Clinical Policy: Ranibizumab (Byooviz, Lucentis, Susvimo)

Reference Number: LA.PHAR.186
Effective Date: 09.21
Last Review Date: 075.2241
Line of Business: Medicaid

Coding Implications
Revision Log

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

Description
Ranibizumab (Lucentis®, Susvimo™) and ranibizumab-nuna (Byooviz™) are) is a 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 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, Lucentis and Susvimo are ~~is~~ **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 ~~Member must use~~ 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;
~~5.~~6. Dose does not exceed one of the following (a, b, or c):
   a. For DME and DR: 0.3 mg per month;
   b. For ~~AMD,~~ RVO or~~, and~~ mCNV: 0.5 mg per month.
   c. For AMD, either i or ii:
      i. If request is for Lucentis or Byooviz: 0.5 mg per month;
      ~~b.~~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
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Ophthalmic Disease (must meet all):
1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Detained neovascularization;
   b. Improvement in visual acuity;
   c. Maintenance of corrected visual acuity from prior treatment;
   d. Supportive findings from optical coherence tomography or fluorescein angiography;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):~~:~~
   a. DME and DR: 0.3 mg per month;
   b. ~~AMD,~~ RVO or~~, and~~ mCNV: 0.5 mg per month.
   c. For AMD, either i or ii:
      i. If request is for Lucentis or Byooviz: 0.5 mg per month;
      ~~b.~~ii. If request is for Susvimo: 2 mg per 6 months.

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

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B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

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
DME: diabetic macular edema
DR: diabetic retinopathy
FDA: Food and Drug Administration
mCNV: myopic choroidal neovascularization
RVO: retinal vein occlusion
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):
  - Lucentis, Byooviz, Susvimo: Ocular or periocular infections
  - Lucentis, Byooviz, Susvimo: Hypersensitivity
  - Susvimo: active intraocular inflammation
- Boxed warning(s): ~~none reported~~
  - Lucentis, Byooviz: none reported
  - Susvimo: Susvimo implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab.

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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)	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 without DME	0.3 mg (0.05 mL) administered by intravitreal injection once a month	0.3 mg/month
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

- ~~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~~

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Drug Name	Availability
Ranibizumab-nuna (Byooviz)	Single-dose glass vial: 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~~www.lucentis.com~~. Accessed November~~October~~ 9~~14~~, 2021~~0~~.
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~~1.~~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.
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~~8.~~10. 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

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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

Reviews, Revisions, and Approvals	Date
Converted corporate to local policy	**05.2021**
Converted redirection language from "must use" to "Failure of" bevacizumab intravitreal solution; added Byoorivz and Susvimo to policy; references reviewed and updated.	**07.22**

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.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.