

MEDICAL POLICY

POLICY TITLE	PHOTODYNAMIC OR PHOTOCOAGULATION THERAPY FOR CHOROIDAL NEOVASCULARIZATION
POLICY NUMBER	MP 4.008

CLINICAL BENEFIT	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	9/1/2024

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I. POLICY

Verteporfin photodynamic therapy (PDT) as monotherapy may be considered **medically necessary** as a treatment of choroidal neovascularization (CNV) associated with age-related macular degeneration, chronic central serous chorioretinopathy, choroidal hemangioma, pathologic myopia, or presumed ocular histoplasmosis.

Verteporfin photodynamic therapy is considered **investigational** as monotherapy for other ophthalmologic disorders. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

Verteporfin photodynamic therapy is considered **investigational** when used in combination with one or more of the anti-vascular endothelial growth factor therapies (anti-VEGF), i.e., pegaptanib (Macugen®), ranibizumab (Lucentis®), bevacizumab (Avastin®), aflibercept (Eylea®) as a treatment of CNV associated with age-related macular degeneration, chronic central serous chorioretinopathy, choroidal hemangioma, pathologic myopia, presumed ocular histoplasmosis, or for other ophthalmologic disorders. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

Photocoagulation therapy as a treatment of CNV is considered **not medically necessary**. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

Policy Guidelines

U.S. Food and Drug Administration (FDA) labeling for verteporfin indicates that the physician should reevaluate the patient every 3 months and, if choroidal neovascularization leakage is detected on fluorescein angiography, therapy should be repeated. However, total number of treatments is not addressed by FDA. Evidence defining when treatment should stop is not available, but experts have suggested stopping “when the situation is judged to be ‘futile’.” FDA labeling states that the “safety and efficacy of Visudyne beyond 2 years have not been demonstrated.”

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Acute central serous chorioretinopathy refers to self-limiting disease that resolves spontaneously over a few months without any treatment. Chronic central serous chorioretinopathy has been defined as a serous macular elevation, visible biomicroscopically or detected by optical coherence tomography, that is associated with retinal pigment epithelial atrophic areas and subtle leaks or ill-defined staining by fluorescein angiography, and which does not resolve spontaneously within a few months.

Cross-references:

- MP 2.028** Eye Care
- MP 2.103** Off-Label Use of Medications and Other Interventions
- MP 2.149** Aqueous Shunts and Stents for Glaucoma
- MP 2.159** Intravitreal and Punctum Corticosteroid Implants
- MP 4.023** Transpupillary Thermotherapy for the Treatment of Choroidal Neovascular Conditions
- MP 4.032** Suprachoroidal Delivery of Pharmacologic Agents

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO: Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

III. DESCRIPTION/BACKGROUND

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Vision Loss

Severe vision loss can occur with ocular neovascularization, the growth of abnormal blood vessels in the retina or choroid. Neovascularization occurs in a number of ocular diseases, including age-related macular degeneration (AMD).

Age-Related Macular Degeneration

AMD is a degenerative disease of the retina that results in loss of central vision. Two distinctive forms, known as dry and wet degeneration, may be observed. The dry form (also known as atrophic or areolar) is more common and is often a precursor of the wet form (also known as exudative neovascular or disciform). The wet form is more devastating and characterized by serous or hemorrhagic detachment of the retinal pigment epithelium and development of choroidal neovascularization (CNV), which greatly increases the risk of developing severe irreversible loss of vision. CNV is categorized as classic or occult. Classic CNV appears as an initial lacy pattern of hyperfluorescence followed by more irregular patterns as the dye leaks into

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the subretinal space. Occult CNV lacks the characteristic angiographic pattern. Classic CNV carries a worse prognosis for vision than occult CNV, suggesting that the proliferative response that obscures new vessels may also favorably alter the clinical course of AMD.

Pathologic Myopia

Pathologic myopia refers to an abnormal elongation of the eye associated with severe near-sightedness. It generally occurs among people older than 30 years of age and can result in a progressive, severe loss of vision, frequently related to the development of CNV. Verteporfin photodynamic therapy (VPDT) has also been investigated in patients with CNV related to pathologic myopia. Antivascular endothelial growth factor (anti-VEGF) therapy is now considered a first-line intervention in patients with myopic CNV.

Presumed Ocular Histoplasmosis

Presumed ocular histoplasmosis may be the second most common cause of blindness in patients younger than 50 years of age in certain endemic areas (Ohio and Mississippi River Valleys in the United States). This condition is characterized by a positive skin test for histoplasmosis, miliary opacities of the lungs, tiny choroidal scars, peripapillary disruption of the choriocapillaris, and exudation or hemorrhage from choroidal lesions in or near the macula. The condition is asymptomatic and benign, unless the CNV lesions, which may develop many years after chorioretinal scarring has taken place, affect the macula.

