Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/06/2024

Ranibizumab Policy

Byooviz™ (ranibizumab-nuna)
Cimerli™ (ranibizumab-eqrn)
Lucentis® (ranibizumab)
Susvimo™ (ranibizumab)

HCPCS: Byooviz Q5124; Cimerli Q5128; Lucentis J2778; Susvimo J2779

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Treatment with bevacizumab or a bevacizumab biosimilar has been ineffective, not tolerated or contraindicated
   d. For Susvimo only
      i. Must have experienced disease stability or improvement following at least 2 injections in the same eye of either Beovu®, Eylea™, or Lucentis prior to Susvimo therapy
      ii. Supplemental treatment is allowed only with Lucentis if ONE of the following are met:
         a) A decrease in visual acuity by half from the baseline visual acuity
         b) Increase of 150 µm or more in retinal thickness
   e. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met
   f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: For at least 60 days and up to one year at a time
      i. For Susvimo only: Up to 2 supplemental Lucentis injections per affected eye allowed per 6 month refill
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Intravitreal injections of anti-vascular endothelial growth factor (VEGF) have been widely used by ophthalmologists to treat a variety of ocular diseases. They are injected directly into the eye to prevent the formation of new blood vessels and reduce blood vessel leakage and inflammation. The following anti-VEGF therapies are currently available to treat the following indications:
    - Byooviz: macular edema due to retinal vein occlusion (RVO), myopic choroidal neovascularization (mCNV), and neovascular (wet) age-related macular degeneration (AMD)
    - Cimerli: diabetic macular edema (DME), diabetic retinopathy (DR), macular edema due to RVO, mCNV, and wet AMD
    - Lucentis: DME, DR, macular edema due to RVO, mCNV, and wet AMD
    - Susvimo: neovascular AMD in those who have previously responded to at least two intravitreal injections of a VEGF inhibitor
- Age-related Macular Degeneration
    - Age-related macular degeneration is a degenerative disease of the macula that results primarily in loss of central vision. Wet AMD is characterized by growth of abnormal vessels into the subretinal space. These abnormal blood vessels leak leading to collections of subretinal fluid and/or blood beneath the retina. The 2022 American Academy of Ophthalmologists (AAO) Age-Related Macular Degeneration Preferred Practice Pattern Guidelines recommend observation and early detection, antioxidant vitamin and mineral supplements, and intravitreal injections of anti-VEGF agents for the management of wet AMD. Guidelines recommend Eylea™, Avastin®, Vabysmo™, or Lucentis for treatment. The guidelines have not been updated with Beovu®, Byooviz, and Susvimo.
- Diabetic Retinopathy and Diabetic Macular Edema
    - Diabetic retinopathy and DME are common complications and the ocular manifestations of end-organ damage in diabetes mellitus. The 2022 AAO Diabetic Retinopathy Preferred Practice Pattern Guidelines state the goals of therapy for DR and DME include improvement or stabilization of visual function, improvement in vision-related quality of life, and optimal control of blood glucose, blood pressure, and other metabolic risk factors. Patients should always be treated with anti-VEGF therapy if they have severe non-proliferative DR or proliferative DR with center-involved macular edema. In cases of mild to moderate non-proliferative DR with center-involved macular edema, patients should also receive intravitreal injections. The guidelines support the use of Lucentis, Eylea, Vabysmo, and Avastin. AAO recommendations were based on trials comparing Eylea, Avastin, and Lucentis to focal laser treatment. All trials showed that treatment with VEGF inhibitors resulted in statistically and clinically significant improvements in visual acuity in patients with DME after one to two years compared to laser treatment.

- Retinal Vein Occlusion

    - Retinal vein occlusion occurs when there is partial or complete obstruction of a retinal vein. Vision loss can occur with RVO and is associated with macular ischemia or edema, retinal hemorrhages, vitreous hemorrhage, or epiretinal membrane formation. The 2019 AAO Retinal Vein Occlusions Preferred Practice Pattern Guidelines recommend anti-VEGF therapy as first-line treatment for macular edema caused by RVO. The guidelines support the use of Lucentis, Eylea, and Avastin. The guidelines state VEGF inhibitors, Eylea, Avastin, and Lucentis, are more effective than sham injection or laser therapy in maintaining or improving visual acuity in patients with macular edema secondary to RVO.

