Clinical Policy: Ranibizumab (Lucentis)

Reference Number: CP.PHAR.186
Effective Date: 03.16
Last Review Date: 02.18 Coding Implications
Line of Business: Commercial, Medicaid Revision Log
See Important Reminder at the end of this policy for important regulatory and legal information.

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

It is the policy of health plans affiliated with Centene Corporation® 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 of a trial of bevacizuamb unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed:
   a. DME and DR: 0.3 mg via intravitreal injection once a month;
   b. AMD, RVO, and mCNV: 0.5 mg via intravitreal injection once a month.

Approval duration:
Medicaid - mCNV: 3 months; All other indications: 6 months
Commercial – Length of benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Member is responding positively to therapy as evidenced by one of the following:
   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;
4. If request is for a dose increase, new dose does not exceed:
   a. DME and DR: 0.3 mg via intravitreal injection once a month;
   b. AMD, RVO, and mCNV: 0.5 mg via intravitreal injection once a month.

Approval duration:
Medicaid - mCNV: 3 months; All other indications: 6 months
Commercial – Length of benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage document;

B. Concomitant use with other anti-vascular endothelial growth factor (VEGF) medications.

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)	**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: 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 syringe: 0.5 mg/0.05 mL
Single-use glass vials: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL

VII. References

1. Lucentis Prescribing Information. South San Francisco, CA: Genentech, Inc.; April 2017. Available at: www.lucentis.com. Accessed November 14, 2017.
2. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; January 2015. Available at: www.aao.org/ppp. Accessed November 14, 2017.

3. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Retinal Vein Occlusions. San Francisco, CA: American Academy of Ophthalmology; November 2015. Available at: www.aao.org/ppp. Accessed November 14, 2017.
4. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Diabetic Retinopathy. San Francisco, CA: American Academy of Ophthalmology; February 2016. Available at: www.aao.org/ppp. Accessed November 14, 2017.
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.

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
C9233	Injection, ranibizumab, 0.5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Medicaid: Policy converted to new template and split from CP.PHAR.39 AMD Retinal Disorder Treatments. Criteria: added age and max dose; monotherapy defined as "other anti-VEGF drugs" since Visudyne is sometimes used with anti-VEGF drugs in nonresponsive cases; removed requests for documentation.	03.16	03.16
Medicaid: Removed age restriction. Added new FDA-approved indication, mCNV; approval periods are set at 3 months. Removed hypersensitivity safety criteria. Modified "once a month" to "every 28 days." For re-auth: modified "Currently receiving…" to "Previously received…"; modified documentation of positive response criterion to be open-ended; added criterion to verify that Lucentis is not being used with other anti-VEGF therapies.	03.17	03.17
1Q18 annual review: - Policy combined for Medicaid and commercial	11.28.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
- Added fluorescein angiography as an acceptable documentation for positive response to therapy Medicaid: - Added specialist requirement - Removed criteria checking for contraindications (ocular infections) due to its ophthalmic nature and addition of specialist requirement - Moved initial and continued therapy criterion "not used concomitantly with other VEGF therapies" to section III. Diagnoses/indications NOT authorized. - Added bevacizuamb redirection - Added age limit - References reviewed and updated		

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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.