MEDICAL POLICY

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

Effective Date:	12/1/2023

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.”

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.

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

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

Top

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

Top

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 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 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 choridal 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

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 neovacularized 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.

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

Top

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.

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 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

Top

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.

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

Top

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

Top

Capital Blue Cross's 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

Top

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						

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

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

ICD-10-CM Diagnosis Codes	Description
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
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

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

ICD-10-CM Diagnosis Codes	Description
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

XI. REFERENCES

Top

1. *Gragoudas ES, Adamis AP, Cunningham ET, et al. Pegaptanib for neovascular age-related macular degeneration. N Engl J Med. Dec 30, 2004; 351(27): 2805-16. PMID 15625332*

2. *Chakravarthy U, Adamis AP, Cunningham ET, et al. Year 2 efficacy results of 2 randomized controlled clinical trials of pegaptanib for neovascular age-related macular degeneration. Ophthalmology. Sep 2006; 113(9): 1508.e1-25. PMID 16828500*
3. *Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med. Oct 05, 2006; 355(14): 1432-44. PMID 17021319*
4. *Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Photodynamic Therapy for Subfoveal Choroidal Neovascularization. TEC Assessments. 2000;Volume 15:Tab 18, PMID: 11503675*
5. *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials--TAP report. Treatment of age-related macular degeneration with photodynamic therapy (TAP) Study Group. Arch Ophthalmol. Oct 1999; 117(10): 1329-45. PMID 10532441*
6. *Bressler NM. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials-tap report 2. Arch Ophthalmol. Feb 2001; 119(2): 198-207. PMID 11176980*
7. *Blumenkranz MS, Bressler NM, Bressler SB, et al. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration: three-year results of an open-label extension of 2 randomized clinical trials--TAP Report no. 5. Arch Ophthalmol. Oct 2002; 120(10): 1307-14. PMID 12365909*
8. *Bressler NM, Arnold J, Benchaboune M, et al. Verteporfin therapy of subfoveal choroidal neovascularization in patients with age-related macular degeneration: additional information regarding baseline lesion composition's impact on vision outcomes-TAP report No. 3. Arch Ophthalmol. Nov 2002; 120(11): 1443-54. PMID 12427056*
9. *Rubin GS, Bressler NM. Effects of verteporfin therapy on contrast on sensitivity: Results From the Treatment of Age-Related Macular Degeneration With Photodynamic Therapy (TAP) investigation-TAP report No 4. Retina. Oct 2002; 22(5): 536-44. PMID 12441717*
10. *Kaiser PK. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: 5-year results of two randomized clinical trials with an open-label extension: TAP report no. 8. Graefes Arch Clin Exp Ophthalmol. Sep 2006; 244(9): 1132-42. PMID 16538452*
11. *Verteporfin In Photodynamic Therapy Study Group. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization--verteporfin in photodynamic therapy report 2. Am J Ophthalmol. May 2001; 131(5): 541-60. PMID 11336929*
12. *Wormald R, Evans J, Smeeth L, et al. Photodynamic therapy for neovascular age-related macular degeneration. Cochrane Database Syst Rev. Jul 18, 2007; (3): CD002030. PMID 17636693*
13. *Azab M, Benchaboune M, Blinder KJ, et al. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: meta-analysis of 2-year safety results in three randomized clinical trials: Treatment Of Age-Related Macular*

Degeneration With Photodynamic Therapy and Verteporfin In Photodynamic Therapy Study Report no. 4. Retina. Feb 2004; 24(1): 1-12. PMID 15076937

