

Blue Cross Blue Shield of Massachusetts is an Independent Licenses of the Blue Cross and Blue Shield Association

Medical Policy Intravitreal Angiogenesis Inhibitors for Choroidal Vascular Conditions

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Policy Number: 343

BCBSA Reference Number: 9.03.24A NCD/LCD: N/A

Related Policies

- Epiretinal Radiation Therapy for Age-Related Macular Degeneration, #610
- Photodynamic Therapy for Choroidal Neovascularization, #599
- Transpupillary Thermotherapy for Treatment of Choroidal Neovascularization, #600

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Anti-vascular endothelial growth factor therapies (anti-VEGF), ie., pegaptanib (Macugen®*), ranibizumab (Lucentis^{™*}), bevacizumab (Avastin[™]), and aflibercept (Eylea^{™*}) for the treatment of neovascular (wet) age-related macular degeneration may be <u>MEDICALLY NECESSARY</u>.

Anti-vascular endothelial growth factor therapies (anti-VEGF) are <u>MEDICALLY NECESSARY</u> for Choroidal neovascularization due to the following conditions:

- Angioid streaks,
- Central serous chorioretinopathy,
- Choroidal rupture or trauma,
- Idiopathic choroidal neovascularization,
- Multifocal choroiditis,
- Pathologic myopia,
- Presumed ocular histoplasmosis syndrome, and
- Uveitis.

Anti-vascular endothelial growth factor therapies (anti-VEGF) are **INVESTIGATIONAL** for the treatment of chorioretinal scars.

*FDA-approved indication

Prior Authorization Information

Pre-service approval is required for all inpatient services for all products.

See below for situations where prior authorization may be required or may not be required for outpatient services.

Yes indicates that prior authorization is required.

No indicates that prior authorization is not required.

N/A indicates that this service is primarily performed in an inpatient setting. Outpatient

Commercial Managed Care (HMO and POS)	 Prior authorization for commercial managed care members is required for this service when it is obtained through a home infusion company. Prior authorization is required when these drugs are purchased by the physician and administered in the office. Home infusion providers should use form <u>#430 Home Infusion Therapy Prior Authorization Form</u>.
Commercial PPO and Indemnity	 Prior authorization for commercial PPO members is required for this service when it is obtained through a home infusion company. Prior authorization is not required when these drugs are purchased by the physician and administered in the office in accordance with this medical policy. Home infusion providers should use form <u>#430 Home Infusion Therapy Prior Authorization Form</u>.
Medicare HMO Blue sm	No
Medicare PPO Blue sm	No

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above <u>medical necessity criteria MUST</u> be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
67028	Intravitreal injection of a pharmacologic agent

HCPCS Codes

HCPCS	
codes:	Code Description
C9257	Injection, bevacizumab, 0.25 mg
J0178	Injection, aflibercept, 1 mg
J2503	Injection, pegaptanib sodium, 0.3 mg
J2778	Injection, ranibizumab, 0.1 mg

J9035 Injection, bevacizumab, 10 mg		J9035	Injection, bevacizumab, 10 mg
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Description

Vascular endothelial growth factor has been implicated in the pathogenesis of a variety of ocular vascular conditions characterized by choroidal neovascularization (CNV) and macular edema.

Neovascular age related macular degeneration (AMD) is characterized by CNV which is the growth of abnormal choroidal blood vessels beneath the macula. This abnormal vascular growth causes severe loss of vision and is responsible for most of the loss of vision caused by AMD. Angiostatic agents block a stage in the vascular growth pathway leading to new blood vessel formation (angiogenesis) and therefore are disease modifying by inhibiting the development of newly formed vessels. Angiogenesis inhibitors are also being evaluated for the treatment of other disorders of choroidal circulation, including central serous chorioretinopathy pathologic myopia, presumed ocular histoplasmosis syndrome, angioid streaks, idiopathic CNV, uveitis, choroidal rupture or trauma, and chorioretinal scars.

