Clinical Policy: Ranibizumab (Byooviz, Cimerli, Lucentis, Susvimo)

Reference Number: LA.PHAR.186
Effective Date: 09.18.21
Last Review Date: ~~07.22~~06.02.23 Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Ranibizumab (Lucentis®, Susvimo™~~)~~), ranibizumab-nuna (Byooviz®), and ranibizumab-~~nuna (Byooviz®)~~eqrn (Cimerli™~~)~~ are vascular endothelial growth factor (VEGF) inhibitors.

FDA Approved Indication(s)
Byooviz is indicated for the treatment of:
- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Myopic choroidal neovascularization (mCNV)

Lucentis ~~is~~and Cimerli are indicated for the treatment of:
- Neovascular (wet) AMD
- Macular edema following RVO
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR)
- mCNV

Susvimo is indicated for the treatment of patients with neovascular (wet) AMD who have previously responded to at least two intravitreal injections of a VEGF inhibitor.

Policy/Criteria
~~Prior authorization is required.~~ *Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of Louisiana Healthcare Connections that Byooviz, Cimerli, Lucentis, and Susvimo are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. Ophthalmic Disease (must meet all)**:**
1. Diagnosis of one of the following (a, b, c, d, or e):
   a. Neovascular (wet) AMD;
   b. Macular edema following RVO;
   c. DME;
   d. DR;
   e. mCNV;

2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. Failure of bevacizumab intravitreal solution, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for bevacizumab intravitreal solution. Requests for IV formulations of Avastin, Mvasi, and Zirabev will not be approved*
5. If request is for Susvimo, member meets both of the following (a and b):
   a. Member has previously responded to at least 2 intravitreal injections of a VEGF inhibitor (e.g., intravitreal bevazicumab);
   b. Request is for the treatment of neovascular (wet) AMD;
6. Dose does not exceed one of the following (a, b, or c):
   a. For DME or DR: 0.3 mg per month;
   b. For RVO or mCNV: 0.5 mg per month;
   c. For AMD, either i or ii:
      i. If request is for Byooviz, Cimerli, or Lucentis ~~or Byooviz~~: 0.5 mg per month;
      ii. If request is for Susvimo: 2 mg per 6 months.

Approval duration:
mCNV: 3 months
All other indications: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
   ~~1. If the requested use (e.g., If request is for Susvimo: 2 mg per 6 months.~~

~~**Approval duration:**~~
~~**mCNV: 3 months**~~
~~**All other indications: 6 months**~~

~~**B. Other diagnoses/indications**~~
~~1.~~2. ~~Refer to the off-label use policy if~~ diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized~~): LA~~) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53 ~~for Medicaid~~.

~~**II.**~~ **Continued Therapy**
II.

~~**A.**~~ **Ophthalmic Disease** (must meet all)**:**
A.

~~1. Member meets one of the following (a or b):~~
~~2. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;~~
1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
~~3.~~2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Detained neovascularization;

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b. Improvement in visual acuity;
c. Maintenance of corrected visual acuity from prior treatment;
d. Supportive findings from optical coherence tomography or fluorescein angiography;

~~4.~~3. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):

~~b.~~a. For DME or DR: 0.3 mg per month;
~~c.~~b. For RVO or mCNV: 0.5 mg per month;
~~d.~~c. For AMD, either i or ii:

1. If request is for Byooviz, Cimerli, or Lucentis ~~or Byooviz~~: 0.5 mg per month;

~~ii.~~i. ~~If request is for Susvimo: 2 mg per 6 months.~~

~~**Approval duration:**~~
~~**mCNV:** 3 months~~
~~**All other indications:** 6 months~~

~~**B.**~~**A.** ~~**Other diagnoses/indications** (must meet 1 or 2)**:**~~

2. If request is for Susvimo: 2 mg per 6 months.

~~1. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.~~

Approval duration: ~~**Duration of request**~~
mCNV: 3 months
All other indications: 6 months

