Clinical Policy: Ranibizumab (Lucentis)

Reference Number: PA.CP.PHAR.186
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

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

FDA Approved Indication(s)
Lucentis 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)

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Lucentis 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 intravitreal of bevacizuamb unless contraindicated or clinically significant adverse effects are experienced;
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:
***mCNV*: 3 months**
***All other indications*: 6 months**

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Previously received medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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:
***mCNV*: 3 months**
***All other indications*: 6 months**

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

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 policies – PA.CP.PMN.53 or evidence of coverage document;

Background

Description/Mechanism of Action:

Lucentis (ranibizumab) is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment. Ranibizumab binds to and inhibits the biologic activity of human vascular endothelial growth factor A (VEGF-A). VEGF-A has been shown to cause neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular AMD, mCNV, diabetic retinopathy, DME, and macular edema following RVO. The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.

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
Avastin® (bevacizumab), Mvasi™ (bevacizumab-awwb)	**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):
  - 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).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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

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

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	Approval Date
Added bevacizumab redirection, Added specific documentation of positive response to therapy required for continued approval. Added "not used concomitantly with other VEGF therapies" to section III. Diagnoses/indications NOT authorized. Added specialist requirement Removed criteria checking for contraindications (ocular infections) due to its ophthalmic nature and addition of specialist requirement. Added age limit following safety guidance. References reviewed and updated.	02/18	
1Q 2019 annual review: reduced approval durations from length of benefit to 3 months for mCNV and 6 months for all other indications; removed section III: concomitant use with other anti-vascular endothelial growth factor (VEGF) medications; references reviewed and updated.	01/19	

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