# INTRAVITREAL ANGIogenesis INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

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.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

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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INTRAVITREAL ANGIOGENESIS INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS (cont.)

Description:

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.

The anti-VEGF agents Avastin® (bevacizumab), Eylea™ (aflibercept), Lucentis™ (ranibizumab) and Macugen® (pegaptanib) are used to treat choroidal neovascularization associated with age-related macular degeneration (AMD) and have been investigated for the treatment of other disorders of choroidal circulation.

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). 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.

Age-Related Macular Degeneration (AMD):
Gradual painless loss of central vision due to a breakdown of a portion of the retina known as the macula.

The non-neovascular form (also known as dry, nonexudative, or atrophic) is more common and progresses slowly, characterized by the accumulation of small, yellowish deposits called drusen that form within the layers of the retina. Non-neovascular AMD may suddenly develop into neovascular AMD.

The neovascular form (also known as wet, exudative or disciform) is characterized by choroidal neovascularization, the proliferation of fine blood vessels at the back of the eye that begin to leak or exude fluid, causing hemorrhage, swelling and scar tissue which may result in permanent central vision loss within days or weeks.

Central Serous Chorioretinopathy:
A disease in which a serous detachment of the macula occurs due to leakage of fluid from the choriocapillaris through the retinal pigment epithelium. Choroidal neovascularization may occur as a secondary complication.

Choroidal Neovascularization (CNV):
The proliferative growth of abnormal new blood vessels, called neovascular membranes, originating from the choroid (between the retina and the sclera) that begin to leak or exude fluid, causing hemorrhage, swelling and scar tissue which can lead to rapid irreversible loss of vision.
INTRAVITREAL ANGIOGENESIS INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS (cont.)

Description: (cont.)

Pathologic Myopia:
Abnormal elongation of the eye associated with severe near-sightedness. It can result in a progressive, severe loss of vision, frequently related to the development of CNV.

Presumed Ocular Histoplasmosis:
Characterized by tiny choroidal scars, peripapillary scarring and exudation or hemorrhage from choroidal lesions in or near the macula along with a positive skin test for histoplasmosis and miliary opacities of the lungs.

Other Choroidal Neovascular Conditions:
Other conditions include but are not limited to angioid streaks, uveitis, choroidal rupture or trauma, chorioretinal scars and multifocal choroiditis.

Criteria:

For Avastin, Eylea, Lucentis and Macugen for retinal vascular conditions, see BCBSAZ Medical Coverage Guideline #O720, “Intravitreal Angiogenesis Inhibitors for Retinal Vascular Conditions”.

- Intravitreal injection of Avastin (bevacizumab), Eylea (aflibercept) or Lucentis (ranibizumab) or Macugen® (pegaptanib) is considered medically necessary with documentation of ANY of the following:
  1. Neovascular (wet) age-related macular degeneration (AMD)
  2. Choroidal neovascularization due to ANY of the following:
     - Angioid streaks
     - Central serous chorioretinopathy
     - Choroidal rupture or trauma
     - Idiopathic choroidal neovascularization
     - Multifocal choroiditis
     - Pathologic myopia
     - Presumed ocular histoplasmosis syndrome
     - Uveitis
INTRAVITREAL ANGIOGENESIS INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS (cont.)

Criteria: (cont.)

➢ Intravitreal injection of Avastin (bevacizumab), Eylea (aflibercept) or Lucentis (ranibizumab) for the treatment of all other choroidal 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:

• Chorioretinal scars

Resources:

Literature reviewed 04/25/17. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

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

INTRAVITREAL ANGIogenesis INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un interprete, llame al 602-864-4884.

Navajo: Díí kwe’ é atah níllíñíí Blue Cross Blue Shield of Arizona haada yít’éego bína’idílklídgo éí doodago Háída bíjá aniyeedííi t’áadoo le’é yina’íldílídgo beehaz’áanníí hólo díí t’áá hazaad’éhí háhí a’doooolgo bee haz’a’ doo báą̀q ilínígóó. Atá’ halne’ilgíí kojí’ bích’i’ hodiilíníí 877-475-4799.

Chinese: 如果您，或您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو أدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona غير إجابة على السؤال أو المعلومات الضرورية بلغتك من دون إجابة تكلفة، للتحدث مع مترجم اتصل ب 877-475-4799.
INTRAVITREAL ANGIOGENESIS INHIBITORS FOR CHOROIDAL VASCULAR CONDITIONS (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관하여 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言葉でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi: اگر شما یا کسی که شما به او کمک می‌کنید، سوال‌هایی در مورد Blue Cross Blue Shield of Arizona دارید یا اطلاعاتی به زبان خود را به طور رایگان دریافت می‌پذیری‌ید، شما می‌توانید به شماره 877-475-4799 تماس حاصل نمایید.

Assyrian: "Blue Cross Blue Shield of Arizona"-نین ناسیه کتیانی، یارانه‌ای چۆک خۆرایەوە، ئەکەرە نزیک 24 ساعت ڕۆژیەوە، 877-475-4799

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomagate ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคุณ หรือผู้ที่คุณช่วยเหลือมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona เช่น เข้าใจไม่ได้หรือต้องการความช่วยเหลือ ต้องติดต่อที่ 877-475-4799