Photodynamic Therapy for Choroidal Neovascularization

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company considers verteporfin photodynamic therapy (VPDT) as monotherapy as a treatment of choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD), chronic central serous chorioretinopathy, choroidal hemangioma, pathologic myopia, or presumed ocular histoplasmosis to be eligible for coverage.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers verteporfin photodynamic therapy (VPDT) as monotherapy for all other ophthalmologic disorders to be investigational.*

Based on review of available data, the Company considers verteporfin photodynamic therapy (VPDT) when used in combination with one or more of the antivascular endothelial growth factor (anti-VEGF) therapies, i.e., pegaptanib (Macugen®)‡, ranibizumab (Lucentis®)‡, bevacizumab (Avastin®)‡, aflibercept (Eylea™)‡ as a treatment of choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD), chronic central serous chorioretinopathy, choroidal hemangioma, pathologic myopia, presumed ocular histoplasmosis, or for other ophthalmologic disorders to be investigational.*

Background/Overview
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 AMD. 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.

**FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

In 2000, verteporfin (Visudyne®, Novartis)², an intravenous photodynamic therapy agent, was approved by the U.S. FDA 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.

Centers for Medicare and Medicaid Services (CMS)

Since 2001, use of ocular photodynamic therapy (OPT) with verteporfin has been covered by Medicare for the treatment predominantly classical subfoveal CNV (i.e., occupies ≥50% of the area of the entire lesion) associated with AMD only when used in conjunction with verteporfin. However, there was no national Medicare coverage policy for other indications. In 2004, Medicare found evidence to conclude that OPT may be “reasonable and necessary” for patients with AMD with “subfoveal occult or minimally classic CNV … 4 disk areas or less in size … [with] evidence of progression within the three months prior to initial treatment.” Medicare also reiterated that use of OPT with verteporfin for indications such as “pathologic myopia or the presumed histoplasmosis syndrome” may be “eligible for coverage through individual contractor discretion.”

**Rationale/Source**

**AGE-RELATED MACULAR DEGENERATION**

AMD is a degenerative disease of 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 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.

The use of VPDT in CNV has decreased substantially with the availability of anti-VEGF therapy. Subsequent to FDA approval of VPDT in 2000, FDA approved pegaptanib in 2004 and ranibizumab in 2006 for treatment of AMD-related CNV. The approval of pegaptanib was based on a sham-controlled randomized controlled trial (RCT) while ranibizumab was approved based on a head-to-head comparison with VPDT in the ANCHOR trial. Intravitreal injections of anti-VEGF drugs such as ranibizumab and bevacizumab have shown superior efficacy compared to VPDT in multiple head-to-head trials. Currently,
VPDT is used for patients in whom VEGF inhibitors are contraindicated or for those who fail to benefit from VEGF inhibitors.

**VPDT vs Placebo**

A 2000 TEC Assessment concluded that fewer patients treated with VPDT compared to placebo experienced a clinically significant loss of visual acuity (38.8% vs 53.6%, respectively; p<0.001). These conclusions were based on the 1-year follow-up results of 609 patients enrolled in 2 similar, multicenter, double-masked, randomized placebo-controlled trials called TAP published in 1999. Subgroup analysis showed that efficacy was limited to patients in whom the area of classic CNV occupied 50% or more of the area of the lesion. Subsequently in 2001, 2-year results of the TAP trials showed that beneficial outcomes for visual acuity and contrast sensitivity observed after 1-year of follow-up were sustained through 24 months. At 2 years, 53% of the VPDT arm compared to 38% of the placebo arm lost fewer than 15 letters. Further, average number of VPDT treatments required was lower in the second year compared to the first year (2.2 vs 3.4, respectively). Subgroup analysis confirmed the earlier findings that efficacy was limited to patients in whom the area of classic CNV occupied 50% or more of the area of the lesion. Since 2001, several additional reports from the TAP trials have been published. They demonstrated positive outcomes with the use of VPDT for subfoveal CNV, and further supported the findings of the earlier TAP trial reports. In 2006, Kaiser reported results of a 3-year open-label extension of the TAP trials. Of 402 VPDT-treated patients who completed the 24-month randomized study, 320 (80%) enrolled in the extension protocol. Of the 320 enrolled, 193 (60%) completed the 60-month examination, 122 (38%) discontinued prematurely, and 3 (1%) were noncompliant. Yearly treatment rates declined from 3.5 treatments in the first year to 0.1 in the fifth year; patients who remained in the study lost an additional 2.3 lines of letters over the 3-year extension.

The Verteporfin in Photodynamic Therapy (VIP) trial (2001) randomized 339 patients to VPDT or placebo. Most (76%) patients had occult disease while the remainder had early classic CNV with good visual acuity. The primary outcome was the proportion of eyes with fewer than 15 letters of visual acuity loss. While there was no significant difference between the treatment and placebo groups at 12 months, by 24 months a significantly lower percentage of those with occult CNV who were treated with VPDT (55%) had lost vision compared with those who received placebo (68%; p=0.032). These results contrast with those of the TAP trials, although the patient populations differed. The TAP trials required all patients to have some percentage of classic CNV, while the VIP trial recruited patients with occult disease without evidence of classic CNV. In addition, the VIP trial required patients with occult disease to have experienced recent deterioration in vision. Results for the subgroup of patients with classic CNV but good visual acuity were not reported separately.

