

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

Reference Number: ERX.SPA.55

Effective Date: 01.11.17

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[RevisionLog](#)

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

Description

Ranibizumab (Lucentis[®], Susvimo[™]), ranibizumab-nuna (Byooviz[®]), and ranibizumab-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 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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] 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 \geq 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 bevacizumab);
 - 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: 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Ophthalmic Disease (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. 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: 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 not be a formulary agent and 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 or periocular infections, 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. <u>Alternative dosing:</u> 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), ranibizumab-eqrn (Cimerli) | 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

| 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) | <ul style="list-style-type: none"> • 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

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| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|----------|-------------------|
| 1Q18 annual review: Converted to new template. Added fluorescein angiography as an acceptable documentation for positive response to therapy Added specialist requirement Added bevacizumab redirection Added age limit | 11.28.17 | 02.18 |
| 1Q 2019 annual review: removed requirement against concomitant use with other VEGF medications; references reviewed and updated. | 11.20.18 | 02.19 |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 12.18.19 | 02.20 |
| Ad Hoc update: clarified redirection from bevacizumab to Avastin as compounding pharmacies often break standard Avastin vials into smaller dosages specifically for ophthalmic use and there is a temporary CPT code not currently available to biosimilars. | 10.01.20 | |
| 1Q 2021 annual review: no significant changes; references reviewed and updated. | 12.01.20 | 02.21 |
| Ad Hoc update: updated redirection to “bevacizumab intravitreal solution” given availability of generic bevacizumab intravitreal solution and considering goal was to minimize use of IV bevacizumab products, most notably biosimilars; converted redirection language to “must use” | 03.04.21 | |
| Ad Hoc update: converted redirection language from “must use” to “Failure of” bevacizumab intravitreal solution. | 08.03.21 | |
| 1Q 2022 annual review: no significant changes; RT4: added Byooviz and Susvimo to policy; references reviewed and updated. | 11.09.21 | 02.22 |
| Spelling corrected for “refill” in Section V. | 04.28.22 | |
| RT4: added Cimerli to policy. | 08.23.22 | |

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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