14. *Schmidt-Erfurth U, Sacu S. Randomized multicenter trial of more intense and standard early verteporfin treatment of neovascular age-related macular degeneration. Ophthalmology. Jan 2008; 115(1): 134-40. PMID 18166408*
15. *Heier JS, Boyer DS, Ciulla TA, et al. Ranibizumab combined with verteporfin photodynamic therapy in neovascular age-related macular degeneration: year 1 results of the FOCUS Study. Arch Ophthalmol. Nov 2006; 124(11): 1532-42. PMID 17101999*
16. *Antoszyk AN, Tuomi L, Chung CY, et al. Ranibizumab combined with verteporfin photodynamic therapy in neovascular age-related macular degeneration (FOCUS): year 2 results. Am J Ophthalmol. May 2008; 145(5): 862-74. PMID 18321465*
17. *Kaiser PK, Boyer DS, Cruess AF, et al. Verteporfin plus ranibizumab for choroidal neovascularization in age-related macular degeneration: twelve-month results of the DENALI study. Ophthalmology. May 2012; 119(5): 1001-10. PMID 22444829*
18. *Larsen M, Schmidt-Erfurth U, Lanzetta P, et al. Verteporfin plus ranibizumab for choroidal neovascularization in age-related macular degeneration: twelve-month MONT BLANC study results. Ophthalmology. May 2012; 119(5): 992-1000. PMID 22424834*
19. *Ba J, Peng RS, Xu D, et al. Intravitreal anti-VEGF injections for treating wet age-related macular degeneration: a systematic review and meta-analysis. Drug Des Devel Ther. 2015; 9: 5397-405. PMID 26451092*
20. *Tong Y, Zhao KK, Feng D, et al. Comparison of the efficacy of anti-VEGF monotherapy versus PDT and intravitreal anti-VEGF combination treatment in AMD: a Meta-analysis and systematic review. Int J Ophthalmol. 2016; 9(7): 1028-37. PMID 27500113*
21. *Semeraro F, Russo A, Delcassi L, et al. Treatment of Exudative Age-Related Macular Degeneration with Ranibizumab combined with Ketorolac Eyedrops or Photodynamic Therapy. Retina. Aug 2015; 35(8): 1547-54. PMID 25784358*
22. *Williams PD, Callanan D, Solley W, et al. A prospective pilot study comparing combined intravitreal ranibizumab and half-fluence photodynamic therapy with ranibizumab monotherapy in the treatment of neovascular age-related macular degeneration. Clin Ophthalmol. 2012; 6: 1519-25. PMID 23055673*
23. *Lim JY, Lee SY, Kim JG, et al. Intravitreal bevacizumab alone versus in combination with photodynamic therapy for the treatment of neovascular maculopathy in patients aged 50 years or older: 1-year results of a prospective clinical study. Acta Ophthalmol. Feb 2012; 90(1): 61-7. PMID 20337606*
24. *Lazic R, Gabric N. Verteporfin therapy and intravitreal bevacizumab combined and alone in choroidal neovascularization due to age-related macular degeneration. Ophthalmology. Jun 2007; 114(6): 1179-85. PMID 17544776*
25. *Lee JH, Lee WK. One-Year Results of Adjunctive Photodynamic Therapy for Type 1 Neovascularization Associated with Thickened Choroid. Retina. May 2016; 36(5): 889-95. PMID 27115853*
26. *Piermarocchi S, Sartore M, Lo Giudice G, et al. Combination of photodynamic therapy and intraocular triamcinolone for exudative age-related macular degeneration and long-*

term chorioretinal macular atrophy. Arch Ophthalmol. Oct 2008; 126(10): 1367-74. PMID 18852414