Multiple systematic reviews and meta-analysis have included TAP and VIP trials and corroborated the treatment benefit of VPDT in preventing vision loss. A 2003 Cochrane review concluded that VPDT was effective at preventing vision loss in classic and occult CNV due to AMD. In a 2004 meta-analysis of the safety of VPDT, Azab et al analyzed data from the 24-month TAP A and B and VIP trials (total N=948 patients with AMD). Reviewers concluded that the safety profile of VPDT did not differ statistically from placebo. An updated Cochrane review in 2007 evaluated results from the 3 RCTs (total N=1022 patients),
which included the TAP and VIP trials. Meta-analysis showed a 24-month risk ratio of losing 6 or more lines of visual acuity of 0.62 compared with the control group. Reviewers concluded that VPDT was probably effective for treating CNV due to AMD, although the effect size was uncertain.

Result of a 2008 multicenter RCT that compared 2 intensities of initial VPDT—every 2 or 3 months for first 6 months in 203 patients with CNV caused by AMD—showed no differences on overall outcomes for visual acuity or lesion anatomic features.

**Section Summary: VPDT vs Placebo**
The evidence for efficacy of VPDT includes multiple RCTs that have established its superiority compared to placebo. However, the efficacy is limited to a subgroup of patients with classic CNV. The use of VPDT has now been largely replaced by anti-VEGF therapies.

**VPDT Plus Anti-VEGF Therapy**
Because VPDT and ranibizumab target different disease components of AMD, it has been hypothesized that combining them might lead to a synergistic effect, with decrease in need for monthly VEGF injection and increased durability of response while maintaining visual acuity. The open-label, phase 2 PROTECT study demonstrated that same-day administration of ranibizumab and VPDT was well tolerated and vision was maintained. Results of the phase 1/2 FOCUS trial further supported the idea that combination treatment might be more effective than monotherapy. In this trial, 162 patients with classic CNV secondary to AMD were randomized to VPDT plus ranibizumab (n=106) or to VPDT plus sham (n=56). VPDT was repeated only if fluorescein angiography revealed persistent or recurrent leakage from CNV at evaluation visits (3-month intervals). Intention-to-treat (ITT) analysis showed an average improvement in acuity of 5 letters at both 12 and 24 months (85% retention) with ranibizumab compared with a decrease of 8 letters in the VPDT-alone group. Visual acuity improved by 15 or more letters in 25% of patients treated with ranibizumab (plus VPDT as needed) compared with 7% of patients treated with VPDT alone. However, the FOCUS trial did not include a ranibizumab monotherapy arm. Subsequently, the 2 larger phase 3 confirmatory trials—DENALI and MONT BLANC—failed to show the superiority of ranibizumab plus VPDT over ranibizumab alone.

DENALI was a multicenter, double-masked, randomized phase 3b trial that tested the noninferiority of ranibizumab plus VPDT to VPDT alone. In this trial, patients were randomized to ranibizumab plus standard fluence VPDT (n=104) or reduced fluence (n=105) or ranibizumab plus sham VPDT (n=112). Patients received 3 consecutive monthly injections of ranibizumab followed by as-needed retreatments. The 2 main outcome measures were change in best-corrected visual acuity (BCVA) from baseline and the proportion of patients in the combination therapy groups with a treatment-free interval of 3 months or more. An improvement in mean BCVA score was observed in all treatment groups, with the largest mean change from baseline in the ranibizumab monotherapy group. The mean change in BCVA at 12 months was +5.3, +4.4, and 8.1 for ranibizumab plus standard fluence VPDT, ranibizumab plus reduced fluence VPDT, and ranibizumab plus sham VPDT, respectively. Noninferiority for visual acuity was not demonstrated. Trials failed to demonstrate the superiority of combination treatment to reduce treatment-free interval period. The proportion of patients with a treatment-free interval of 3 months or more was 92.6% (95% confidence
interval [CI], 85.4% to 97.0%) in the ranibizumab plus standard fluence VPDT and 83.5% (95% CI, 74.6% to 90.3%) in the reduced fluence arm. Percentages for ranibizumab monotherapy were not reported.