Central Serous Chorioretinopathy

Central serous chorioretinopathy (CSC) refers to an idiopathic disease in which there is a serious detachment of the macula due to leakage of fluid from the choriocapillaris through the retinal pigment epithelium. This condition is avascular; however, neovascularization can occur as a secondary complication. In most cases, CSC resolves spontaneously in 3 to 4 months. However, in a few cases, chronic progression or recurrence can lead to the progressive decline of visual acuity. CSC has been treated with medication and laser photocoagulation, but these treatments have limited efficacy. Multiple definitions have been used in the literature to classify CSC as acute or chronic based cutoff time points (e.g., persistent fluid for <3, 4 or 6 months) or less frequently based on the timing of treatment. For example, acute CSC defined as the first attempted treatment to improve visual acuity, and chronic CSC is defined as being refractory to treatment. Further multiple VPDT strategies that use either reduced dose or half-fluency have been evaluated for the treatment of CSC because full-dose VPDT used in AMD has shown a potentially higher risk of developing choroidal ischemia and retinal atrophic changes.

Polypoidal Choroidal Vasculopathy

Polypoidal choroidal vasculopathy arises primarily from abnormal choroidal circulation, resulting in characteristic lesions comprising well-defined vascular networks of vessels ending in polyp-like structures. A less common subtype is polypoidal CNV, and it may be considered a subtype of AMD. Eyes that develop a cluster of grape-like polypoidal dilations are at high risk for severe vision loss.

Choroidal Hemangioma

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Choroidal hemangioma is an uncommon, benign vascular tumor, manifesting as an orange-red mass in the posterior pole of the eye. Visual loss may be progressive and irreversible because of chronic foveal detachment.

Angioid Streaks

Angioid streaks result from crack-like breaks in the Bruch membrane (the innermost layer of the choroid) and occur in patients spontaneously or due to blunt trauma or associated with some systemic diseases such as pseudoxanthoma elasticum, Paget disease of bone, or sickle hemoglobinopathy. Vision loss in eyes with angioid streaks occurs most frequently as a result of CNV.

Treatment

Available therapeutic options for CNV include anti-VEGF inhibitors, VPDT, antioxidants, thermal laser photocoagulation, and corticosteroids. The safety and efficacy of each treatment depends on the form and location of the neovascularization.

VPDT is a treatment modality designed to selectively occlude ocular choroidal neovascular tissue. The therapy is a 2-step process, consisting of an injection of the photosensitizer verteporfin, followed 15 minutes later by laser treatment to the targeted sites of retinal neovascularization. The laser treatment selectively damages the vascular endothelium and occludes the neovascularized tissue. Patients may be retreated if leakage from CNV persists.

Monotherapy with VEGF inhibitors is now standard treatment of CNV due to AMD and pathologic myopia. Combining VPDT with anti-VEGF inhibitors, concurrently or sequentially, has a biologic basis and has been investigated in multiple trials particularly in the treatment of CNV due to AMD and pathologic myopia.

The use of verteporfin photodynamic therapy in choroidal neovascularization has decreased substantially with the availability of antivascular endothelial growth factor therapy. Subsequent to U.S. Food and Drug Administration (FDA) approval of verteporfin photodynamic therapy in 2000, the FDA approved pegaptanib in 2004 and ranibizumab in 2006 for treatment of age-related macular degeneration related choroidal neovascularization. The approval of pegaptanib was based on a sham-controlled RCT while ranibizumab was approved based on a head-to-head comparison with verteporfin photodynamic therapy in the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration (ANCHOR) trial. Intravitreal injections of antivascular endothelial growth factor drugs such as ranibizumab and bevacizumab have shown superior efficacy compared with verteporfin photodynamic therapy in multiple head-to-head trials. Currently, verteporfin photodynamic therapy is used for patients in whom vascular endothelial growth factor inhibitors are contraindicated or for those who fail to benefit from vascular endothelial growth factor inhibitors.

Thermal laser photocoagulation is no longer recommended for subfoveal CNV treatment. There still remains a possible role for thermal laser surgery treatment in eyes with extrafoveal and peripapillary CNV lesions. The current trend is to use anti-VEGF agents in preference to laser photocoagulation surgery.

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Regulatory Status

In 2000, verteporfin (Visudyne®; Novartis), an intravenous photodynamic therapy agent, was approved by the U.S. Food and Drug Administration for the treatment of AMD in patients with predominantly classic subfoveal CNV. Subsequently, in 2001, the indication was expanded to include presumed ocular histoplasmosis and pathologic myopia.

