Local Coverage Determination (LCD):
Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (L36962)

Links in PDF documents are not guaranteed to work. To follow a web link, please use the MCD Website.

Contractor Information

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LCD Information

Document Information

**LCD ID**
L36962

**LCD Title**
Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases

**Proposed LCD in Comment Period**
N/A

**Source Proposed LCD**
N/A

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CMS National Coverage Policy

This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies may be found in the following Internet-Only Manuals (IOMs) published on the CMS Web site.

Internet Only Manual (IOM) Citations:

- CMS IOM Publication 100-04, Medicare Claims Processing Manual,
  • Chapter 17, Section 40 Discarded Drugs and Biologicals
- CMS IOM Publication 100-08, Medicare Program Integrity Manual,
  • Chapter 13, Section 13.5.4 Reasonable and Necessary Provision in an LCD

Social Security Act (Title XVIII) Standard References:

- Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.
• Title XVIII of the Social Security Act, Section 1862(a)(7). This section excludes routine physical examinations.
• Title XVIII of the Social Security Act, Section 1833(e) states that no payment shall be made to any provider for any claim that lacks the necessary information to process the claim.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

History/Background and/or General Information

Vascular endothelial growth factor (VEGF) plays an important role in both physiologic and pathologic angiogenesis and contributes to increased permeability across both the blood-retinal and blood-brain barriers.\(^1\) VEGF is a protein that stimulates the growth, proliferation, and survival of vascular endothelial cells. After two decades of extensive research into the VEGF families and receptors, specific molecules have been targeted for drug development, and several medications have received US Food and Drug Administration (FDA) approval.\(^1\)

VEGF, through its promotion of angiogenesis and vascular permeability, is a central component of the pathologic process driving wet age-related macular degeneration (AMD), as well as other choroidal and retinal vascular disorders. The VEGF inhibitors referenced within this LCD are administered via intravitreal injection.

Please refer to the Local Coverage Article: Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (A56716) for billing and coding of VEGF described in this LCD. The appropriate selection of patients for therapy is based on product labeling, clinical guidelines and clinical studies.

Vascular Endothelial Growth Factor Inhibitors

Pegaptanib sodium injection is a sterile, aqueous solution containing pegaptanib sodium. Pegaptanib is a selective VEGF antagonist. Pegaptanib binds to VEGF and inhibits its binding to cellular receptors. Pegaptanib sodium’s anti-VEGF activity is expected to inhibit abnormal blood vessel proliferation and, therefore, decrease the vision loss associated with the proliferation of abnormal blood vessels.

Ranibizumab injection is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment designed for intraocular use. Ranibizumab binds to and inhibits the biologic activity of human vascular endothelial growth factor A (VEGF-A). 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.

Bevacizumab which was initially approved by the FDA in 2004 for the treatment of metastatic colon cancer, is a monoclonal antibody that binds to VEGF. Non-FDA approved intravitreal use of bevacizumab has been widely reported by practicing ophthalmologists to be beneficial in select individuals with neovascular AMD. Consistent with the statement by the American Academy of Ophthalmology (AAO) in support of intravitreal use of bevacizumab, physicians should provide appropriate informed consent with respect to the off-label use of this drug and maintain it in the patient’s chart.

Based on published reports and widespread clinical use, there is compelling evidence of bevacizumab’s safety and efficacy for choroidal neovascularization in AMD and also in proliferative diabetic retinopathy, neovascular glaucoma, DME, retinal and iris neovascularizations and macular edema following branch and central retinal vein occlusions.

Aflibercept is a VEGF inhibitor administered as an intravitreal injection. Aflibercept is a fully human recombinant
fusion protein that binds all isoforms of VEGFA, and prevents their binding to VEGFR-1 and VEGFR-2. Aflibercept also binds to Placental Growth Factor (PIGF) inhibiting binding to VEGFR-1. Inhibiting the binding to these receptors decreases inflammation and vascular permeability, prevents the progression of neovascular AMD, and prevents further loss of vision.

**Covered Indications**

Pegaptanib sodium injection will be covered for Food and Drug Administration (FDA) approved labeled indications. See the FDA drug label for the FDA approved indications and dosages. https://labels.fda.gov/.

Pegaptanib sodium injection will be covered for the following off-label indication:

- Diabetic macular edema (DME)

Physicians should provide appropriate informed consent with respect to the off-label use of this drug and maintain it in the patient chart.

Ranibizumab injection will be covered for Food and Drug Administration (FDA) approved labeled indications. See the FDA drug label for the FDA approved indications and dosages. https://labels.fda.gov/.

Bevacizumab is a monoclonal antibody that binds to VEGF and is covered for Food and Drug Administration (FDA) approved labeled indications. See the FDA drug label for the FDA approved indications and dosages. https://labels.fda.gov/.

Bevacizumab is covered for the following off-label indications:

- Neovascular (wet) age-related macular degeneration (ARMD/AMD).
- Macular edema following branch retinal vein occlusion (BRVO).
- Macular edema following central retinal vein occlusion (CRVO).
- Diabetic macular edema (DME).
- Diabetic retinopathy (DR) in members with DME.
- Proliferative diabetic retinopathy.
- Secondary angle-closure glaucoma resulting from neovascularization (i.e., neovascular glaucoma).
- Stage 3 retinopathy of prematurity (ROP).
- Cystoid macular degeneration of retina
- Retina edema
- Rubeosis iridis
- Retinal neovascularization
- BRVO with retinal neovascularization
- CRVO with retinal neovascularization

Physicians should provide appropriate informed consent with respect to the off-label use of bevacizumab.

Aflibercept will be covered for Food and Drug Administration (FDA) approved labeled indications. See the FDA drug label for the FDA approved indications and dosages. https://labels.fda.gov/.