MONT BLANC was similar to DENALI in terms of design and outcome measures, except that the former did not include a reduced-fluence VPDT arm. In this trial, 255 patients were randomized to ranibizumab plus standard fluence VPDT (n=122) or ranibizumab plus sham VPDT (n=133). Patients received 3 consecutive monthly injections of ranibizumab followed by as-needed retreatments. A difference in mean BCVA within 7 letters was designated as noninferiority margin. The mean change in BCVA at 12 months was +2.5 letters in ranibizumab plus standard fluence VPDT group and +4.4 letters in the ranibizumab plus sham VPDT group, yielding a mean difference (MD) of 1.88. Because this difference was within the noninferiority margin, authors concluded that ranibizumab plus VPDT was noninferior to VPDT alone. At 12 months, the proportion of patients with a treatment-free interval of 3 months or more was similar in the 2 groups (96% combination therapy vs 92% monotherapy). With the sample size of 125 in each arm, the trial as designed had 80% power to identify treatment difference of 20% or more in the proportion of patients with 3 or more months of treatment-free interval in the combination arm versus monotherapy arm. After 12 months, the proportion of patients with 3 or more months of treatment-free interval was 96% and 92% in the combination and monotherapy arm, respectively (difference in proportion, 4%; 95% CI, -0.02 to 0.09). Thus, the trial failed to show the superiority of ranibizumab plus VPDT over VPDT alone in increasing the treatment-free interval.

A systematic review of anti-VEGF injections for treating wet AMD was published in 2015, including a comparison of anti-VEGF monotherapy to anti-VEGF combination therapy plus VPDT. Results showed a significant difference in BCVA of 2.74 letters (95% CI, 0.26 to 5.21 letters; p=0.03) in favor of the monotherapy group (note that the conclusions of the systematic review indicated that the difference favored the combination group, which is incorrect). There were no differences between groups on central retinal thickness or lesion size. Reviewers did not report combined analysis of the number of anti-VEGF injections performed in each group. Similar results were reported in a meta-analysis published in 2016.

In addition to the above trials, several smaller randomized trials have been published. In 2015, Semeraro et al published an RCT of 75 patients with treatment-naive exudative CNV due to AMD. Patients were randomized into 3 groups: ranibizumab monotherapy, ranibizumab plus reduced-fluence VPDT, and ranibizumab plus ketorolac eye drops. At the 12-month follow-up, BCVA was superior in the ranibizumab plus ketorolac group (-0.25 logMAR [logarithm of the minimum angle of resolution]) compared with ranibizumab monotherapy (-0.14 logMAR) or ranibizumab combined with VPDT (-0.10 logMAR). In a multicenter, unmasked trial, Williams et al (2012) randomized 60 patients to ranibizumab with half-fluence VPDT or ranibizumab alone. BCVA improved by 9.9 letters in the ranibizumab group and by 2.6 letters in the combined treatment group. The proportion of patients who gained 15 or more letters was 33% in the monotherapy arm and 31% in the combination arm. A small RCT by Lim et al (2012) included 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy who were randomized to bevacizumab monotherapy or to bevacizumab plus VPDT. At 12 months, the monotherapy and combined treatment groups showed similar improvements in BCVA and central foveal thickness, and the total number of bevacizumab injections was not reduced when VPDT was given. A 2007 randomized, open-label assessor-
blinded trial from Croatia with short-term (3-month) follow-up evaluated combination treatment with bevacizumab plus VPDT (N=165 eyes). At 3-month follow-up, 22 (42%) of 52 patients improved by more than 0.2 logMAR following combined treatment compared with 1 (2%) patient treated with bevacizumab alone and none treated with VPDT alone.

Data from a retrospective study for adjunctive VPDT in patients refractory to anti-VEGF monotherapy has suggested favorable effect on visual acuity and anatomic outcomes. Lee and Lee (2016) reported data from a retrospective analysis of 28 eyes of 28 patients who showed persistent subretinal and/or intraretinal fluid after at least 4 anti-VEGF injections in the 6 months before adjunctive VPDT and subsequently received additional VPDT and anti-VEGF therapies. Patient charts were reviewed until 12 months after the initial VPDT. During a 1-year follow-up, 17 (60.7%) eyes did not demonstrate recurrent fluid accumulation. Among the 11 eyes requiring retreatment, 7 eyes initially showed complete fluid absorption after the initial PDT. At 12 months, BCVA had improved by 0.3 logMAR or more or was maintained compared with baseline in 27 (96.4%) eyes.

Section Summary: VPDT Plus Anti-VEGF Therapy
The evidence for the efficacy VPDT plus anti-VEGF therapies compared to anti-VEGF therapies alone includes 2 confirmatory RCTs (and their multiple analyses), multiple smaller RCTs, and a meta-analysis. This evidence does not demonstrate improvements in BCVA with 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.

VPDT Plus Corticosteroids and/or VEGF Inhibitors
Three RCTs have evaluated combination of VPDT with corticosteroids—1 trial from Italy, RETINA, and 1 trial from Iran. The Italian RCT (2008) assigned 84 treatment-naive patients with exudative AMD to VPDT alone (n=41) or combination intravitreal triamcinolone acetonide plus VPDT (n=43). Mean visual acuity increased at 1 month of follow-up but decreased progressively by the 24-month point in both groups. In the RETINA trial (2009), 100 patients with CNV due to AMD were randomized to VPDT alone or VPDT plus intravitreal triamcinolone. Combination treatment did not result in a significant difference in the primary outcome of visual acuity at 1 year compared with VPDT alone. The Iranian trial randomized 84 treatment-naive patients with CNV due to AMD to VPDT plus bevacizumab with and without intravitreal triamcinolone. There were no significant differences in the BCVA at week 12 and other time points.