IV. RATIONALE

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SUMMARY OF EVIDENCE

Age-Related Macular Degeneration

For individuals who have classic CNV due to age-related macular degeneration who receive VPDT, the evidence includes RCTs and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Multiple RCTs have supported the superiority of VPDT in reducing vision loss and decreasing retinal thickness compared with placebo or sham procedure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have CNV due to age-related macular degeneration who receive VPDT plus anti-VEGF therapy, the evidence includes two confirmatory RCTs (and their multiple analyses), multiple smaller RCTs, and a meta-analysis of existing trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. This evidence does not demonstrate improvements in visual acuity using combination therapy compared with anti-VEGF monotherapy. Combination therapy may reduce the number of intravitreal injections needed, but this result has not been consistently reported across studies. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have CNV due to AMD who receive VPDT plus corticosteroids and/or anti-VEGF therapy, the evidence includes three small RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The evidence does not demonstrate improvements in visual acuity with combination therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have extrafoveal and peripapillary CNV lesions who receive laser photocoagulation, the evidence is insufficient to determine the effects of the technology on health outcomes.

Pathologic Myopia

For individuals who have CNV due to pathologic myopia who receive VPDT, the evidence includes a subgroup analysis from large RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The subgroup analysis showed VPDT was more effective than placebo in preventing vision loss at one year but not in the second year. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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For individuals who have CNV due to pathologic myopia who receive VPDT plus anti-VEGF therapy, the evidence includes a small RCT and a retrospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The single RCT was likely underpowered to detect a clinically meaningful change in visual acuity outcomes. The retrospective cohort study did not demonstrate improvements in visual acuity with combination treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

Presumed Ocular Histoplasmosis

For individuals who have CNV due to presumed ocular histoplasmosis who receive VPDT, the evidence includes a small RCT and a prospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Lack of a control arm in the prospective cohort study and 50% lost to follow-up in the RCT preclude a meaningful interpretation of data of observed improvements in visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Central Serous Chorioretinopathy

For individuals who have CNV due to acute central serous chorioretinopathy who receive VPDT, the evidence includes two RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although the evidence has demonstrated that full and reduced doses VPDT result in a small improvement in visual acuity outcomes, the improvements did not meet clinically meaningful thresholds. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have CNV due to chronic central serous chorioretinopathy who receive VPDT, the evidence includes multiple retrospective studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although this relatively large body of retrospective studies has shown that half-dose VPDT yields positive functional and anatomic outcomes while, at the same time, reducing the potential adverse events associated with conventional VPDT, data from RCTs for multiple VPDT strategies are lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

Polypoidal Choroidal Vasculopathy

For individuals who have CNV due to polypoidal choroidal vasculopathy who receive VPDT, the evidence includes several prospective cohort studies and a meta-analysis of 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Prospective cohort studies have reported favorable anatomic and visual acuity outcomes for patients treated with VPDT. RCTs comparing VPDT with anti-VEGF therapies have reported no statistical differences in visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have CNV due to polypoidal choroidal vasculopathy who receive VPDT plus anti-VEGF therapy, the evidence includes three small RCTs, a meta-analysis, and two

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retrospective cohort studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Results of the RCTs failed to demonstrate statistical differences in visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Choroidal Hemangioma

For individuals who have CNV due to choroidal hemangioma who receive VPDT, the evidence includes a systematic review and a prospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although the prospective cohort suggested a favorable effect of VPDT on various visual acuity and anatomic outcomes in patients with choroidal hemangioma, data from RCTs are lacking. The evidence is insufficient to determine the effects of the technology on health outcomes.

Angioid Streaks

For individuals who have CNV due to angioid streaks who receive VPDT, the evidence includes a systematic review of case series. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Data from multiple case series have shown conflicting results for visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Inflammatory Chorioretinal Conditions

For individuals who have CNV due to inflammatory chorioretinal conditions who receive VPDT, the evidence includes a systematic review of case reports. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Methodologic limitations restrict the conclusions drawn from 15 case reports (total N=115 patients) of multiple disease indications. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2012 supported the use of verteporfin photodynamic therapy for pathologic myopia, presumed ocular histoplasmosis, chronic central serous chorioretinopathy, and choroidal hemangioma. Therefore, verteporfin photodynamic therapy may be considered medically necessary for these indications.

V. DEFINITIONS

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ANGIOGENESIS refers to the development of blood vessels.

CHOROID is the thin, highly vascular membrane covering the posterior five sixths of the eye between the retina and the sclera.

CHOROIDAL NEOVASCULARIZATION refers to the abnormal formation of new blood vessels usually on or under the retina, usually seen in diabetic retinopathy, blockages of central retinal vision and macular degeneration.

EXUDATION refers to the pathological oozing of fluids, usually the result of inflammation.

