

Corporate Medical Policy: Ocular Angiogenesis Inhibitor Agents "Notification" POLICY EFFECTIVE JANUARY 1, 2025

Restricted Product(s):

- brolucizumab-dbll (Beovu®) intravitreal injection for administration by a healthcare professional
- aflibercept (Eylea[®]) intravitreal injection for administration by a healthcare professional
- aflibercept (Eylea[®] HD) intravitreal injection for administration by a healthcare professional
- ranibizumab-nuna (Byooviz[™]) intravitreal injection for administration by a healthcare professional
- ranibizumab-eqrn (Cimerli[™]) intravitreal injection for administration by a healthcare professional
- ranibizumab (Lucentis®) intravitreal injection for administration by a healthcare professional
- ranibizumab (Susvimo[™]) intravitreal implant for administration by a healthcare professional
- faricimab-svoa (Vabysmo®) intravitreal injection for administration by a healthcare professional

FDA Approved Use:

- Brolucizumab-dbll (Beovu[®])
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of diabetic macular edema (DME)
- Aflibercept (Eylea®)
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of macular edema following retinal vein occlusion (RVO)
 - For treatment of diabetic macular edema (DME)
 - For treatment of diabetic retinopathy (DR)
 - For treatment of retinopathy of prematurity (ROP)
- Aflibercept (Eylea[®] HD)
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of diabetic macular edema (DME)
 - For treatment of diabetic retinopathy (DR)
- Ranibizumab (Lucentis[®])
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of macular edema following retinal vein occlusion (RVO)
 - For treatment of diabetic macular edema (DME)
 - For treatment of diabetic retinopathy (DR)
 - For treatment of myopic choroidal neovascularization (mCNV)
- Ranibizumab-nuna (Byooviz[™])



- For treatment of neovascular (Wet) age-related macular degeneration (AMD)
- For treatment of macular edema following retinal vein occlusion (RVO)
- For treatment of myopic choroidal neovascularization (mCNV)
- Ranibizumab-eqrn (Cimerli[™])
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of macular edema following retinal vein occlusion (RVO)
 - For treatment of diabetic macular edema (DME)
 - For treatment of diabetic retinopathy (DR)
 - For treatment of myopic choroidal neovascularization (mCNV)
- Ranibizumab (Susvimo[™])
 - For treatment of neovascular (wet) age-related macular degeneration (AMD) in patients who have previously responded to at least two intravitreal injections of a vascular endothelial growth factor (VEGF) inhibitor

NOTE: On October 18, 2022, Susvimo was voluntarily withdrawn from the market by the manufacturer due to safety concerns related to the septum of the ocular implant. The manufacturer plans to make adjustments to the manufacturing process to resolve safety concerns. Susvimo will be unavailable for new implantation, but continued refill procedures may occur in eligible patients with existing implants.

- Faricimab-svoa (Vabysmo[®])
 - For treatment of neovascular (wet) age-related macular degeneration (AMD)
 - For treatment of diabetic macular edema (DME)
 - For treatment of macular edema following retinal vein occlusion (RVO)

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

- 1. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; OR
- 2. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; OR
- 3. The requested agent is **brolucizumab-dbll (Beovu)**; **AND**
 - a. The patient has ONE of the following diagnoses:
 - i. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR



- ii. Diabetic Macular Edema (DME); AND
- b. BOTH of the following:
 - i. ONE of the following:
 - 1. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; AND
 - ii. ONE of the following:
 - 1. The patient has tried and had an inadequate response to one of the following: aflibercept (Eylea), aflibercept (Eylea HD), ranibizumab (Lucentis), ranibizumab-nuna (Byooviz), ranibizumab-eqrn (Cimerli), faricimab-svoa (Vabysmo) [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all of the following: aflibercept (Eylea), aflibercept (Eylea HD), ranibizumab (Lucentis), ranibizumab-nuna (Byooviz), ranibizumab-eqrn (Cimerli), faricimab-svoa (Vabysmo) [medical record documentation required]; OR
- 4. The requested agent is aflibercept (Eylea); AND
 - a. The patient has ONE of the following diagnoses:
 - i. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR
 - ii. Macular Edema following Retinal Vein Occlusion (RVO); OR
 - iii. Diabetic Macular Edema (DME); OR
 - iv. Diabetic Retinopathy (DR); OR
 - v. Retinopathy of Prematurity (ROP); AND
 - b. ONE of the following:
 - i. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; OR
- 5. The requested agent is aflibercept (Eylea HD); AND
 - a. The patient has ONE of the following diagnoses:
 - i. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR
 - ii. Diabetic Macular Edema (DME); OR
 - iii. Diabetic Retinopathy (DR); AND