Examples of angiogenesis inhibiting drugs for treating choroidal vascular conditions are Pegaptanib (Macugen®) from Eyetech and Pfizer, ranibizumab (Lucentis™), and Bevacizumab (Avastin®) from Genentech. All other angiogenesis inhibiting drugs for treating choroidal vascular conditions are considered investigational regardless of the commercial name, the manufacturer, or FDA approval status except as noted in the policy statement.

Summary

The available literature from randomized controlled trials supports the use of anti-VEGF therapies (ranibizumab, bevacizumab, pegaptanib, aflibercept) as monotherapy for the treatment of CNV associated with AMD. The use of anti-VEGF therapies for CNV secondary to other relatively rare disorders of choroidal circulation (angioid streaks, central serous chorioretinopathy, choroidal rupture or trauma, idiopathic choroidal neovascularization, multifocal choroiditis, pathologic myopia, presumed ocular histoplasmosis syndrome, and uveitis) is supported by a few small randomized trials, numerous case series, and clinical input. Therefore, anti-VEGF therapies (ranibizumab, bevacizumab, pegaptanib aflibercept) may be considered medically necessary for CNV associated with these conditions. Anti-VEGF therapies are considered investigational for the treatment of chorioretinal scars.

Policy History

Date	Action
12/2019	Clarified coding information
3/2018	Prior authorization table clarified. 3/23/2018
8/2016	Clarified coding information.
5/2015	New references added from BCBSA National medical policy.
7/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective
	10/2015.
5/2014	New references from BCBSA National medical policy.
5/2013	New references from BCBSA National medical policy.
2/2013	BCBSA National medical policy review.
	New medically necessary indications described. Effective 2/4/2013.
11/2011-	Medical policy ICD 10 remediation: Formatting, editing and coding updates.
4/2012	No changes to policy statements.
1/1/2012	New policy, effective (01/01/2012), describing covered and non-covered indication.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use Managed Care Guidelines Indemnity/PPO Guidelines

Clinical Exception Process

References

- Vedula SS, Krzystolik MG. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration. Cochrane Database Syst Rev 2008; (2):CD005139.
- 2. Gragoudas ES, Adamis AP, Cunningham ET, Jr. et al. Pegaptanib for neovascular age-related macular degeneration. N Engl J Med 2004; 351(27):2805-16.
- 3. Brown DM, Kaiser PK, Michels M et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006; 355(14):1432-44.
- 4. Brown DM, Michels M, Kaiser PK et al. Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: two-year results of the ANCHOR study. Ophthalmology 2009; 116(1):57-65 e5.
- 5. Bressler NM, Chang TS, Fine JT et al. Improved vision-related function after ranibizumab vs photodynamic therapy: a randomized clinical trial. Arch Ophthalmol 2009; 127(1):13-21.
- Singer MA, Awh CC, Sadda S et al. HORIZON: an open-label extension trial of ranibizumab for choroidal neovascularization secondary to age-related macular degeneration. Ophthalmology 2012; 119(6):1175-83.
- 7. Bressler NM, Boyer DS, Williams DF et al. Cerebrovascular accidents in patients treated for choroidal neovascularization with ranibizumab in randomized controlled trials. Retina 2012; 32(9):1821-8.
- 8. Tufail A, Patel PJ, Egan C et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. BMJ 2010; 340:c2459.
- 9. U.S. Food and Drug Administration. Drug approval package for Eylea (aflibercept) injection. 2011. Available online at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/125387s0000TOC.cfm. Last accessed February, 2014.
- 10. Heier JS, Brown DM, Chong V et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 2012; 119(12):2537-48.
- Schmidt-Erfurth U, Kaiser PK, Korobelnik JF et al. Intravitreal Aflibercept Injection for Neovascular Age-related Macular Degeneration: Ninety-Six-Week Results of the VIEW Studies. Ophthalmology 2014; 121(1):193-201.
- 12. CATT Research Group, Martin DF, Maguire MG et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. N Engl J Med 2011; 364(20):1897-908.
- 13. Chan A, Duker JS, Ko TH et al. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. Arch Ophthalmol 2006; 124(2):193-8.
- 14. Rosenfeld PJ. Bevacizumab versus Ranibizumab The Verdict. N Engl J Med 2011; 364(20):1966-7.
- 15. Comparison of Age-related Macular Degeneration Treatments Trials Research G, Martin DF, Maguire MG et al. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology 2012; 119(7):1388-98.
- Investigators IS, Chakravarthy U, Harding SP et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology 2012; 119(7):1399-411.
- Chakravarthy U, Harding SP, Rogers CA et al. Alternative treatments to inhibit VEGF in age-related choroidal neovascularisation: 2-year findings of the IVAN randomised controlled trial. Lancet 2013; 382(9900):1258-67.
- Kodjikian L, Souied EH, Mimoun G et al. Ranibizumab versus Bevacizumab for Neovascular Agerelated Macular Degeneration: Results from the GEFAL Noninferiority Randomized Trial. Ophthalmology 2013; 120(11):2300-9.
- 19. Krebs I, Schmetterer L, Boltz A et al. A randomised double-masked trial comparing the visual outcome after treatment with ranibizumab or bevacizumab in patients with neovascular age-related macular degeneration. Br J Ophthalmol 2013; 97(3):266-71.
- 20. Zehetner C, Kirchmair R, Huber S et al. Plasma levels of vascular endothelial growth factor before and after intravitreal injection of bevacizumab, ranibizumab and pegaptanib in patients with agerelated macular degeneration, and in patients with diabetic macular oedema. Br J Ophthalmol 2013.
- 21. Schmucker C, Ehlken C, Agostini HT et al. A safety review and meta-analyses of bevacizumab and ranibizumab: off-label versus goldstandard. PLoS One 2012; 7(8):e42701.