Section Summary: VPDT Plus Corticosteroids and/or VEGF Inhibitors
The evidence for the efficacy of triple-therapy VPDT plus corticosteroid and anti-VEGF includes 3 small RCTs. This evidence does not demonstrate improvements in BCVA with this triple therapy compared to anti-VEGF monotherapy. Comparative trials are needed to evaluate the efficacy of this triple therapy.

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. VPDT has also been investigated in patients with
CNV related to pathologic myopia. Anti-VEGF therapy is now considered a first-line intervention in patients with myopic CNV. The initial evidence was based primarily on retrospective studies and clinician experience. RADIANCE, a 2014 multicenter RCT compared intravitreal ranibizumab to VPDT in the treatment of myopic CNV and reported improved visual acuity at 12 months in the ranibizumab treatment arm. Zhu et al (2016) published a Cochrane review that found treatment with anti-VEGF therapies was more likely to restore visual acuity than VPDT.

**VPDT vs Placebo**

A second arm of the VIP trial focused on 120 patients with pathologic myopia and CNV, either classic, occult, or mixed (although 90% of patients had classic CNV) who were randomized in a 2:1 ratio to receive VPDT or placebo. Patients received an average of 3.4 VPDT treatments over 12 months. The primary outcome was the proportion of eyes with fewer than 8 letters of visual acuity lost at 12 months by ITT analysis. At month 12, VPDT-treated eyes lost fewer than 8 letters on a standard eye chart in 58 (72%) of patients versus 17 (44%) receiving placebo. Improvement of at least 5 letters was observed in 26 (32%) VPDT-treated eyes compared with 6 (15%) placebo-treated eyes. Fluorescein angiography showed progression of classic CNV in 36% of VPDT-treated eyes compared with 54% of the placebo group. The authors concluded that VPDT increased the chance of stabilizing or improving vision compared with placebo for at least 1 year. However, the results at 2 years of follow-up were not statistically significantly in favor of VPDT.

**Section Summary: VPDT vs Placebo**
The evidence for the efficacy of VPDT compared with placebo includes a subgroup analysis from a large RCT. This analysis showed VPDT to be more effective than placebo in preventing vision loss, and these findings have been corroborated in nonrandomized studies. However, the long-term efficacy of VPDT is uncertain. Moreover, use of VPDT for myopic CNV has now been largely replaced by anti-VEGF therapies.

**VPDT Plus With Anti-VEGF Therapy**

Rinaldi et al (2017) randomized 60 patients to VPDT (standard- and reduced-fluence, n=20 each) plus ranibizumab or to ranibizumab monotherapy (n=20). The primary outcomes were mean change in BCVA and mean change in retinal thickening from baseline to week 48. The trial was likely underpowered to detect a clinical meaningful difference in BVCA for between-group comparisons. Mean BCVA change at 48 weeks was +0.2 and +15 letters with standard- and reduced-fluence VPDT plus ranibizumab, respectively, compared with +16.8 letters with ranibizumab monotherapy. At 48 weeks, mean central foveal thickness decreased from baseline was 58 μm, 91.4 μm, and 85 μm for the 3 groups, respectively.

Chen et al (2011) compared bevacizumab monotherapy (n=17) with bevacizumab plus VPDT (n=6) in a retrospective analysis of patients with CNV secondary to causes other than AMD; approximately half of patients had myopic CNV. Most observed differences between groups were not statistically significant, likely due to the small sample size. For example, mean change in visual acuity at 12-month follow-up was 1.7 lines in the monotherapy group and 2.8 lines in the combination therapy group, and 36% of the monotherapy group gained 3 lines or more compared with 60% in the combination therapy group. The combination group received fewer reinjections (average injections, 2.6 vs 4.8), but this difference was not
statistically significant (p=0.11). Subgroup analysis for cases of myopic CNV showed no significant difference between groups in mean acuity gains (2.0 lines in the monotherapy group vs 2.3 lines in the combination therapy group), with fewer reinjections (2 vs 7.2, p<0.05) needed in the combination group during the 12-month follow-up. No serious ocular complications were observed. Prospective comparison with a larger number of patients is needed.

Section Summary: VPDT in Plus Anti-VEGF Therapy
The evidence for efficacy of VPDT plus anti-VEGF therapy includes 1 small RCT and 1 retrospective study. This evidence does not demonstrate improvements in BCVA. Comparative trials are needed to evaluate the efficacy of this combination therapy versus relevant comparators.

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.