27. *Maberley D, Shortt S, Erasmus M, et al. Photodynamic therapy and intravitreal triamcinolone for neovascular age-related macular degeneration: a randomized clinical trial. Ophthalmology. Nov 2009; 116(11): 2149-57.e1. PMID 19748675*
28. *Piri N, Ahmadieh H, Taei R, et al. Photodynamic Therapy and Intravitreal Bevacizumab with Versus without Triamcinolone for Neovascular Age-related Macular Degeneration; a Randomized Clinical Trial. J Ophthalmic Vis Res. Oct-Dec 2014; 9(4): 469-77. PMID 25709773*
29. *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): 682-92.e2. PMID 24326106*
30. *Zhu Y, Zhang T, Xu G, et al. Anti-vascular endothelial growth factor for choroidal neovascularisation in people with pathological myopia. Cochrane Database Syst Rev. Dec 15, 2016; 12: CD011160. PMID 27977064*
31. *Verteporfin in Photodynamic Therapy Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. 1-year results of a randomized clinical trial--VIP report no. 1. Ophthalmology. May 2001; 108(5): 841-52. PMID 11320011*
32. *Blinder KJ, Blumenkranz MS, Bressler NM, et al. Verteporfin therapy of subfoveal choroidal neovascularization in pathologic myopia: 2-year results of a randomized clinical trial--VIP report no. 3. Ophthalmology. Apr 2003; 110(4): 667-73. PMID 12689884*
33. *Rinaldi M, Semeraro F, Chiosi F, et al. Reduced-fluence verteporfin photodynamic therapy plus ranibizumab for choroidal neovascularization in pathologic myopia. Graefes Arch Clin Exp Ophthalmol. Mar 2017; 255(3): 529-539. PMID 27680013*
34. *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. Nov 2011; 31(10): 2078-83. PMID 21691258*
35. *Ramaiya KJ, Blinder KJ, Ciulla T, et al. Ranibizumab versus photodynamic therapy for presumed ocular histoplasmosis syndrome. Ophthalmic Surg Lasers Imaging Retina. Jan-Feb 2013; 44(1): 17-21. PMID 23410808*
36. *Salehi M, Wenick AS, Law HA, et al. Interventions for central serous chorioretinopathy: a network meta-analysis. Cochrane Database Syst Rev. Dec 22, 2015; (12): CD011841. PMID 26691378*
37. *Chan WM, Lai TY, Lai RY, et al. Half-dose verteporfin photodynamic therapy for acute central serous chorioretinopathy: one-year results of a randomized controlled trial. Ophthalmology. Oct 2008; 115(10): 1756-65. PMID 18538401*
38. *Zhang YL, You ZP, Wang CY. Different doses of verteporfin photodynamic therapy for central exudative chorioretinopathy. Chin J Exp Ophthalmol. 2012;30(11):1030-1035. PMID*

39. *Zhao M, Zhang F, Chen Y, et al. A 50% vs 30% dose of verteporfin (photodynamic therapy) for acute central serous chorioretinopathy: one-year results of a randomized clinical trial. JAMA Ophthalmol. Mar 2015; 133(3): 333-40. PMID 25555191*
40. *Bae SH, Heo JW, Kim C, et al. A randomized pilot study of low-fluence photodynamic therapy versus intravitreal ranibizumab for chronic central serous chorioretinopathy. Am J Ophthalmol. Nov 2011; 152(5): 784-92.e2. PMID 21742303*
41. *Semeraro F, Romano MR, Danzi P, et al. Intravitreal bevacizumab versus low-fluence photodynamic therapy for treatment of chronic central serous chorioretinopathy. Jpn J Ophthalmol. Nov 2012; 56(6): 608-12. PMID 22915299*
42. *Coskun E, Gurler B, Erbagci I. Combined half dose photodynamic therapy with verteporfin and intravitreal bevacizumab for chronic central serous chorioretinopathy [abstract]. Ophthalmologica 2014;232(Supp 2):56. PMID*
43. *Chan WM, Lai TY, Lai RY, et al. Safety enhanced photodynamic therapy for chronic central serous chorioretinopathy: one-year results of a prospective study. Retina. Jan 2008; 28(1): 85-93. PMID 18185143*
44. *Nicolo M, Zoli D, Musolino M, et al. Association between the efficacy of half-dose photodynamic therapy with indocyanine green angiography and optical coherence tomography findings in the treatment of central serous chorioretinopathy. Am J Ophthalmol. Mar 2012; 153(3): 474-480.e1. PMID 22019224*
45. *Lai TY, Chan WM, Li H, et al. Safety enhanced photodynamic therapy with half dose verteporfin for chronic central serous chorioretinopathy: a short-term pilot study. Br J Ophthalmol. Jul 2006; 90(7): 869-74. PMID 16597666*
46. *Valmaggia C, Haueter I, Niederberger H. Photodynamic therapy in the treatment of persistent central serous chorioretinopathy: a two-year follow-up. Klin Monbl Augenheilkd. Apr 2012; 229(4): 323-6. PMID 22389262*
47. *Rouvas A, Stavrakas P, Theodossiadis PG, et al. Long-term results of half-fluence photodynamic therapy for chronic central serous chorioretinopathy. Eur J Ophthalmol. May-Jun 2012; 22(3): 417-22. PMID 21928269*
48. *Jirarattanasopa P, Ooto S, Tsujikawa A, et al. Assessment of macular choroidal thickness by optical coherence tomography and angiographic changes in central serous chorioretinopathy. Ophthalmology. Aug 2012; 119(8): 1666-78. PMID 22521082*
49. *Senturk F, Karacorlu M, Ozdemir H, et al. Microperimetric changes after photodynamic therapy for central serous chorioretinopathy. Am J Ophthalmol. Feb 2011; 151(2): 303-9.e1. PMID 21168824*
50. *Fujita K, Shinoda K, Imamura Y, et al. Correlation of integrity of cone outer segment tips line with retinal sensitivity after half-dose photodynamic therapy for chronic central serous chorioretinopathy. Am J Ophthalmol. Sep 2012; 154(3): 579-85. PMID 22818904*
51. *Fujita K, Yuzawa M, Mori R. Retinal sensitivity after photodynamic therapy with half-dose verteporfin for chronic central serous chorioretinopathy: short-term results. Retina. Apr 2011; 31(4): 772-8. PMID 20890236*
52. *Boni C, Kloos P, Valmaggia C. New guidelines in the treatment of persistent central serous chorioretinopathy: PDT with half-dose verteporfin. Klin Monbl Augenheilkd. Apr 2012; 229(4): 327-30. PMID 22495997*

