radiation retinopathy]

<b>H40.50X0-H40.53X4</b>	Glaucoma secondary to other eye disorders [neovascular glaucoma]
<b>H40.89</b>	Other specified glaucoma [neovascular glaucoma]
<b>H44.20-H44.23</b>	Degenerative myopia
<b>H44.2A1-H44.2A9</b>	Degenerative myopia with choroidal neovascularization
<b>Q82.8</b>	Other specified congenital malformations of skin [pseudoxanthoma elasticum]
<b>T66.XXXA-T66.XXS</b>	Radiation sickness, unspecified [specified as radiation retinopathy]

#### Intravitreal injections of ranibizumab [Lucentis] [Byooviz]

##### CPT

<b>67028</b>	Intravitreal injection of a pharmacologic agent [ <i>when billed in conjunction with intravitreal injection of ranibizumab HCPCS code listed below</i> ] <i>*Inclusion of this code in the clinical policy is informational only and does not denote a requirement for pre or post service medical necessity review.</i>
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##### HCPCS

<b>J2778</b>	Injection, ranibizumab; 0.1 mg [Lucentis]
<b>J3490</b>	Unclassified drugs (when specified as (ranibizumab-nuna) [Byooviz])

##### ICD-10 Diagnosis

<b>E08.311-E08.3519</b>	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
<b>E08.3521-E08.3599</b>	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
<b>E09.311-E09.3519</b>	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E09.311 and ranges E09.3211-E09.3219, E09.3311-E09.3319, E09.3411-E09.3419, E09.3511-E09.3519, and E09.319 when specified as proliferative diabetic retinopathy]
<b>E09.3521-E09.3599</b>	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E10.311-E10.3519</b>	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, and E10.319 when specified as proliferative diabetic retinopathy]
<b>E10.3521-E10.3599</b>	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E11.311-E11.3519</b>	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, and E11.319 when specified as proliferative diabetic retinopathy]
<b>E11.3521-E11.3599</b>	Type 2 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E13.311-E13.3519</b>	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]
<b>E13.3521-E13.3599</b>	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>H21.1X1-H21.1X9</b>	Other vascular disorders of iris and ciliary body (neovascularization)
<b>H34.8110</b>	Central retinal vein occlusion, right eye, with macular edema
<b>H34.8120</b>	Central retinal vein occlusion, left eye, with macular edema
<b>H34.8130</b>	Central retinal vein occlusion, bilateral, with macular edema
<b>H34.8190</b>	Central retinal vein occlusion, unspecified eye, with macular edema
<b>H34.8310</b>	Tributary (branch) retinal vein occlusion, right eye, with macular edema
<b>H34.8320</b>	Tributary (branch) retinal vein occlusion, left eye, with macular edema
<b>H34.8330</b>	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
<b>H34.8390</b>	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
<b>H35.3210-H35.3293</b>	Exudative age-related macular degeneration
<b>H35.9</b>	Unspecified retinal disorder [specified as radiation retinopathy]
<b>H44.20-H44.23</b>	Degenerative myopia
<b>H44.2A1-H44.2A9</b>	Degenerative myopia with choroidal neovascularization



<b>T66.XXXA-T66.XXXS</b>	Radiation sickness, unspecified [specified as radiation retinopathy]
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### Intravitreal injections of aflibercept [Eylea]

#### CPT

<b>67028</b>	Intravitreal injection of a pharmacologic agent [ <i>when billed in conjunction with intravitreal injection of aflibercept HCPCS code listed below</i> ] *Inclusion of this code in the clinical policy is informational only and does not denote a requirement for pre or post service medical necessity review.
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#### HCPCS

<b>J0178</b>	Injection, aflibercept, 1 mg [Eylea]
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#### ICD-10 Diagnosis

<b>E08.311-E08.3519</b>	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
<b>E08.3521-E08.3599</b>	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
<b>E10.311-E10.3519</b>	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, and E10.319 when specified as proliferative diabetic retinopathy]
<b>E10.3521-E10.3599</b>	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E11.311-E11.3519</b>	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, and E11.319 when specified as proliferative diabetic retinopathy]
<b>E11.3521-E11.3599</b>	Type 2 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>E13.311-E13.3519</b>	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]
<b>E13.3521-E13.3599</b>	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
<b>H34.8110</b>	Central retinal vein occlusion, right eye, with macular edema
<b>H34.8120</b>	Central retinal vein occlusion, left eye, with macular edema
<b>H34.8130</b>	Central retinal vein occlusion, bilateral, with macular edema
<b>H34.8190</b>	Central retinal vein occlusion, unspecified eye, with macular edema
<b>H34.8310</b>	Tributary (branch) retinal vein occlusion, right eye, with macular edema
<b>H34.8320</b>	Tributary (branch) retinal vein occlusion, left eye, with macular edema
<b>H34.8330</b>	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
<b>H34.8390</b>	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
<b>H35.3210-H35.3293</b>	Exudative age-related macular degeneration
<b>H35.9</b>	Unspecified retinal disorder [specified as radiation retinopathy]