There are few published data on the use of VPDT to treat patients with CNV related to ocular histoplasmosis. FDA approval in 2001 was based on a prospective single-arm study involving 26 patients with ocular histoplasmosis. Visual acuity improved by an average of more than 1 line (6.7 letters) on a standard eye chart at 12 months, with 28% of patients experiencing improvement of at least 3 lines (15 letters). Visual acuity decreased by less than 3 lines in 88% of patients during the same period from a historical control. Ramaiya et al (2013) reported results from a small RCT that assigned 19 patients to ranibizumab or PDT with rescue ranibizumab. The primary outcome measure was the change in visual acuity at 1 year. Data from 10 of the 19 randomized patients was excluded from analysis because of lack of follow-up data. The number of injections in the ranibizumab arm was 7.7 (range, 1-11). The mean number of PDT treatments administered was 2.5 (range, 2-3). All patients in the VPDT group required rescue ranibizumab therapy with a mean of 2.5 (range, 2-3) injections. Mean change in the Early Treatment Diabetic Retinopathy Study visual acuity at 1-year follow-up was 19.6 letters in the ranibizumab group versus 21 letters in the PDT group. Four (80%) of 5 patients showed a greater than 15 letter gain at 1 year in the ranibizumab group, whereas 1 of 2 patients in the VPDT group showed a greater than 15 letter gain. Because of 50% lost to follow-up, small sample (<6 patients per arm) and incomplete reporting of the trial results, interpretation of data is difficult.

Section Summary: Presumed Ocular Histoplasmosis
The evidence for the efficacy of VPDT includes 1 small prospective single-arm study and 1 RCT. Lack of a control arm in the single-arm study and 50% loss to follow-up in the RCT preclude meaningful interpretation of the data on observed improvements in visual acuity. Comparative trials are needed to evaluate the efficacy of combination VPDT plus anti-VEGF therapy.
Central serous chorioretinopathy (CSC) refers to an idiopathic disease in which there is a serous 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 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 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 treatment of CSC because full-dose VPDT used in AMD has shown a potentially higher risk of developing choroidal ischemia and retinal atrophic changes.

A Cochrane review with network meta-analysis on various treatments for CSC that included both acute and chronic CSC was published in 2015. Only RCTs were included. Pairwise (direct) comparison for VPDT included anti-VEGF versus VPDT, anti-VEGF plus 50% VPDT versus 50% VPDT alone, 50% VPDT versus 50% VPDT versus VPDT. (Percentages refer to the dose of verteporfin used.) The primary outcome was visual acuity at 12 months. Low-quality evidence from 1 study (58 participants) suggested that half-dose VPDT for acute CSC probably resulted in a small improvement in vision (MD = -0.10 logMAR; 95% CI, -0.18 to -0.02 logMAR) compared to sham treatment. Moderate-quality evidence from 2 studies suggested that 30% VPDT results in a small improvement in vision compared to VPDT (MD = -0.16 logMAR; 95% CI, -0.22 to -0.10 logMAR) and compared to 50% VPDT (MD = -0.12 logMAR; 95% CI, -0.15 to -0.08 logMAR). Visual acuity scores at 12 months did not differ between anti-VEGF versus VPDT or anti-VEGF plus 50% VPDT versus 50% VPDT alone, or 50% VPDT versus observation or sham treatment.

Acute Central Serous Chorioretinopathy
Chan et al (2008) conducted a randomized, double-masked, placebo-controlled trial of 63 patients who were randomized in a 2:1 ratio to half-dose VPDT or placebo. Thirty-nine patients in the VPDT and 19 in the placebo arm completed the trial. The primary outcome measure (the proportion of eyes with absence of subretinal fluid at the macula at 12 months) was observed in 37 (95%) eyes in the VPDT arm and 11 (58%) eyes in the placebo arm. Mean increase of BCVA was 1.8 and 0.6 lines in the VPDT and placebo arm, respectively. The treatment difference was 1.2 lines, which fell below the threshold of 3 lines considered clinically meaningful. A responder analysis was not reported.

In 2015, Zhao et al reported a double-masked, randomized, noninferiority trial with 131 patients that compared a 50% versus a 30% dose of VPDT for acute (<6 months) CSC. The 2 primary outcome measures were the proportion of eyes with complete absorption of subretinal fluid and the proportion of eyes with complete disappearance of fluorescein leakage at 6 and 12 months. The 30% dose was not shown to be noninferior to the 50% dose, demonstrating a fluorescein angiography–based improvement rate of 68.9% versus 91.1% at 6 months (p=0.001) and 68.9% versus 92.9% at 12 months (p=0.001).
Salehi et al (2015), in their meta-analysis which included a total of 25 studies (total N=1098 patients; 1098 eyes), judged this study to be at low risk of bias in most domains with the exception of attrition bias (6% of the 30% VPDT group were lost to follow-up vs 13% of the 50% VPDT group) and selective outcomes reporting (primary and secondary outcomes were designated differently on the trial register entry and the published report). The 30% dose did not achieve noninferiority. At 12 months, the proportion of eyes with complete absorption of retinal fluid was 75.4% in the 30%-dose group and 94.6% in the half-dose group (p=0.004). Complete disappearance of fluorescein leakage at 12 months was observed in 68.9% of the 30%-dose group versus 92.9% of the half-dose group (p=0.001). Visual acuity (a secondary outcome measure) improved from 20/32 to 20/20 in both groups, with a mean between-group difference of 1.7 letters. In the 30%-dose group, 4 (6.6%) eyes lost 5 or more letters compared with 0 eyes in the half-dose group. This study did not provide sufficient evidence of a functional benefit that would outweigh the potential risk of treatment with VPDT for acute CSC.

