

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

### Background

Ranibizumab (Lucentis®) is a vascular endothelial growth factor (VEGF) inhibitor. Ranibizumab 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ranibizumab	mCNV	0.5 mg (0.05 mL) administered by intravitreal injection once a	0.5

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

(Lucentis®)	month for up to 3 months. Patients may be retreated if needed.	mg/month
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## 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.

### 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. Currently receiving medication that has been authorized by RxAdvance or member has previously 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**

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	Maximum Dose
Avastin® (bevacizumab), Mvasi® (bevacizumab- awwb), Zirabev® (bevacizumab- bvzr)	<b>Neovascular (wet) AMD:</b> 1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	<b>Neovascular glaucoma:</b> 1.25 mg administered by intravitreal injection every 4 weeks	1.25 mg/month
	<b>Macular edema secondary to RVO:</b> 1 mg to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	<b>DR:</b> 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	<b>DME:</b> 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	<b>mCNV:</b> 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):
  - 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**

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Review/Revision History	Review/Revised Date-	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: <ol style="list-style-type: none"> <li>1. Policy title table was updated.</li> <li>2. Dosing information was updated to accompany updated indications.</li> <li>3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance...”.</li> <li>4. Age symbols and approval duration was updated in initial and continued therapy approval.</li> <li>5. Appendix B brands were updated.</li> <li>6. References were updated.</li> </ol>	07/13/2020	09/14/2020