53. *Wu ZH, Lai RY, Yip YW, et al. Improvement in multifocal electroretinography after half-dose verteporfin photodynamic therapy for central serous chorioretinopathy: a randomized placebo-controlled trial. Retina. Jul-Aug 2011; 31(7): 1378-86. PMID 21836413*
54. *Uetani R, Ito Y, Oiwa K, et al. Half-dose vs one-third-dose photodynamic therapy for chronic central serous chorioretinopathy. Eye (Lond). May 2012; 26(5): 640-9. PMID 22573069*
55. *Chan WM, Lim TH, Pece A, et al. Verteporfin PDT for non-standard indications--a review of current literature. Graefes Arch Clin Exp Ophthalmol. May 2010; 248(5): 613-26. PMID 20162298*
56. *Tang K, Si JK, Guo DD, et al. Ranibizumab alone or in combination with photodynamic therapy vs photodynamic therapy for polypoidal choroidal vasculopathy: a systematic review and Meta-analysis. Int J Ophthalmol. 2015; 8(5): 1056-66. PMID 26558226*
57. *Silva R, Arias L, Nunes S, et al. Efficacy and Safety of Intravitreal Aflibercept Treat and Extend for Polypoidal Choroidal Vasculopathy in the ATLANTIC Study: A Randomized Clinical Trial. Ophthalmologica. 2022; 245(1): 80-90. PMID 34348351*
58. *Hikichi T, Ohtsuka H, Higuchi M, et al. Factors predictive of visual acuity outcomes 1 year after photodynamic therapy in Japanese patients with polypoidal choroidal vasculopathy. Retina. May 2011; 31(5): 857-65. PMID 21124252*
59. *Akaza E, Yuzawa M, Mori R. Three-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy. Jpn J Ophthalmol. Jan 2011; 55(1): 39-44. PMID 21331691*
60. *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. Sep 2012; 32(8): 1453-64. PMID 22426346*
61. *Kang HM, Kim YM, Koh HJ. Five-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy. Am J Ophthalmol. Mar 2013; 155(3): 438-447.e1. PMID 23218705*
62. *Kim SJ, Yu HG. Efficacy of combined photodynamic therapy and intravitreal bevacizumab injection versus photodynamic therapy alone in polypoidal choroidal vasculopathy. Retina. Oct 2011; 31(9): 1827-34. PMID 21734621*
63. *Blasi MA, Tiberti AC, Scupola A, et al. Photodynamic therapy with verteporfin for symptomatic circumscribed choroidal hemangioma: five-year outcomes. Ophthalmology. Aug 2010; 117(8): 1630-7. PMID 20417564*
64. *American Academy of Ophthalmology Retina Panel. Age-related macular degeneration PPP - Updated 2015. 2019*
65. *National Institute for Health and Care Excellence (NICE). Age-related macular degeneration [NG82]. 2018 A, Hodge W, Cruess A, et al. Management of Neovascular Age-related Macular Degeneration: Systematic Drug Class Review and Economic Evaluation (Canadian Agency for Drugs and Technologies in Health). 2008*
66. *Centers for Medicare and Medicaid Services. Decision Memo for Ocular Photodynamic Therapy with Verteporfin for Macular Degeneration (CAG-00066R3). 2004*