~~**C.**~~**B.** **Other diagnoses/indications** (must meet 1 or ~~**6 months (whichever is less);**~~ ~~or~~2)**:**

1. ~~Refer to the off-label use policy if~~If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized~~): LA~~) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53 ~~for Medicaid.~~

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III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53 ~~for Medicaid, or evidence of coverage documents.~~

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AMD: age-related macular degeneration	mCNV: myopic choroidal neovascularization
DME: diabetic macular edema	
DR: diabetic retinopathy	RVO: retinal vein occlusion
FDA: Food and Drug Administration	VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Bevacizumab (Avastin®)	**Neovascular (wet) AMD:** 1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	Neovascular glaucoma: 1.25 mg administered by intravitreal injection every 4 weeks	1.25 mg/month
	Macular edema secondary to RVO: 1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	DR: 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	DME: 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	mCNV: 0.05 mL initial intravitreal injection, followed by monthly evaluation for additional injections as needed	0.5 mL/month

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Byooviz, Cimerli, Lucentis, Susvimo: ~~Ocular~~ocular or periocular infections; hypersensitivity
  - ~~Byooviz, Lucentis, Susvimo: Hypersensitivity~~
  - Susvimo: active intraocular inflammation
- Boxed warning(s):
  - Byooviz, Cimerli, Lucentis: none reported
  - Susvimo: associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab

Appendix D: General Information

- In the Comparison of AMD Treatments Trials study, the difference in mean visual acuity improvement for patients treated with Avastin compared to Lucentis was -1.4 letters (95% [CI],- 3.7 to 0.8) at two years. The proportion of patients with arteriothrombotic events was similar in the Lucentis-treated patients (4.7%) compared to the Avastin-treated patients (5.0%; p=0.89). The proportion of patients with one or more systemic serious adverse events was higher with Avastin (39.9%) than Lucentis (31.7%; adjusted risk ratio, 1.30; 95% CI, 1.07-1.57; p = 0.009). Serious systemic adverse events included

all-cause mortality, non-fatal stroke, non-fatal myocardial infarction, vascular death, venous thrombotic events and hypertension.

- In the ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularisation in AMD (ANCHOR) trial, the number of patients that lost fewer than 15 letters at 12 months was achieved by 96.4% of patients treated with Lucentis 0.5 mg compared to 64.3% of patients treated with Visudyne ($p < 0.001$). Rate of intraocular inflammation was higher for patients treated with Lucentis 0.5 mg at 15% compared to Visudyne at 2.8%.
- In the VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (VIEW)-1 trial, the difference in the number of patients who lost fewer than 15 letters at 52 weeks between Eylea every 8 weeks compared to Lucentis was 0.6% (95.1% CI -0.32, 4.4). In terms of the number of patients who gained at least 15 letters, the mean difference between Eylea every 8 weeks was 6.6% (95.1% CI -1.0, 14.1). There were no adverse events that were found to be significant from the Lucentis arm.
- In a trial comparing Eylea, Avastin and Lucentis, the Diabetic Retinopathy Clinical Research Network found in patients with diabetic macular edema that when the initial visual-acuity letter score was 78 to 69 (equivalent to approximately 20/32 to 20/40) (51% of participants), the mean improvement was 8.0 with Eylea, 7.5 with Avastin, and 8.3 with Lucentis ($p > 0.50$ for each pair wise comparison). When the initial letter score was less than 69 (approximately 20/50 or worse), the mean improvement was 18.9 with Eylea, 11.8 with Avastin, and 14.2 with Lucentis ($p < 0.001$ for Eylea vs. Avastin, $p = 0.003$ for Eylea vs. Lucentis, and $p = 0.21$ for Lucentis vs. Avastin).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ranibizumab (Lucentis), ranibizumab-nuna (Byooviz), ranibizumab-eqrn (Cimerli)	Neovascular (wet) AMD	0.5 mg (0.05 mL) administered by intravitreal injection once a month. Alternative dosing: Once monthly injections for three months followed by 4-5 doses dispersed among the following 9 months; or treatment may be reduced to one injection every 3 months after the first four injections if monthly injections are not feasible.	0.5 mg/month
	Macular edema following RVO	0.5 mg (0.05 mL) administered by intravitreal injection once a month.	0.5 mg/month
	mCNV	0.5 mg (0.05 mL) administered by intravitreal injection once a month for up to 3 months. Patients may be retreated if needed.	0.5 mg/month
Ranibizumab (Lucentis),	DME and DR with or	0.3 mg (0.05 mL) administered by intravitreal injection once a month	0.3 mg/month