Section Summary: Acute Central Serous Chorioretinopathy
The evidence for the efficacy of VPDT for acute CSC includes 2 RCTs. This evidence, although demonstrating that full- and reduced-dose VPDT results in small improvements in BCVA, did not meet the clinically meaningful threshold. Comparative and adequately powered trials are needed to evaluate the efficacy of VPDT in acute CSC.

Chronic Central Serous Chorioretinopathy
Reductions in subretinal fluid and improvement in retinal anatomy, visual acuity and retinal sensitivity have been observed in 70% to 100% of cases in multiple retrospective studies. Use of reduced-dose VPDT for chronic CSC also has been reported. Uetani et al (2012) compared half-dose versus one-third dose VPDT in a small (N=16 eyes) prospective open-label trial. At 3 months, all 10 (100%) eyes in the half-dose VPDT group and 2 (33%) eyes in the one-third-dose VPDT group had complete resolution of subretinal fluid. Patients in the half-dose VPDT group gained an average of 5.4 letters while patients in the one-third-dose group gained 1.7 letters (p=NS). Chan et al (2008) also reported on reduced-dose verteporfin for the treatment of chronic CSC in a prospective series of 48 patients. Mean duration of CSC was 8.2 months (range, 3-40 months). At 12 months after VPDT, mean BCVA improved from 0.31 to 0.15 logMAR, an improvement of 1.6 lines.

Section Summary: Chronic Central Serous Chorioretinopathy
The evidence for the efficacy of VPDT for chronic CSC includes multiple retrospective studies. Although this relatively large body of studies has indicated that half-dose VPDT yields positive functional and anatomic outcomes while, at the same time, reducing the potential adverse events associated with conventional VPDT, no comparative data have shown the relative efficacy of multiple VPDT strategies. Comparative trials are needed to evaluate the efficacy of VPDT strategies in chronic CSC.

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.

**Verteporfin Photodynamic Therapy**

The 2010 systematic review by Chan et al included 30 studies on VPDT in patients with polypoidal choroidal vasculopathy. Chan et al found numerous case series reporting favorable anatomic outcomes and visual acuity for patients treated with VPDT. Some of these studies are described below. Tang et al (2015) also published a systematic review and meta-analysis evaluating treatment for polypoidal choroidal vasculopathy. Two RCTs Compared VPDT with ranibizumab and reported the weighted MD in visual acuity was 0.06 logMAR (95% CI, -0.01 to 0.12 logMAR) in favor of ranibizumab, but this difference was not statistically significant.

Several nonrandomized studies from Asia have been reported. Hikichi et al (2011) reported the largest prospective consecutive series of 220 eyes of 210 Japanese patients with polypoidal choroidal vasculopathy who were followed for 1 year after the primary VPDT. A single physician diagnosed, treated, and followed all patients (not masked). Retreatment was considered every 3 months based on the findings of examinations, and there was an average of 1.37 treatments. Fluid, exudates, and hemorrhages had resolved in 205 (93%) eyes at 1-year follow-up. Average visual acuity improved by more than 0.3 logMAR in 55 (25%) of eyes, remained stable in 143 (65%) of eyes, and decreased more than 0.3 logMAR in 21 (10%) of eyes.

Akaza et al (2011) reported 3-year follow-up of 43 eyes (43 patients) treated with VPDT for polypoidal choroidal vasculopathy in the narrow sense and 3 (7%) exhibited polypoidal choroidal vasculopathy. Number of treatment sessions during follow-up ranged from 1 to 8. At 3-year follow-up, mean visual acuity decreased to below baseline. Polypoidal lesions recurred in 33 (77%) of the 43 eyes at 3 years, although the 3 eyes with polypoidal CNV showed little change except enlargement and recurrence. Long-term visual outcomes following VPDT showed a high frequency of recurrent polypoidal lesions as well as enlargement and neovascular changes of abnormal vascular networks. However, because polypoidal lesions recurred after VPDT in some cases, further study is needed to confirm the long-term effectiveness of VPDT for polypoidal choroidal vasculopathy.

**Section Summary: VPDT in Polypoidal Choroidal Vasculopathy**

Available evidence on the efficacy of VPDT for polypoidal choroidal vasculopathy consists of a several retrospective studies and 1 meta-analysis that included 2 RCTs. Retrospective studies have reported favorable anatomic outcomes and visual acuity for patients treated with VPDT. RCTs comparing VPDT with anti-VEGF therapies have reported no statistical differences in visual acuity. Controlled trials are needed to permit conclusions on the efficacy of VPDT monotherapy in polypoidal choroidal vasculopathy.