67. Jian L, Panpan Y, Wen X. Current choroidal neovascularization treatment. Ophthalmologica. 2013;230(2):55-61. doi:10.1159/000351660
68. Kent C. Macular Degeneration: Is Laser Still Relevant? Review of Ophthalmology. Published August 13, 2009
69. *Blue Cross Blue Shield Association Medical Policy Reference Manual. 9.03.08, Photodynamic Therapy for Choroidal Neovascularization. April 2023.*

X. POLICY HISTORY

TOP

MP 4.008	**CAC 10/29/02**
	CAC 10/28/03
	CAC 11/30/04
	CAC 4/26/05
	CAC 1/31/06
	CAC 9/26/06
	CAC 9/25/07
	CAC 7/29/08
	CAC 7/28/09
	CAC 7/27/2010 Minor review. Statements clarified for use of PDT.
	CAC 4/04/2011 Minor review. Policy revised to add new indication for Ozurdex for the treatment of non-infectious uveitis affecting the posterior segment of the eye.
	CAC 10/25/2011 Minor revision. Criteria for Ozurdex removed and placed in MP-2.159 "Intravitreal Corticosteroid Implants." Criteria for Anecortave Acetate (Retaane®) was removed from the policy, as it was not FDA approved. Criteria for ranibizumab (Lucentis), bevacizumab (Avastin); pegaptanib (Macugen) other than for indications when combined with photodynamic therapy were removed and placed in MP 2.163 Intravitreal Angiogenesis Inhibitors for Choroidal Vascular Conditions; and MP-2.164 Intravitreal Angiogenesis Inhibitors for Retinal Vascular Conditions.
	CAC 10/28/2012 Adopting BCBSA. • Added PDT monotherapy as medically necessary for central serous chorioretinopathy and choroidal hemangioma. Previously was only medically necessary as a treatment of choroidal neovascularization (CNV) associated with age-related macular degeneration, pathologic myopia, or presumed ocular histoplasmosis. • Added aflibercept (Eylea™) to the list of investigational agents when used in combination with one or more of the anti-vascular endothelial growth factor therapies (anti-VEGF) 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 • Deleted information regarding destruction of macular drusen by

	photocoagulation and photocoagulation (feeder vessel technique). Now silent on these procedures. • Extracted information regarding Suprachoroidal Delivery of Pharmacologic Agents and Transpupillary Thermotherapy for Treatment of Choroidal Neovascularization from this policy and new policies created. • Changed FEP variation to reference FEP Medical Policy Manual MP 9.03.08 Photodynamic Therapy for Choroidal Neovascularization • Title changed to Photodynamic Therapy for Choroidal Neovascularization (formerly Ocular Therapy) • Codes reviewed 9/19/12
	CAC 11/26/2013 Consensus review. References updated, no changes to the policy statements. Rationale added.
	CAC 11/25/2014 Consensus review. No change to policy statements. References and rationale updated**.**
	Coding reviewed. 0124T- and 0186T deleted codes replaced with 68399, 67299. Needs coding review. 11/12/2014
	CAC 11/24/2015 Consensus review. No changes to the policy statements. Reference and rationale update. Coding reviewed.
	CAC 11/29/2016 Consensus review. No change to policy statements. References and rationale updated. Variation reformatting. Coding reviewed. New Diagnosis codes added effective 10/01/16
	CAC 1/30/2018 Minor revision. Clarification added to the policy statements; photodynamic therapy now described as verteporfin photodynamic therapy (PDT). Investigation statement added regarding use of visudyne (verteporfin for injection) beyond 2 years. Cross-Reference, Description/Background, Rationale and Reference sections updated. Coding updated.
	3/6/2019 Consensus review. No change to policy statements. Background and references updated. Rationale condensed. FEP variation updated.
	10/1/2019 Admin update. Updated diagnosis codes.
	4/14/2020 Minor review. Change to match policy to BCBSA for full adoption. References updated. FEP variation updated.
	6/8/2021 Consensus review. No change to policy statement. Reference and coding reviewed.
	6/16/2022 Minor review. Added NMN statement regarding photocoagulation. Updated FEP, background, and references. Added G0186 and 67220 to coding table as NMN.
	6/23/2023 Consensus review. No change to policy statement. Background and rationale updated. References updated. Coding reviewed.