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ranibizumab-eqrn (Cimerli)	without DME		
Ranibizumab (Susvimo)	Neovascular (wet) AMD	2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the Susvimo implant with refills every 24 weeks (approximately 6 months)	2 mg/6 months

VI. Product Availability

Drug Name	Availability
Ranibizumab-nuna (Byooviz)	Single-dose glass vial: 0.5 mg/0.05 mL
Ranibizumab-eqrn (Cimerli)	Single-dose glass vials: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL
Ranibizumab (Lucentis)	• Single-use prefilled syringes: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL • Single-use glass vials: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL
Ranibizumab (Susvimo)	Single-dose glass vial: 100 mg/mL

VII. References

1. Lucentis Prescribing Information. South San Francisco, CA: Genentech, Inc.; March 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125156s117lbl.pdf. Accessed November ~~9, 2021~~17, 2022.
2. Byooviz Prescribing Information. Cambridge, MA: Biogen Inc.; June 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761202s000lbl.pdf. Accessed November ~~22, 2021~~17, 2022.
3. Susvimo Prescribing Information. South San Francisco, CA: Genentech, Inc.; October 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761197s000lbl.pdf. Accessed November ~~22, 2021~~17, 2022.
4. Cimerli Prescribing Information. Redwood City, CA: Coherus BioSciences, Inc.; August 2022. Available at: https://www.cimerli.com/pdf/prescribing-information.pdf. Accessed August 23, 2022.
~~4.~~5. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: www.aao.org/ppp. Accessed November ~~9, 2021~~17, 2022.
~~5.~~6. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: www.aao.org/ppp. Accessed November ~~9, 2021~~17, 2022.
~~6.~~7. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; September 2019. Available at: www.aao.org/ppp. Accessed November ~~9, 2021~~17, 2022.

~~7.~~8.Wolf S, Valciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. *Ophthalmology*. 2014; 121(3):682-92.e2. doi: 10.1016/j.ophtha.2013.10.023. Epub 2013 Dec 8.

~~8.~~9.El Matri L, Chebil A, and Kort F. Current and emerging treatment options for myopic choroidal neovascularization. *Clinical Ophthalmology*. 2015:9 733–744.

~~9.~~10. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. *N Engl J Med*. 2015;372(13):1193-203. doi: 10.1056/NEJMoa1414264.

~~10.~~11. Cheung C, Arnold JJ, Holz FG, et al. American Academy of Ophthalmology: Myopic choroidal neovascularization: review, guidance, and consensus statement on management. *Ophthalmology*. 2017; 124:1690:1711. http://dx.doi.org/10.1016/j.ophtha.2017.04.028

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2778	Injection, ranibizumab, 0.1 mg
J2779	Injection, ranibizumab, via intravitreal implant (susvimo), 0.1 mg
Q5124	Injection, ranibizumab-nuna, biosimilar, (byooviz), 0.1 mg
TBD	Injection, ranibizumab-eqrn, biosimilar (cimerli), 0.1 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy	05.21	09.18.21
Converted redirection language from "must use" to "Failure of" bevacizumab intravitreal solution; added Byooviz and Susvimo to policy; references reviewed and updated.	07.22	08.18.22
Added Cimerli to to policy; added HCPCS codes for Susvimo, Byooviz, and Cimerli. Template changes applied to other diagnoses/indications and continued therapy section. References reviewed and updated. Added verbiage this policy is for medical benefit only.	06.02.23	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing

this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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