**VPDT Plus Anti-VEGF Therapy**

Tang et al published a systematic review in 2015 evaluating treatment for polypoidal choroidal vasculopathy. A single RCT that compared VPDT to VPDT plus ranibizumab reported a nonsignificant weighted MD of -0.08 logMAR (95% CI, -0.20 to 0.04 logMAR) in favor of combination therapy.
Lim et al (2012) randomized 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy to bevacizumab alone or to bevacizumab plus VPDT. Bevacizumab was administered at 6-week intervals for the first 18 weeks, and then at 3-month intervals as needed. At 12 months, the monotherapy and combined treatment groups showed similar improvements in BCVA and central foveal thickness. Patients with polypoidal choroidal vasculopathy did not show significant improvement in BCVA ($p=0.050$) or central foveal thickness ($p=0.088$) when analyzed alone; however, the study was likely underpowered for this subset analysis.

EVEREST (2012) was a small, exploratory, multicenter, double-masked, randomized trial of VPDT, ranibizumab, or VPDT plus ranibizumab in 61 treatment-naive Asian patients with polypoidal choroidal vasculopathy. Patients in the VPDT-only group (angio-occlusive) received sham ranibizumab, and patients in the ranibizumab monotherapy group (antiangiogenic and antipermeability) received sham VPDT. The primary end point (the proportion of patients with complete regression of polyps at 6 months) showed VPDT alone (71.4%) or in combination with ranibizumab (77.8%) to be superior to ranibizumab monotherapy (28.6%) in achieving complete polyp regression. Mean improvement in BCVA was generally similar for the 3 groups (7.5 letters for VPDT, 10.9 letters for combined treatment, 9.2 letters for ranibizumab alone). The proportion of patients gaining at least 15 letters was 19% in the VPDT group, 21% in the combination group, and 33% in the ranibizumab monotherapy group. Interpretation of the visual acuity results is limited, because the study was not powered to assess differences in BCVA. There were no new safety findings.

Observational studies have also been published. Kang et al (2013) reported 5-year retrospective follow-up for 42 eyes (36 patients) treated with VPDT for polypoidal choroidal vasculopathy. Patients received a mean of 2.21 VPDT treatments during the study, with additional intravitreal injections of anti-VEGF agents if exudative changes were observed. During follow-up, recurrence was observed in 33 (78.6%) eyes, and the mean number of anti-VEGF injections was 6.42 in eyes with recurrence. In the entire group, BCVA improved from 0.78 logMAR at baseline (20/120 Snellen equivalent) to 0.67 logMAR (20/93 Snellen equivalent) at 5 years. Using a change of at least 0.3 logMAR as a threshold, BCVA improved in 14 (33.3%) eyes, remained stable in 23 (54.8%) eyes, and decreased in 5 (11.9%) eyes. Interpretation of this study is difficult, because all patients received combination treatment with intravitreal VEGF antagonists without comparison groups. Kim and Yu (2011) retrospectively reviewed 39 consecutive patients with polypoidal choroidal vasculopathy who received VPDT (before April 2007) or combination VPDT plus intravitreal bevacizumab (after April 2007). During 12 months of follow-up, patients in the monotherapy group (n=19) received a mean of 1.89 VPDT applications, and patients in the combined therapy group (n=20) received a mean of 1.30 VPDT applications and 2.90 bevacizumab injections. BCVA improved by 3.0 lines in the combined therapy group compared with 1.6 lines in the VPDT-only group. This level of improvement in BCVA was achieved in 55.0% in the combined therapy group and 36.8% in the monotherapy group.

Section Summary: VPDT Plus Anti-VEGF Therapy in Polypoidal Choroidal Vasculopathy
Available evidence on the efficacy of VPDT for polypoidal choroidal vasculopathy consists of 2 small RCTs, 1 meta-analysis, and 2 retrospective studies. While results of the RCT reported no difference in visual acuity for patients treated with VPDT plus anti-VEGF therapy versus VPDT alone, the other trial reported improvement in visual acuity but the effect was not statistically significant. Adequately powered controlled...
trials are needed to permit conclusions on the efficacy of combination VPDT plus anti-VEGF therapy in polypoidal choroidal vasculopathy.

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.

The 2010 systematic review by Chan et al included 11 case series on VPDT in patients with choroidal hemangioma. VPDT has been reported to induce complete and irreversible occlusion of the microvasculature, although this may require more than 1 treatment. Several case series have demonstrated encouraging visual acuity and anatomic outcomes in 150 patients with circumscribed choroidal hemangioma treated with various VPDT regimens.

In 2010, Blasi et al reported on 5-year outcomes for a prospective series of 25 consecutive patients with symptomatic choroidal hemangioma. Twenty-two (88%) patients received a single VPDT session and 3 eyes received a second VPDT session. Follow-up examinations were performed 2 weeks, 1 month, 3 months, and every 6 months after treatment. All tumors were reduced in size, and there were no recurrences through 5 years of follow-up. At 1 year, BCVA improved by an average of 18.2 letters. Visual acuity improved by 2 or more lines in 20 (80%) eyes and by 3 or more lines in 12 (48%) eyes. No treated eyes lost visual acuity between the 1- and 5-year follow-ups. Foveal center thickness decreased from a mean of 386.20 μm to 179.2 μm at 5 years, and there was resolution of macular exudation in all cases. No treatment-related adverse events were identified.

