



MEDICAL COVERAGE GUIDELINES
SECTION: VISION

ORIGINAL EFFECTIVE DATE: 04/16/13
LAST REVIEW DATE: 04/15/14
LAST CRITERIA REVISION DATE: 04/29/13
ARCHIVE DATE:

INTRAVITREAL ANGIOGENESIS INHIBITORS FOR RETINAL VASCULAR CONDITIONS

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Angiogenesis inhibitors, e.g., Avastin™ * (bevacizumab), Eylea™ (aflibercept), Lucentis® (ranibizumab) and Macugen® (pegaptanib sodium) have been investigated for the treatment of disorders of retinal circulation. Angiogenesis inhibitors bind to and inhibit vascular endothelial growth factor (VEGF) to prevent the formation of new blood vessels. VEGF inhibitors are also referred to as anti-vascular endothelial growth factors (anti-VEGF) or angiogenesis inhibitors.

- * Avastin is approved for the treatment of metastatic cancers including colorectal and lung cancer. Avastin is the full-length monoclonal antibody from which the Lucentis fragment is derived. Use of Avastin is included in the American Academy of Ophthalmology (AAO) preferred practice pattern for Age-Related Macular Degeneration (AMD).¹² Although prospective randomized trials with bevacizumab for AMD have not yet been conducted, community experience demonstrating the beneficial impact on vision have resulted in acceptance as standard in the medical community.

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Description: (cont.)

Diabetic Retinopathy:

At its earliest stage (nonproliferative retinopathy), microaneurysms occur. With disruption of the blood-retinal barrier, macular retinal vessels become permeable, leading to exudation of serous fluid and lipids into the macula (macular edema). As the disease progresses, blood vessels that provide nourishment to the retina are blocked, triggering the growth of new and fragile blood vessels (proliferative retinopathy). Severe vision loss with proliferative retinopathy arises from vitreous hemorrhage. Moderate vision loss can also arise from macular edema (fluid accumulating in the center of the macula) during the proliferative or nonproliferative stages of the disease. Although proliferative disease is the main blinding complication of diabetic retinopathy, macular edema is more frequent and is the leading cause of moderate vision loss in people with diabetes.

Central and Branch Retinal Vein Occlusions:

Retinal vein occlusions are classified by whether there is a central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO). CRVO is also categorized as ischemic or non-ischemic. Ischemic CRVO is associated with a poor visual prognosis, with macular edema and permanent macular dysfunction occurring in virtually all individuals. Non-ischemic CRVO has a better visual prognosis, but many individuals will have macular edema, and it may convert to the ischemic type within 3 years. Most of the vision loss associated with CRVO results from the main complications, macular edema and intraocular neovascularization. BRVO is a common retinal vascular disorder in adults between 60 and 70 years of age and occurs approximately 3 times more commonly than CRVOs. Macular edema is the most significant cause of central visual loss in BRVO.

Retinopathy of Prematurity:

This is a neovascular retinal disorder that primarily affects premature infants of low birth weight. It is one of the most common causes of childhood blindness in the United States. Typically, retinal vascularization begins at the optic nerve when the eye begins to develop (16 weeks' gestation) and reaches the edge of the retina at 40 weeks' gestation. If an infant is born prematurely, normal vessel growth may stop, followed by neovascularization at the interface between the vascular and avascular retinal areas.

Other Retinal Vascular Conditions:

Other retinal vascular conditions that have been investigated for treatment with VEGF inhibitors are cystoid macular edema resulting from vasculitis, Coats disease, Eales disease, idiopathic macular telangiectasia type II, neovascularization of the iris/neovascularization of the angle/neovascular glaucoma, pseudoxanthoma elasticum, radiation retinopathy, retinal neovascularization, rubeosis, Von Hippel-Lindau and vitreous hemorrhage secondary to retinal neovascularization.

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Criteria:

- Intravitreal injection of Lucentis (ranibizumab), or Avastin (bevacizumab) is considered **medically necessary** with documentation of **ANY** of the following:
 1. Diabetic macular edema
 2. Proliferative diabetic retinopathy as an adjunctive treatment to vitrectomy or photocoagulation
 3. Macular edema following branch retinal vein occlusion (BRVO)
 4. Macular edema following central retinal vein occlusion (CRVO)
 5. Neovascular glaucoma
 6. Rubeosis (neovascularization of the iris)
- Intravitreal injection of ranibizumab or bevacizumab for the treatment of all other retinal vascular disorders not previously listed is considered **experimental or investigational** based upon:
 1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 2. Insufficient evidence to support improvement of the net health outcome, and
 3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
 4. Insufficient evidence to support improvement outside the investigational setting.
- Intravitreal injection of Avastin (bevacizumab) for the treatment of retinopathy of prematurity is considered **medically necessary**.
- Intravitreal injection of Eylea (afibercept) is considered **medically necessary** for treatment of the following retinal conditions:
 1. Diabetic macular edema
 2. Macular edema following central retinal vein occlusion (CRVO)

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INTRAVITREAL ANGIOGENESIS INHIBITORS FOR RETINAL VASCULAR CONDITIONS (cont.)

Criteria: (cont.)

- Intravitreal injection of Eylea (afibercept) for all other retinal vascular disorders not previously listed is considered ***experimental or investigational*** based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
4. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- Proliferative diabetic retinopathy
- Macular edema following branch retinal vein occlusion (BRVO)

- Intravitreal injection of Macugen (pegaptanib) for treatment of retinal vascular disorders is considered ***experimental or investigational*** based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
4. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- Proliferative diabetic retinopathy
- Diabetic macular edema
- Branch retinal vein occlusion (BRVO)
- Central retinal vein occlusion (CRVO)

Resources:

Resources prior to 04/16/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. 9.03.27 BCBS Association Medical Policy Reference Manual . Intravitreal Angiogenesis Inhibitors for Retinal Vascular Conditions. Re-issue date 03/13/2014, issue date 10/04/2011.