POLICY – MPP – Vascular Endothelial Growth Factor Inhibitors for Ocular Indications

Department/Team	Medical Management/Medical Payment Policy (MPP)
Approval By	Pharmacy and Therapeutics Committee
Approval Date	2/27/20
Effective Date	8/20/20
Line of Business	☒ CCC+ ☐ Exchange ☒ Medallion 4.0 ☒ D-SNP ☐ MAPD

PURPOSE

This policy outlines guidelines and criteria for coverage determination of vascular endothelial growth factor inhibitors for vascular indications.

DESCRIPTION

Vascular endothelial growth factor (VEGF) is a naturally occurring substance in the body responsible for the growth of new blood vessels (neovascularization). In the retina however, VEGF may stimulate growth of abnormally fragile vessels prone to leakage. This leakage causes scarring in the macula and eventually leads to loss of central vision.

Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is a major cause of painless central vision loss and is a leading cause of blindness in people over 60. The neovascular (wet) form of the disease is responsible for the majority of cases of severe vision loss and is due to proliferation of abnormal blood vessels behind the retina. These new blood vessels tend to be very fragile and often leak blood and fluid into the retina, that causes visual abnormalities, and cause scar tissue that destroys the central retina. For most patients with AMD and neovascularization, treatment with intravitreal bevacizumab, ranibizumab, or aflibercept is recommended. In a systematic review of 16 randomized trials (6347 participants) evaluating VEGF inhibitors, outcomes for bevacizumab and ranibizumab were similar and both improved visual acuity, as well as morphologic parameters, compared with placebo. (Solomon SD, 2019) Another review concludes that intravitreal injection of ranibizumab every four weeks, bevacizumab (off-label) every four weeks, or aflibercept every eight weeks appear to have similar efficacy in the treatment of wet AMD. (VEGF inhibitors for AMD and diabetic macular edema.)

Central Retinal Vein Occlusion

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder. The exact etiology is unknown, however may be caused by arteriosclerotic changes in the central retinal artery or from a thrombotic occlusion of the central retinal vein. Occlusion of the central retinal vein leads to backup of the blood in the retinal venous system and increases resistance to the venous blood flow. This increased resistance causes stagnation of the blood and ischemia to the retina. Ischemic damage to the retina stimulates increase production of vascular endothelial growth factor (VEGF), and increased levels of VEGF stimulate neovascularization of the

posterior and anterior segment of the eye. Retinal vein occlusion can lead to macular edema or growth of fragile new blood vessels. Intravitreal anti-VEGF drugs are first-line therapy for macular edema associated with CRVO. Only ranibizumab and aflibercept are approved for treatment of RVO by the US Food and Drug Administration (FDA). There are no evidence-based criteria for determining which of these drugs to use, and clinical decisions are based mostly on medication cost.

Diabetic Macular Edema

Diabetic Macular Edema (DME) is the consequence of retinal microvascular changes from poorly controlled diabetes and diabetic retinopathy. DME is associated with thickening of the basement membrane and reduction of pericytes which are believed to increase permeability of the retinal vasculature. This compromises the blood-retinal barrier causing a leakage of plasma constituents and subsequent retinal edema and hypoxia, all of which stimulates the production of vascular endothelial growth factor (VEGF). DME damages the central retina, which impairs color and pinpoint vision, leading to blurry, washed-out vision. DME can be classified as either focal or diffuse types. Routine prophylactic treatment of DME that is not associated with impaired visual acuity is not recommended. In a trial comparing intravitreal aflibercept, focal/grid laser photocoagulation, or observation in 702 adults with center-involving DME and good visual acuity (20/25 or better), there was no difference in vision loss at two years among the three groups (eyes with a ≥5-letter visual acuity decrease occurred in 16, 17, and 19 percent, respectively). (Baker CW, 2019) For patients with DME and impaired visual acuity, intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents is recommended as initial therapy. In the only comparison trial, aflibercept, bevacizumab, and ranibizumab all had similar efficacy when visual acuity was better than 20/50. When the baseline visual acuity was 20/50 or worse, aflibercept improved visual acuity more than the other two drugs. (Diabetic Retinopathy Clinical Research Network, 2015) There was no difference in improvement in visual acuity between ranibizumab and bevacizumab.

GUIDELINES/INSTRUCTIONS

Initial approval period 12 injections in 12 months.

Renewal as necessary per the support of clinical documentation.