- 22. Curtis LH, Hammill BG, Schulman KA et al. Risks of mortality, myocardial infarction, bleeding, and stroke associated with therapies for age-related macular degeneration. Arch Ophthalmol 2010; 128(10):1273-9.
- Gower EW, Cassard S, Shu L et al. Adverse event rates following intravitreal injection of Avastin or Lucentis for treating age-related macular degeneration. *The Association for Research in Vision and Ophthalmology (ARVO), May 1-5* 2011. Available online at: http://www.abstractsonline.com/Plan/ViewAbstract.aspx?sKey=3a667d20-f42d-421e-a859e1b680de80ed&cKey=4e534aee-b678-4b9d-91dc-20a9d6ae0c56&mKey=%7B6F224A2D-AF6A-4533-8BBB-6A8D7B26EDB3%7D. Last accessed February, 2014.
- 24. Heier JS, Brown D, Ciulla T et al. Ranibizumab for choroidal neovascularization secondary to causes other than age-related macular degeneration: a phase I clinical trial. Ophthalmology 2011; 118(1):111-8.
- 25. Chen L, Miller JW, Vavvas D et al. Anti-vascular endothelial growth factor monotherapy versus combination treatment with photodynamic therapy for subfoveal choroidal neovascularization secondary to causes other than age-related macular degeneration. Retina 2011; 31(10):2078-83.
- 26. Gliem M, Finger RP, Fimmers R et al. Treatment of choroidal neovascularization due to angioid streaks: a comprehensive review. Retina 2013; 33(7):1300-14.
- Bae SH, Heo J, Kim C et al. Low-Fluence Photodynamic Therapy versus Ranibizumab for Chronic Central Serous Chorioretinopathy: One-Year Results of a Randomized Trial. Ophthalmology 2014; 121(2):558-65.
- 28. Lim JW, Ryu SJ, Shin MC. The effect of intravitreal bevacizumab in patients with acute central serous chorioretinopathy. Korean J Ophthalmol 2010; 24(3):155-8.
- 29. Artunay O, Yuzbasioglu E, Rasier R et al. Intravitreal bevacizumab in treatment of idiopathic persistent central serous chorioretinopathy: a prospective, controlled clinical study. Curr Eye Res 2010; 35(2):91-8.
- 30. Parodi MB, Iacono P, Kontadakis DS et al. Bevacizumab vs photodynamic therapy for choroidal neovascularization in multifocal choroiditis. Arch Ophthalmol 2010; 128(9):1100-3.
- 31. Parodi MB, Iacono P, Papayannis A et al. Laser photocoagulation, photodynamic therapy, and intravitreal bevacizumab for the treatment of juxtafoveal choroidal neovascularization secondary to pathologic myopia. Arch Ophthalmol 2010; 128(4):437-42.
- 32. Iacono P, Parodi MB, Papayannis A et al. Intravitreal ranibizumab versus bevacizumab for treatment of myopic choroidal neovascularization. Retina 2012; 32(8):1539-46.
- Gharbiya M, Giustolisi R, Allievi F et al. Choroidal neovascularization in pathologic myopia: intravitreal ranibizumab versus bevacizumab--a randomized controlled trial. Am J Ophthalmol 2010; 149(3):458-64 e1.
- 34. Lai TY. Anti-vascular endothelial growth factor therapy for myopic choroidal neovascularization: do we need more evidence? Retina 2012; 32(8):1443-5.
- Oishi A, Kojima H, Mandai M et al. Comparison of the effect of ranibizumab and verteporfin for polypoidal choroidal vasculopathy: 12-month LAPTOP study results. Am J Ophthalmol 2013; 156(4):644-51.
- 36. Koh A, Lee WK, Chen LJ et al. EVEREST study: efficacy and safety of verteporfin photodynamic therapy in combination with ranibizumab or alone versus ranibizumab monotherapy in patients with symptomatic macular polypoidal choroidal vasculopathy. Retina 2012; 32(8):1453-64.
- 37. American Academy of Ophthalmology Retina Panel. Preferred Practice Pattern Guidelines. Agerelated macular degeneration. 2008. Available online at: www.aao.org/ppp. Last accessed February, 2014.
- American Academy of Ophthalmology. Age-related macular degeneration PPP. 2011. Available online at: http://one.aao.org/preferred-practice-pattern/agerelated-macular-degeneration-ppp-september-200. Last accessed February, 2014.
- 39. American Academy of Ophthalmology. Age-related macular degeneration summary benchmarkhttp://one.aao.org/summary-benchmark-detail/agerelated-macular-degenerationsummary-benchmark-. 2013. Available online at: http://one.aao.org/summary-benchmarkdetail/agerelated-macular-degeneration-summary-benchmark-. Last accessed February, 2014.
- 40. Canadian Agency for Drugs and Technologies in Health (CADTH). Technology Overview. Management of Neovascular Age-related Macular Degeneration: Systematic Drug Class Review and