### Intravitreal injections of (brolucizumab-dbl) [Beovu]

#### CPT

<b>67028</b>	Intravitreal injection of a pharmacologic agent [ <i>when billed in conjunction with intravitreal injection of brolucizumab HCPCS code listed below</i> ] *Inclusion of this code in the clinical policy is informational only and does not denote a requirement for pre or post service medical necessity review.
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#### HCPCS

<b>J0179</b>	J0179 : Injection, brolucizumab-dbl, 1 mg [Beovu]
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#### ICD-10 Diagnosis

<b>H35.3210-H35.3293</b>	Exudative age-related macular degeneration
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## Document History

Revised: 11/19/2021

Document History:

- 01/28/2022 – Step therapy table updates.
- 11/19/2021- Annual Review: Add clinical criteria and quantity limit for new biosimilar Byovoiz; update diabetic retinopathy criteria to include moderate to severe non-proliferative disease; update Lucentis quantity limit to break out by diagnosis for clarity and to include all diagnoses; wording and formatting updates. Step therapy table update. Coding Reviewed: Added HCPCS J3490 for Byovoiz.
- 11/20/2020- Annual Review: Clarify diabetic macular edema applies to individuals with all types of diabetic retinopathy; update step therapy to move Beovu to non-preferred and to allow continuation of use; update references; wording and formatting changes. Coding Reviewed: Removed CPT code 67028 from Avastin.
- 02/21/2020- Select Review: Add bevacizumab products as potential preferred in VEGF step therapy with override; update references. Coding Reviewed: No changes. 7/13/2020 Removed T66.XXXA-T66.XXXS radiation sickness for Eylea per clinical guideline. 8/21/2020-Removed HCPCS J3590, J3490.
- 11/15/2019- Annual Review: Add prior authorization and quantity limit to new agent Beovu; add Beovu as potential preferred to step therapy; update quantity limit override criteria for Lucentis. Added HCPCS 67028, and J0179, and ICD-10-CM H35.3210-H35.3293 for Beovu
- 09/09/2019- Select Review: Wording and formatting updates; add new Eylea dosage form to quantity limits.
- 08/16/2019- Select Review: Add biosimilar Zirabev to bevacizumab criteria; add non-preferred bevacizumab reference and biosimilar step therapy for ophthalmologic indications; add quantity limits to Mvasi and Zirabev. Coding Reviewed: Added HCPCS code Q5118 for Zirabev
- 11/16/2018– Annual Review: Add references for off-label uses; add biosimilar Mvasi to bevacizumab criteria, clarify off-label uses of bevacizumab; remove bevacizumab from step therapy. HCPCS Coding Review: no change. HCPCS Coding Review: Deleted J3490 and J3590 for Mvasi and added Q5107 effective 1/1/2019. Deleted ICD-10 E09.311-E09.3519, E09.3521-E09.3599 from Eylea criteria due to removal of indication for radiation retinopathy. Added HCPCS codes J3490 and J3590 back in for Avastin and Mvasi because NOC codes are used for some intravitreal formulations.

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**ING-CC-0072 Selective VEGF Inhibitors**

**Commercial Medical Benefit**

<b>Effective Date</b>	<b>Preferred Agents</b>	<b>Non-Preferred Agents</b>
10/1/2020	Avastin Mvasi Zirabev Eylea	Lucentis Macugen Beovu
3/1/2022	Avastin Eylea	Lucentis *Byooviz Macugen Beovu

\*Effective 5/1/2022

**Medicaid Medical Benefit**

<b>Effective Date</b>	<b>Preferred Agents</b>	<b>Non-Preferred Agents</b>
1/1/2021 - AR, GA, IA, MD, NJ, NV, NY, SC, TN, VA, WI, WNY  2/1/2021 – CA, LA  3/1/2021 - IN	Avastin Mvasi Zirabev	Eylea Lucentis Macugen Beovu
3/1/2022 – AR,CA, GA, IA, IN, LA, MD, NJ, NV, NY, SC, TN, VA, WI, WNY	Avastin	Eylea Lucentis Macugen Beovu

**Medicare Medical Benefit**

<b>Effective Date</b>	<b>Preferred Agents</b>	<b>Non-Preferred Agents</b>
8/1/2020	Avastin Mvasi Zirabev Eylea	Lucentis Macugen Beovu
3/1/2022	Avastin Eylea	Lucentis Macugen Beovu