Bevacizumab (Avastin)

Virginia Premier Health Plan considers bevacizumab, 1.25 mg per eye per month, to be medically necessary for the treatment of the following conditions:

1) Neovascular Glaucoma and tried/failed/intolerance to maximal doses of one antiglaucoma medication, OR
2) Proliferative diabetic retinopathy, OR
3) Macular edema secondary to retinal vein occlusion, OR
4) Diabetic macular edema, OR
5) Neovascular (Wet) Age-Related Macular Degeneration

Ranibizumab (Lucentis)

Virginia Premier Health Plan considers ranibizumab, 0.3 -0.5 mg per eye per month, to be medically necessary for the treatment of the following conditions:

The member must have tried and failed or be intolerant of bevacizumab, AND is diagnosed with one of the following:

1) Neovascular (Wet) age-related macular degeneration (AMD), OR

2) For the treatment of patients with macular edema following retinal vein occlusion, OR
3) For the treatment of patients with diabetic macular edema, OR
4) Diabetic retinopathy in patients with diabetic macular edema

Aflibercept (Eylea)
Virginia Premier Health Plan considers aflibercept, 2 mg per eye per month, to be medically necessary for the treatment of the following conditions:

1) Diagnosis of diabetic macular edema AND initial visual acuity of 20/50 or worse; OR
2) The member must has tried and failed or is intolerant of ranibizumab or bevacizumab, AND is diagnosed with one of the following:
    a. Neovascular (Wet) age-related macular degeneration (AMD), OR
    b. For the treatment of patients with macular edema following retinal vein occlusion, OR
    c. For the treatment of patients with diabetic macular edema, OR
    d. Diabetic retinopathy in patients with diabetic macular edema

Pegaptanib Sodium Injection (Macugen)

Virginia Premier Health Plan considers pegaptanib sodium injection, 0.3 mg per eye every 6 weeks, to be medically necessary for the treatment of the following conditions:

The member must have tried and failed or be intolerant of ranibizumab or bevacizumab, AND is diagnosed with one of the following:

1) Neovascular age-related macular degeneration (AMD)
2) Diabetic macular edema

NOT MEDICALLY NECESSARY

Virginia Premier Health Plan considers Bevacizumab (Avastin), Ranibizumab (Lucentis), Aflibercept (Eylea), and Pegaptanib Sodium Injection (Macugen) to be experimental and investigational and not medically necessary for all other indications and in all other dosages not specified in the medical policy above.

Concurrent use of more than one VEGF inhibitor in the same eye is considered experimental and investigational because the safety and effectiveness of combinational use of VEGF inhibitors for ocular indications has not been established.

CODING

HCPCS codes covered if selection medical necessity is met:
67028 Intravitreal injection of a pharmacologic agent
J2503 Injection pegaptanib sodium, 0.3 mg
J2778 Injection ranibizumab, 0.1 mg
J9035 Injection bevacizumab, 10 mg
C9257 Injection, bevacizumab, 0.25 mg

Q5107 Injection, bevacizumab-awwb, biosimilar, 10 mg
J0178 Injection aflibercept, 1 mg

ICD-10 Codes which justify medical necessity:

E11.3111 - E11.3119, E11.3211 - E11.3219, E11.3311 - E11.3219, E11.3411 - E11.3419, E11.3511 - E11.3519	Type II diabetes with retinopathy with macular edema
E08.311 - E08.3599, E09.311 - E09.3599, E10.311 - E10.3599, E11.311 - E11.3599, E13.311 - E13.3599	Diabetes mellitus with retinopathy
H35.3210 - H35.3293	Exudative age-related macular degeneration
H35.101 - H35.179	Retinopathy of prematurity
H34.8110 - H34.8192	Central retinal vein occlusion
H34.8310 - H34.8392	Tributary (branch) retinal vein occlusion
H35.051 - H35.059	Retinal neovascularization, unspecified [myopic]
H35.81	Retinal edema
H44.20 - H44.23	Degenerative myopia
H44.2A1 - H44.2A9	Degenerative myopia with choroidal neovascularization

REFERENCES

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2) https://www.uptodate.com/contents/diabetic-retinopathy-prevention-and-treatment?source=history_widget Accessed 1/31/2020
3) https://www.uhcprovider.com/content/dam/provider/docs/public/policies/medadv-guidelines/e/eylea-aflibercept.pdf ACCESSED 1/29/20
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8) Lanzetta, P, Lowenstein, A. Fundamental principles of an anti-VEGF treatment regimen: optimal application of intravitreal anti-vascular endothelial growth factor therapy of macular diseases. Graefes Arch Clinc Exp Ophthalmol, (2017) 255; 1259-1273.

Related Documents

Revision History		
Date	**By**	**Description**
8/13/20	P&T Committee	Update criteria for Eylea