- Myopic Choroidal Neovascularization

    - Myopic choroidal neovascularization is a common vision-threatening complication of myopia and pathological myopia. Naïve myopic patients who present with blurred vision, vision loss, or metamorphopsia should be referred to a retinal specialist who can diagnose mCNV. Once mCNV is diagnosed, anti-VEGF therapy should be started immediately. Lucentis has demonstrated improvements in visual acuity in patients with mCNV. A randomized controlled trial compared the effects of Lucentis to photodynamic therapy with verteporfin in patients with mCNV. At month three, treatment with Lucentis demonstrated significant improvements in visual acuity compared to photodynamic therapy with verteporfin. A Cochrane systematic review concluded that there is low to moderate-certainty evidence for the efficacy of VEGF inhibitors to treat mCNV at one year and two years. It also concluded that Lucentis and Avastin are equivalent in terms of efficacy in the treatment of patients with mCNV.

- There are very few randomized control trials that assess the efficacy of one anti-VEGF therapy over another. Of the two that are available, Avastin, Eylea, and Lucentis were all shown to be non-inferior to each other, and because of this, choice of therapy should be based on patient characteristics, side effect profiles, cost, and availability. However, a 2015 study conducted by Wells, et al. did show Eylea was superior to Avastin therapy when patients had a visual acuity of less than or equal to 20/50. In addition, a subcohort analysis of the YOSEMITE AND RHINE trials showed Vabysmo demonstrated BCVA gains similar to aflibercept, while demonstrating numerically greater improvements in anatomic outcomes at years 1 and 2. Therefore, in these scenarios Avastin should not be used prior to Eylea or Vabysmo.

- Susvimo

    - In the ARCHWAY clinical trial, Susvimo was only implanted following at least 3 prior anti-VEGF intravitreal injections of either Avastin, Eylea, or Lucentis within 6 months of screening. Patients in the study had to demonstrate anatomic and visual response to anti-VEGF treatment for nAMD, therefore, Susvimo should not be administered to patients who have not had proven success with prior anti-VEGF therapy.

    - Susvimo was not studied with supplemental doses of other anti-VEGF therapies and therefore, should not be administered with any other intravitreal injections other than Lucentis. Supplemental doses were given when the study participants experienced one of the following: decrease of 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or more from the best-recorded BCVA in the study; an increase of 150 µm or more in retinal thickness measured by central subfield thickness (CST) on spectral domain OCT (SD-OCT) from the lowest CST measurement in the study; or an increase of 100 µm or more in CST on SD-OCT from the lowest CST measurement in the study associated with a decrease of 10 ETDRS letters or more from the best-recorded BCVA during the study. In these scenarios only should patients be considered for additional Lucentis injections. Fifteen ETDRS letters are equivalent to a decrease in visual acuity by half.

- Of the 1.6% of patients who required supplemental injections with Lucentis during the study, a maximum of 2 injections were given per affected eye within the 24 weeks between implantation of the device of the first refill. As such, there is no data available to support more than 2 supplemental injections per 6 months.

References:

1. Lucentis [prescribing information]. South San Francisco, CA: Genentech, Inc.; February 2024.
2. Byooviz [prescribing information]. Cambridge, MA: Samsung Bioepis Co., Ltd; October 2023.
3. Susvimo [prescribing information]. South San Francisco, CA: Genentech, Inc.; April 2022.
4. Cimerli [prescribing information]. Redwood City, California: Coherus BioSciences, Inc,; November 2022.
5. Avastin [prescribing information]. South San Francisco, CA: Genentech, Inc.; January 2021.
6. Martin DF, Maguire MG, Ying GS, et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. NEJM. 2011 May 19; 364 (20): 1897 - 908.
7. Harding S, Rogers C, Chakravarthy U, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one year findings from the IVAN randomized trial. Ophthalmology. 2012 Jul; 119 (7): 1399 - 411.
8. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern. Ophthalmology. 2020 Jan (updated March 2022); 127 (1): P1 - P65.
9. Tufail A, Patel PJ, Egan C, et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomized double masked study. BMJ. 2010; 340: c2459.
10. Zhand H, Liu ZL, Sun P, et al. Intravitreal bevacizumab for treatment of macular edema secondary to central retinal vein occlusion: eighteen-month results of a prospective trial. J Ocul Pharmacol Ther. 2011 Dec; 27 (6): 615 - 21.
11. Ghanem AA, El- Kannishy AM, El- Wehidy AS, et al. Intravitreal bevacizumab (avastin) as an adjuvant treatment in cases of neovascular glaucoma. Middle East Afr J Ophthalmol. 2009; 16: 75 - 9.
12. Michaelides M, Kaines A, Hamilton R, et al. A prospective randomized trial of intravitreal bevacizumab or laser therapy in the management of diabetic macular edema (BOLT Study). Amer Acad Ophth. 2010 Mar; 117 (6): 1078 – 86.
13. El Matri L, Chebil A, & Kort F. Current and emerging treatment options for myopic choroidal neovascularization. Clin Ophthalmology. 2015; 9: 733 – 44.
14. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. NEJM. 2015 March 26; 372 (13): 1193 – 203.
15. Vedula SS & Krzystolik MG. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration. The Cochrane database of systematic reviews. 2008(2):CD005139. PMID: 18425911 6.
16. Solomon SD, Lindsley K, Vedula SS, et al. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. The Cochrane database of systematic reviews. 2019 Mar 4; 3: CD005139. PMID: 30834517.
17. Flaxel CJ, Adelman RA, Bailey ST, et al. Diabetic retinopathy preferred practice pattern. Ophthalmology. 2020 Jan (March 2022); 127 (1): P66 - P145.
18. Flaxel CJ, Adelman RA, Bailey ST, et al. Retinal vein occlusions preferred practice pattern. Ophthalmology. 2019 Sept 25; 127 (2): 288 – 320.
19. Wolf S, Balciuniene V, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. Ophthalmology. 2014; 121: 682 - 92.
20. Zhu Y, Zhang T, Xu G, et al. Anti-vascular endothelial growth factor for choroidal neovascularization in people with pathological myopia (Review). The Cochrane database of systematic reviews. 2016; 12: CD011160.
21. Holekamp NM, Campochiaro PA, Chang M, et al. ARCHWAY randomized phase 3 trial of the port delivery system with ranibizumab for neovascular age-related macular degeneration. Ophthalmology. 2021 Sept 28. Available at: https://doi.org/10.1016/j.ophtha.2021.09.016. Accessed on October 25, 2021.
22. Jhaveri CD, Glassman AR, Ferris FL, et al. Aflibercept monotherapy or bevacizumab first for diabetic macular edema. NEJM. 2022 Aug 25; 387: 692 – 703.

Policy History		
#	Date	Change Description
2.1	Effective Date: 06/06/2024	Annual review of criteria was performed, no changes were made
2.0	Effective Date: 06/08/2023	Updated to add criteria stating the biosimilars will be covered for all FDA approved indications of the innovator product and add a step through Byooviz
1.9	Effective Date: 04/06/2023	New policy. This policy replaces previously approved criteria that was embedded in the Intravitreal Injections for Retinal Conditions Policy which is being split into individual drug policies and retired. The authorization period was updated from up to 1 year to at least 60 days and up to 1 year
1.8	Efffective Date: 10/03/2022	UM medical management system update for BCNA and MAPPO for Cimerli
1.7	Effective Date: 09/01/2022	UM medical management system update for BCN and BCBS for Cimerli
1.6	Efffective Date: 06/06/2022	UM medical management system update for BCNA and MAPPO for Byooviz
1.5	Efffective Date: 03/31/2022	UM medical management system update for BCN and BCBS for Byooviz
1.4	Effective Date: 12/27/2021	UM medical management system update for MAPPO and BCNA for Susvimo
1.3	Effective Date: 11/18/2021	UM medical management system update for BCBSM and BCN for Susvimo
1.2	Effective Date: 01/01/2020	UM medical management system update for BCBS for Lucentis
1.1	Effective Date: 07/05/2017	UM medical management system update for MAPPO and BCNA for Lucentis
1.0	Effective Date: 11/08/2012	UM medical management system update for BCN for Lucentis

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*