- b. ONE of the following:
 - i. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; OR
- 6. The requested agent is ranibizumab (Lucentis); AND
 - a. The patient has a diagnosis of Myopic Choroidal Neovascularization (mCNV); OR
 - b. BOTH of the following:
 - i. The patient has ONE of the following diagnoses:
 - 1. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR
 - 2. Macular Edema following Retinal Vein Occlusion (RVO); OR
 - 3. Diabetic Macular Edema (DME); OR
 - 4. Diabetic Retinopathy (DR); AND
 - ii. ONE of the following:
 - 1. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; OR
- 7. The requested agent is ranibizumab-nuna (Byooviz); AND
 - a. The patient has a diagnosis of Myopic Choroidal Neovascularization (mCNV); OR
 - b. BOTH of the following:
 - i. The patient has ONE of the following diagnoses:
 - 1. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR
 - 2. Macular Edema following Retinal Vein Occlusion (RVO); OR
 - 3. Diabetic Macular Edema (DME); OR
 - 4. Diabetic Retinopathy (DR); AND
 - ii. ONE of the following:
 - 1. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; OR



- 8. The requested agent is ranibizumab-eqrn (Cimerli); AND
 - a. The patient has a diagnosis of Myopic Choroidal Neovascularization (mCNV); OR
 - b. BOTH of the following:
 - i. The patient has ONE of the following diagnoses:
 - 1. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR
 - 2. Macular Edema following Retinal Vein Occlusion (RVO); OR
 - 3. Diabetic Macular Edema (DME); OR
 - 4. Diabetic Retinopathy (DR); AND
 - ii. ONE of the following:
 - 1. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; OR
- 9. The requested agent is ranibizumab (Susvimo); AND
 - a. The patient has a diagnosis of Neovascular (Wet) Age-Related Macular Degeneration (AMD); AND
 - b. BOTH of the following:
 - i. ONE of the following:
 - 1. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; AND
 - ii. ONE of the following:
 - 1. The patient has tried and had an inadequate response to a ranibizumab product (e.g., Byooviz, Cimerli, Lucentis) [medical record documentation required]; OR
 - 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all other ranibizumab products (e.g., Byooviz, Cimerli, Lucentis) that is not anticipated with the requested product [medical record documentation required]; OR
- 10. The requested agent is faricimab-svoa (Vabysmo); AND
 - a. The patient has ONE of the following diagnoses:
 - i. Neovascular (Wet) Age-Related Macular Degeneration (AMD); OR



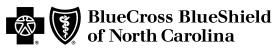
- ii. Diabetic Macular Edema (DME); OR
- iii. Macular Edema following Retinal Vein Occlusion (RVO); AND
- b. ONE of the following:
 - i. The patient has tried and had an inadequate response to bevacizumab intravitreal injection [medical record documentation required]; OR
 - ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all bevacizumab products [medical record documentation required]; AND
- 11. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval: 365 days (1 year)

	FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*	
· /	Related Macular Degeneration (AMD) Diabetic Macular Edema (DME)	 AMD: 6 mg (0.05 mL) administered by intravitreal injection monthly (approximately every 25-31 days) for the first three doses, followed by 6 mg (0.05 mL) once every 8-12 weeks DME: 6 mg (0.05 mL) administered by intravitreal injection every six weeks (approximately every 39-45 days) for the first five doses, followed by 6 mg (0.05 mL) once every 8-12 weeks 	J0179	48 (per treated eye)	



FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
aflibercept (Eylea®) intravitreal injection	Neovascular (Wet) Age- Related Macular Degeneration (AMD) Macular Edema following Retinal Vein Occlusion (RVO)	2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first 3 months, followed by 2 mg (0.05 mL) once every 8 weeks (2 months). [Although dosing may be as frequent as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated in most patients when dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 12 weeks (3 months). Although not as effective as the recommended every 8 week dosing regimen, patients may also be treated with one dose every 12 weeks after one year of effective therapy.]	J0178	ROP: 1.2 (per treated eye) All other
	Diabetic Macular Edema (DME) Diabetic Retinopathy (DR)	 DME: 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 mL) once every 8 weeks (2 months). [Although dosing may be as frequent as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated in most patients when dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).] DR: 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 		diagnoses: 26 (per treated eye)



	FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*	
		frequent as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated in most patients when dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).]			
		ROP: 0.4 mg (0.01 mL or 10 μ L) administered by intravitreal injection. Treatment is initiated with a single injection per eligible eye and may be given bilaterally on the same day. Injections may be repeated in each eye. The treatment interval between doses injected into the same eye should be at least 10 days.			
aflibercept (Eylea [®] HD) intravitreal injection	Related Macular	AMD: 8 mg (0.07 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days) for the first 3 doses, followed by 8 mg (0.07 mL) once every 8 to 16 weeks.			
		DME: 8 mg (0.07 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days) for the first 3 doses, followed by 8 mg (0.07 mL) once every 8 to 16 weeks.	J0177	64 (per treated eye)	
	(DR)	DR: 8 mg (0.07 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days) for the first 3 doses, followed by 8 mg (0.07 mL) once every 8 to 12 weeks.			



FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
ranibizumab-nuna (Byooviz™) intravitreal injection	Neovascular (Wet) Age- Related Macular Degeneration (AMD)	AMD: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days). [Although not as effective, patients may be treated with 3 monthly doses followed by less frequent dosing with regular assessment, or with one dose every 3 months after 4 monthly doses with regular assessment.]		
	Macular Edema Following Retinal Vein Occlusion (RVO)	RVO: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	Diabetic Macular Edema (DME)	DME: 0.3 mg (0.03 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)	Q5124	65 (per treated eye)
	Diabetic Retinopathy (DR)	DR: 0.3 mg (0.03 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	Myopic Choroidal neovascularization (mCNV)	mCNV: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection initially once a month (approximately 28 days) for up to 3 months. May be retreated if needed.		
ranibizumab-eqrn (Cimerli™) intravitreal injection	Related Macular	AMD: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days). [Although not as effective, patients may be treated with 3 monthly	Q5128	65 (per treated eye)



FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
		doses followed by less frequent dosing with regular assessment, or with one dose every 3 months after 4 monthly doses with regular assessment.]		
		RVO: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	Diabetic Macular Edema (DME)	DME: 0.3 mg (0.05 mL of 6 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
		DR: 0.3 mg (0.05 mL of 6 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	5 1	mCNV: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection initially once a month (approximately 28 days) for up to 3 months. May be retreated if needed.		
ranibizumab (Lucentis [®]) intravitreal injection	Neovascular (Wet) Age- Related Macular Degeneration (AMD)	AMD: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days). [Although not as effective, patients may be treated with 3 monthly doses followed by less frequent dosing with regular assessment, or with one dose every 3 months after 4 monthly doses with regular assessment.]	J2778	65 (per treated eye)



FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
	Following Retinal Vein	RVO: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	Diabetic Macular Edema (DME)	DME: 0.3 mg (0.05 mL of 6 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	(DR)	DR: 0.3 mg (0.05 mL of 6 mg/mL solution) administered by intravitreal injection once a month (approximately 28 days)		
	J - I	mCNV: 0.5 mg (0.05 mL of 10 mg/mL solution) administered by intravitreal injection initially once a month (approximately 28 days) for up to 3 months. May be retreated if needed.		
ranibizumab (Susvimo [™]) intravitreal implant		AMD: 2 mg (0.02 mL) continuously administered by intravitreal implant with refills every 24 weeks (approximately every 6 months)	J2779	40 (per treated eye)
faricimab-svoa (Vabysmo®) intravitreal injection	rsmo [®]) Related Macular Degeneration (AMD) itreal injection	Related Macular 6 mg (0.05 mL) administered by intravitreal injection once every 4 weeks (approximately 28 days) for the first 4 doses, then 6 mg	J2777	AMD: 540 (per treated eye)
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	FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*	
		4 weeks compared to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses.]		RVO: 420 (per treated eye)	
	Diabetic Macular Edema (DME)	 DME: 6 mg (0.05 mL) administered by intravitreal injection once every 4 weeks (approximately 28 days) for at least 4 doses, then 6 mg in extensions of every 4 or 8 weeks based on CST and visual acuity evaluations; OR 6 mg (0.05 mL) once every 4 weeks for the first 6 doses, then 6 mg once every 8 weeks (2 months) [Although additional efficacy was not demonstrated in most patients when dosed every 4 weeks compared to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses.] 			
	Macular Edema Following Retinal Vein Occlusion (RVO)	RVO 6 mg (0.05 mL) administered by intravitreal injection once every 4 weeks (approximately every 28) for 6 months			

*Maximum units allowed for duration of approval **Non-specific assigned HCPCS codes, must submit requested product NDC

Other HCPCS codes that may be applicable: C9257

References: all information referenced is from FDA package insert unless otherwise noted below.

- 1. Cheung CMG, Arnold JJ, Holz FG, et al. American Academy of Ophthalmology. Myopic choroidal neovascularization: review, guidance, and consensus statement on management. *Ophthalmology*. 2017;124(11):1690-1711.
- 2. Flaxel CJ, Adelman RA, Bailey ST, et al. American Academy of Ophthalmology. Age-related macular degeneration preferred practice pattern[®]. *Ophthalmology*. 2020 Jan;127(1):1-65.