**Limitations**

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Though the optimal frequency of VEGF inhibitors is yet to be determined, the expectation is that the clinical assessment pre-treatment on date of service (DOS) (or close to it) should support decision making for treatment and subsequent follow-up treatment. Generally, a maximum of monthly intervals (q 4 weeks) should be assessed after the initial 3 months (12 weeks) of treatment for possible alternative frequency (such as q 8 weeks to quarterly etc.) based on the clinical assessment. The treatment frequency should be consistent with the clinical assessment (symptoms, exam, testing when indicated (OCT, FA, etc.) as documented in the medical record. Office based retina diagnostic tests are addressed in other polices. The diagnosis of AMD or other retinal diseases may require fluorescein dye retinal angiography (FA), optical coherence tomography (OCT), as well as other testing per standards of care. After establishment of a diagnosis and during treatment protocol for indicated VEGF Inhibitors OCT, Ultrasound, FA may be necessary to assess new symptoms and/or assess treatment progress for decisions on the subsequent frequency prescription. Documentation must support the need for testing and testing not used for decision making will be denied. Multiple testing modalities on a DOS may be subject to medical review and denial if testing exceeds the medical need.

Injections of drugs that are administered at an excessive frequency are not medically necessary. Frequency is considered excessive when services are performed more frequently than listed in the package insert or generally accepted by peers and the reason for additional services is not justified by documentation. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.

The following are considered not reasonable and necessary and therefore may be denied:

1. It is not reasonable and necessary to inject more than one anti-VEGF medication (pegaptanib sodium, ranibizumab, bevacizumab, aflibercept) in the same eye during the same treatment session.
2. It is not expected to inject one anti-VEGF medication in one eye and another in the other eye. If different medications are injected into each eye during the same date of service, the rationale for this therapy must be documented in the medical record and the billing modifier (RT/LT) must be appended to the correct drug.
3. VEGF inhibitors addressed in this LCD are contraindicated in patients with ocular or periocular infections and in patients with known hypersensitivity to the VEGF inhibitor or any of its inactive ingredients.
4. Frequency is considered excessive when services are performed more frequently than listed in the package insert or generally accepted by peers and the reason for additional services is not justified by documentation. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
5. Multi-dosing from a single eye use vial or syringe or single-dose syringe is not medically reasonable and necessary, and is not a covered service.

As published in the CMS IOM Publication 100-08, Medicare Program Integrity Manual, Chapter 13, Section 13.5.4, an item or service may be covered by a contractor LCD if it is reasonable and necessary under the Social Security Act Section 1862 (a)(1)(A). Contractors shall determine and describe the circumstances under which the item or service is considered reasonable and necessary.

**Provider Qualifications**

The following provider qualification requirements must be met for the service to be considered reasonable and necessary:

- Provider Specialties: Services rendered will be considered medically reasonable and necessary only when furnished by a qualified ophthalmologist.
**Summary of Evidence**

N/A

**Analysis of Evidence**
*(Rationale for Determination)*

N/A

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**Coding Information**

**Bill Type Codes:**

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

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**Revenue Codes:**

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

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**CPT/HCPCS Codes**

**Group 1 Paragraph:**

Please refer to the Local Coverage Article: Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (A56716) for billing and coding requirements that apply to the reasonable and necessary provisions outlined in this LCD.

**Group 1 Codes:**
ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:

Please refer to the Local Coverage Article: Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (A56716) for billing and coding requirements that apply to the reasonable and necessary provisions outlined in this LCD.

Group 1 Codes:

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ICD-10 Codes that DO NOT Support Medical Necessity

Group 1 Paragraph:

N/A

Group 1 Codes:

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Additional ICD-10 Information

N/A

General Information

Associated Information

Documentation Requirements

Please refer to the Local Coverage Article: Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (A56716) for documentation requirements that apply to the reasonable and necessary provisions outlined in this LCD.

Utilization Guidelines

Please refer to the Local Coverage Article: Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases (A56716) for utilization guidelines that apply to the reasonable and necessary provisions outlined in this LCD.
Sources of Information

Contractor is not responsible for the continued viability of websites listed.


Bibliography


37. Wu L, Arevalo F, Roca J, et al. Comparison of two doses of intravitreal bevacizumab (Avastin®) for treatment


### Revision History Information

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<td>Revision Number: 3</td>
<td>• Reconsideration Request</td>
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<td>Publication: July 2019 Connection</td>
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Explanation of Revision: The LCD was revised to be consistent with Change Request 10901 to remove all billing and coding and all language not related to reasonable and necessary provisions (“Bill Type Codes”, “Revenue Codes”, “CPT/HCPCS Codes”, “ICD-10 Codes that Support Medical Necessity”, “Documentation Requirements” and “Utilization Guidelines” sections of the LCD) and place them into a newly created billing and coding article. Also, Internet Only Manuals (IOM) references have been updated and language from the CMS IOM and/or regulations was removed and instead the applicable manual/regulation reference was listed. The effective date of this revision is for claims processed on or after January 08, 2019, for dates of service on or after October 03, 2018.

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<td><strong>Explanation of Revision:</strong> Based on CR 10153 (Annual 2018 ICD-10-CM Update) the LCD was revised. Added ICD-10-CM diagnosis code H44.2A1 – H44.2A3 for procedure code J2778. The effective date of this revision is based on date of service.</td>
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### Associated Documents

**Attachments**

N/A

**Related Local Coverage Documents**

**Article(s)**

A56716 - Billing and Coding: Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases

A56715 - Vascular endothelial growth factor inhibitors for the treatment of ophthalmological diseases revision to the Part A and Part B LCD

**Related National Coverage Documents**

N/A

**Public Version(s)**

Updated on 07/17/2019 with effective dates 07/25/2019 - N/A

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