Economic Evaluation. 2008. Available online at: http://www.cadth.ca/index.php/en/publication/813. Last accessed February, 2014.

- 41. National Institute for Health and Care Excellence (NICE). TA155 Ranibizumab and pegaptanib for the treatment of age-related macular degeneration. 2012. Available online at: http://publications.nice.org.uk/ranibizumab-and-pegaptanib-for-the-treatment-of-age-related-macular-degeneration-ta155. Last accessed February, 2014.
- 42. National Institute for Health and Care Excellence (NICE). TA 294 Aflibercept solution for injection treating wet age-related macular degeneration. 2013. Available online at: http://publications.nice.org.uk/aflibercept-solution-for-injection-for-treating-wet-agerelated-macular-degeneration-ta294. Last accessed February, 2014.
- 43. National Institute for Health and Care Excellence (NICE). TA 298 Ranibizumab for treating choroidal neovascularization associated with pathological myopia 2013. Available online at: http://publications.nice.org.uk/ranibizumab-for-treating-choroidal-neovascularisation-associated-with-pathological-myopia-ta298. Last accessed February, 2014.
- 44. Solomon SD, Lindsley K, Vedula SS, et al. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2014;8:CD005139. PMID 25170575
- 45. Wolf S, Balciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. Ophthalmology. Mar 2014;121(3):682-692 e682. PMID 24326106