Section Summary: Choroidal Hemangioma

Available evidence on the efficacy of VPDT for choroidal hemangioma consists of 1 systematic review that included data from 11 case series and 1 prospective study. This body of evidence has suggested a favorable effect of VPDT on various visual acuity and anatomic outcomes in patients with choroidal hemangioma. Controlled trials with a larger number of patients and longer follow-up are needed to permit conclusions regarding the efficacy of VPDT for this indication.

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.

The 2010 systematic review by Chan et al included 8 case series on VPDT in 148 patients with angioid streaks. Reviewers concluded the VPDT might limit or slow vision loss compared with the expected natural course of CNV due to angioid streaks, but 1 study showed a decrease in visual acuity following VPDT, and others showed that substantial proportions of patients continued to lose visual acuity. Thus, further studies are warranted to assess long-term safety and efficacy of VPDT in these patients.
Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

Section Summary: Angioid Streaks
Available evidence on the efficacy of VPDT for angioid streaks consists of 1 systematic review on case series. The data from case series have reported conflicting results for visual acuity. Controlled trials with a larger number of patients and longer follow-up are needed to permit conclusions on the efficacy of VPDT in angioid streaks, especially if it is effective in limiting the growth of CNV.

INFLAMMATORY CHORIORETINAL CONDITIONS
CNV can occur as a complication of inflammatory conditions such as uveitis, multifocal choroiditis and panuveitis, and punctate inner choroidopathy. About one-third of patients develop CNV, which can result in severe vision loss if it is subfoveal.

The 2010 systematic review by Chan et al included 15 case reports of VPDT in 115 patients with inflammatory eye conditions. Encouraging visual acuity and anatomic improvements have been reported with VPDT for punctuate inner choroidopathy, choroiditis and toxoplasmic retinochoroiditis, and subfoveal CNV secondary to posterior uveitis. While promising, larger and comparative studies are needed to evaluate the effect of VPDT on health outcomes for this indication.

Section Summary: Inflammatory Chorioretinal Conditions
Available evidence on the efficacy of VPDT for inflammatory chorioretinal conditions consists of multiple case reports. Controlled trials are needed to permit conclusions on the efficacy of VPDT in ocular inflammatory conditions.

SUMMARY OF EVIDENCE
Age-Related Macular Degeneration
For individuals who have classic CNV due to AMD 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 to 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 AMD who receive VPDT plus anti-vascular endothelial growth factor (anti-VEGF) therapy, the evidence includes 2 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 3 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.
Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

Pathologic Myopia
For individuals who have CNV due to pathologic myopia who receive VPDT, the evidence includes 1 subgroup analysis from a 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 1 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 1 small RCT and 1 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 clinical 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.

For individuals who have CNV due to presumed ocular histoplasmosis who receive VPDT, the evidence includes 1 small RCT and 1 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 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 CSC who receive VPDT, the evidence includes 2 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 CSC 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 1 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.

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Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

For individuals who have CNV due to polypoidal choroidal vasculopathy who receive VPDT plus anti-VEGF therapy, the evidence includes 2 small RCTs, 1 meta-analysis, and 2 retrospective cohort studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Results of the 2 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 1 systematic review (11 case series) and 1 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 1 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 1 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.

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3. VEGF Inhibition Study in Ocular Neovascularization Clinical Trial Group, Chakravarthy U, Adamis AP, 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 e1501-1525. PMID 16828500
Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017


Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
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Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

05/03/2006 Medical Director review
05/17/2006 Medical Policy Committee approval. Format revision including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
04/04/2007 Medical Director review
04/18/2007 Medical Policy Committee approval. No change to coverage eligibility.
08/06/2008 Medical Director review
08/20/2008 Medical Policy Committee approval. Added Updates from BCBSA to Rationale. Changed the verbiage in the Coverage section from “When Services May Be Eligible for Coverage” to “When Services Are Eligible for Coverage”. Criteria dropped in Coverage section due to redundancy. No change to coverage eligibility.
08/06/2009 Medical Policy Committee approval.
08/26/2009 Medical Policy Implementation Committee approval. No change to coverage eligibility.
08/05/2010 Medical Policy Committee review
08/18/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2011 Medical Policy Committee review
08/02/2012 Medical Policy Committee review
08/15/2012 Medical Policy Implementation Committee approval. New drug listed under investigational section.
08/01/2013 Medical Policy Committee review
08/21/2013 Medical Policy Implementation Committee approval. PDT monotherapy considered eligible for coverage for central serous chorioretinopathy and choroidal hemangioma added as investigational.
08/07/2014 Medical Policy Committee review
08/20/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/01/2014 Coding updated- code G0186 Destruction of localized lesion of choroid (for example, choroidal neovascularization); photoocoagulation, feeder vessel technique (one or more sessions) - added to policy
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/08/2015 Medical Policy Committee review
10/21/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/06/2016 Medical Policy Committee review
10/19/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
10/05/2017 Medical Policy Committee review
10/18/2017 Medical Policy Implementation Committee approval. Added “verteporfin” in front of “photodynamic therapy” in the policy statements and throughout the body of the policy.

Next Scheduled Review Date: 10/2018

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Page 20 of 22
Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

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Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/18/2017

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