- 3. Flaxel CJ, Adelman RA, Bailey ST, et al. American Academy of Ophthalmology. Diabetic retinopathy preferred practice pattern[®]. *Ophthalmology*. 2020 Jan;127(1):66-145.
- 4. Flaxel CJ, Adelman RA, Bailey ST, et al. American Academy of Ophthalmology. Retinal vein occlusions preferred practice pattern[®]. *Ophthalmology*. 2020 Feb;127(2):288-320.
- 5. Ho AC, Scott IU, Kim SJ, et al. American Academy of Ophthalmology Ophthalmic Technology Assessment. Anti–vascular endothelial growth factor pharmacotherapy for diabetic macular edema: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2012 Oct;119(10):2179-88.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q4 annually.

January 2025: Criteria change: For Beovu, added requirement for trial and failure of one of the following products: Eylea, Eylea HD, Lucentis, Byooviz, Cimerli, or Vabysmo. For Lucentis, removed requirement for trial and failure of Byooviz and Cimerli. Adjusted maximum units for Eylea, Lucentis, Byooviz, Cimerli, and Vabysmo for clarity according to FDA labeled dosing. Removed Macugen from policy due to market withdrawal and product discontinuation. Additional minor updates made to formatting throughout policy for clarity. **Policy notification given 11/1/2024 for effective date 1/1/2025**.

April 2024: Coding change: Added HCPCS code J0177 for Eylea HD to dosing reference table effective 4/1/2024; deleted C9161, J3490, and J3590 termed 3/31/2024.

January 2024: Criteria change (Vabysmo): Added new indication for Vabysmo for treatment of macular edema following retinal vein occlusion (RVO) with corresponding criteria and dosing table updates.

January 2024: Coding update: Added HCPCS code C9161 for Eyela HD to dosing reference table effective 1/1/2024; deleted C9399 termed 12/31/2023.

September 2023: Criteria update: Added newly approved Eylea HD to policy for treatment of AMD, DME, and DR, with the same criteria requirements as Eylea for the appropriate FDA labeled indications. Added associated dosing and maximum units, and HCPCS codes C9399, J3490, and J3590 to FDA label reference table.

April 2023: Coding update: Added HCPCS code Q5128 for Cimerli to dosing reference table effective 4/1/2023; deleted C9399, J3490, J3590 termed 3/31/2023.

March 2023: Criteria update: Added new indication for Eylea for treatment of retinopathy of prematurity (ROP) with corresponding criteria and dosing table updates.

October 2022: Criteria change: Added new to market product Cimerli to policy as a co-preferred ranibizumab product with corresponding criteria and dosing table updates. Added note indicating temporary voluntary market withdrawal of Susvimo.



October 2022: Coding update: Added HCPCS code J2777 for Vabysmo to dosing reference table and updated maximum units per code definition effective 10/1/2022; deleted C9097, J3490, and J3590 termed 9/30/2022. Adjusted dosing for Byooviz for DME and DR indications in dosing reference table.

August 2022: Criteria change: Added new indication for Beovu for treatment of diabetic macular edema (DME) with corresponding criteria and dosing table updates.

August 2022: Criteria change: For Lucentis requests, added requirement of a documented serious adverse event that required medical intervention to Byooviz that is not anticipated with Lucentis and a submitted MedWatch Adverse Event Reporting form. For Susvimo requests, changed trial and failure requirement to one ranibizumab product (e.g., Byooviz, Lucentis). **Policy notification given 6/1/2022 for effective date 8/1/2022**.

July 2022: Coding update: Added HCPCS code C9097 for Vabysmo and J2779 for Susvimo to dosing reference table and updated units for Susvimo per code definition effective 7/1/2022, deleted C9399 for Vabysmo and C9093, C9399, J3490, and J3590 for Susvimo termed 6/30/2022.

March 2022: Criteria change: Added new to market product Byooviz to policy with corresponding criteria and dosing table updates; added code C9093 for Susvimo

February 2022: Criteria change: Added newly approved Vabysmo to policy for treatment of neovascular (wet) age-related macular degeneration (AMD) and diabetic macular edema (DME) with requirement of trial and failure of bevacizumab; added associated dosing and maximum units to FDA label reference table.

January 2022: Criteria change: Added newly approved Susvimo to policy for treatment of neovascular (wet) age-related macular

degeneration (AMD) with requirement of trial and failure of bevacizumab and Lucentis; added associated dosing and maximum units to FDA label reference table.

October 2021: Criteria change: Added criteria for patients currently being treated with and stable on therapy with the requested agent for at least 180 days, or at risk if therapy is changed.

October 2021: Original medical policy criteria issued. Policy notification given 7/1/2021 for effective date 10/1/2021.