Clinical Policy Title:	ranibizumab
Policy Number:	RxA.398
Drug(s) Applied:	Lucentis®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Ranibizumab (Lucentis®) is a vascular endothelial growth factor (VEGF) inhibitor. It is indicated for the treatment of:

- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR)
- Myopic choroidal neovascularization (mCNV)

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ranibizumab (Lucentis®)	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
	DME and DR with or without DME	0.3 mg (0.05 mL) administered by intravitreal injection once a month	0.3 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

Dosage Forms

- 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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 intravitreal bevacizumab, unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization is required for bevacizumab.
5. Dose does not exceed:
   a. DME and DR: 0.3 mg per month;
   b. AMD, RVO, and mCNV: 0.5 mg per month.

Approval duration

Commercial: mCNV**:** 3 months; All other indications**:** 6 months**Medicaid:** mCNV**:** 3 months; All other indications**:** 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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:
   a. DME and DR: 0.3 mg per month;
   b. AMD, RVO, and mCNV: 0.5 mg per month.

Approval duration

Commercial: mCNV**:** 3 months; All other indications**:** 6 months

Medicaid: mCNV**:** 3 months; All other indications**:** 6 months

III. Appendices

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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Avastin® (bevacizumab), Mvasi® (bevacizumab-awwb), Zirabev® (bevacizumab-bvzr)	**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 generic (Brand name®) when the drug is available by both generic and brand ; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In patients with ocular or periocular infections.
  - In patients with known hypersensitivity to ranibizumab or any of the excipients in Lucentis®. Hypersensitivity reactions may manifest as severe intraocular inflammation.

- Boxed warning(s):
  - None reported.

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).

References

1. Lucentis® Prescribing Information. South San Francisco, CA: Genentech, Inc.; March 2018. Available at: www.Lucentis.com. Accessed June 1, 2021.
2. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; October 2019. Available at: www.aao.org/ppp. Accessed June 2, 2021.
3. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; October 2019. Available at: www.aao.org/ppp. Accessed June 2, 2021.
4. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; October 2019. Available at: www.aao.org/ppp. Accessed June 2, 2021.
5. 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 March 2014; 121(3):682-92.e2. doi: 10.1016/j.ophtha.2013.10.023. Epub 2013 Dec 8.
6. El Matri L, Chebil A, and Kort F. Current and emerging treatment options for myopic choroidal neovascularization. Clinical Ophthalmology 2015:9 733–744.
7. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. N Engl J Med. 2015 Mar 26;372(13):1193-203. doi: 10.1056/NEJMoa1414264.
8. 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.

Review/Revision History	Review/Revised Date-	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Dosing information was updated to accompany updated indications.	07/13/2020	09/14/2020

3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 4. Age symbols and approval duration was updated in initial and continued therapy approval. 5. Appendix B brands were updated. 6. References were updated.		
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Therapeutic alternative verbiage was updated to “Below are suggested therapeutic alternatives based on clinical guidance...”. 3. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 4. References were reviewed and updated.	06/02/2021	09/14/2021