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MACULAR DEGENERATION refers to loss of pigmentation in the macular region of the retina, usually affecting persons over age fifty (50); a common disease of unknown etiology that produces central visual field loss and is the leading cause of permanent blindness in the United States.

OCULAR refers to the eye or vision.

PHOTODYNAMIC refers to the effects of light on biological, chemical, or physical systems.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Not Medically Necessary; therefore, not covered:

Procedure Codes					
G0186	67220				

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Covered when medically necessary:

Procedure Codes					
J3396	67221	67225			

ICD-10-CM Diagnosis Codes	Description
B39.9	Histoplasmosis, unspecified
D18.09	Hemangioma of other sites
H32	Chorioretinal disorders in diseases classified elsewhere
H35.30	Unspecified macular degeneration
H35.3110	Nonexudative age-related macular degeneration, right eye, stage unspecified
H35.3111	Nonexudative age-related macular degeneration, right eye, early dry stage
H35.3112	Nonexudative age-related macular degeneration, right eye, intermediate dry stage
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement
H35.3114	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement
H35.3120	Nonexudative age-related macular degeneration, left eye, stage unspecified
H35.3121	Nonexudative age-related macular degeneration, left eye, early dry stage
H35.3122	Nonexudative age-related macular degeneration, left eye, intermediate dry stage
H35.3123	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement
H35.3124	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement
H35.3130	Nonexudative age-related macular degeneration, bilateral, stage unspecified
H35.3131	Nonexudative age-related macular degeneration, bilateral, early dry stage
H35.3132	Nonexudative age-related macular degeneration, bilateral, intermediate dry stage
H35.3133	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement
H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement
H35.3190	Nonexudative age-related macular degeneration, unspecified eye, stage unspecified
H35.3191	Nonexudative age-related macular degeneration, unspecified eye, early dry stage
H35.3192	Nonexudative age-related macular degeneration, unspecified eye, intermediate dry stage
H35.3193	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic without subfoveal involvement
H35.3194	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic with subfoveal involvement

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ICD-10-CM Diagnosis Codes	Description
H35.3210	Exudative age-related macular degeneration, right eye, stage unspecified
H35.3211	Exudative age-related macular degeneration, right eye, with active choroidal neovascularization
H35.3212	Exudative age-related macular degeneration, right eye, with inactive choroidal neovascularization
H35.3213	Exudative age-related macular degeneration, right eye, with inactive scar
H35.3220	Exudative age-related macular degeneration, left eye, stage unspecified
H35.3221	Exudative age-related macular degeneration, left eye, with active choroidal neovascularization
0H35.3222	Exudative age-related macular degeneration, left eye, with inactive choroidal neovascularization
H35.3223	Exudative age-related macular degeneration, left eye, with inactive scar
H35.3230	Exudative age-related macular degeneration, bilateral, stage unspecified
H35.3231	Exudative age-related macular degeneration, bilateral, with active choroidal neovascularization
H35.3232	Exudative age-related macular degeneration, bilateral, with inactive choroidal neovascularization
H35.3233	Exudative age-related macular degeneration, bilateral, with inactive scar
H35.3290	Exudative age-related macular degeneration, unspecified eye, stage unspecified
H35.3291	Exudative age-related macular degeneration, unspecified eye, with active choroidal neovascularization
H35.3292	Exudative age-related macular degeneration, unspecified eye, with inactive choroidal neovascularization
H35.3293	Exudative age-related macular degeneration, unspecified eye, with inactive scar
H35.711	Central serous chorioretinopathy, right eye
H35.712	Central serous chorioretinopathy, left eye
H35.713	Central serous chorioretinopathy, bilateral
H35.719	Central serous chorioretinopathy, unspecified eye
H44.20	Degenerative myopia, unspecified eye
H44.21	Degenerative myopia, right eye
H44.22	Degenerative myopia, left eye
H44.23	Degenerative myopia, bilateral
H44.2A1	Degenerative myopia with choroidal neovascularization, right eye
H44.2A2	Degenerative myopia with choroidal neovascularization, left eye
H44.2A3	Degenerative myopia with choroidal neovascularization, bilateral eye
H44.2A9	Degenerative myopia with choroidal neovascularization, unspecified eye

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X. POLICY HISTORY

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MP 4.008	04/14/2020 Minor Review. Change to match policy to BCBSA for full adoption. References updated. FEP variation updated.
	06/08/2021 Consensus Review. No change to policy statement. Reference and coding reviewed.
	06/16/2022 Minor Review. Added NMN statement regarding photocoagulation. Updated FEP, background, and references. Added G0186 and 67220 to coding table as NMN.
	06/23/2023 Consensus Review. No change to policy statement. Background and rationale updated. References updated. Coding reviewed.
	06/07/2024 Consensus Review. No change to policy statement. New references.

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