APPENDIX to Photodynamic Therapy for Subfoveal Choroidal Neovascularization Policy

Prior Authorization Requirements

This service (or procedure) is considered **medically necessary** in certain instances and **investigational** in others (refer to policy for details).

For instances when the indication is **medically necessary**, clinical evidence is required to determine **medical necessity**.

For instances when the indication is **investigational**, you may submit additional information to the Prior Authorization Department.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

Evidence Basis for the Policy

Rationale

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). Available therapeutic options for choroidal neovascularization include photodynamic therapy (PDT), antioxidants, thermal laser photocoagulation, corticosteroids, and vascular endothelial growth factor (VEGF) antagonists or angiostatics. The safety and efficacy of each treatment depends on the form and location of the neovascularization. For those whose visual losses impair their ability to perform daily tasks, low-vision rehabilitative services offer resources to compensate for deficits.

Prior to the availability of PDT, choroidal neovascularization (CNV) was treated with photocoagulation using either argon, green, or infrared lasers. This conventional photocoagulation was limited to extrafoveal lesions due to the risk of retinal burns. Introduction of a scotoma or enlargement of a pre-existing scotoma, with or without visual acuity loss, is an immediate and permanent effect of photocoagulation surgery. Because of the loss of vision

associated with laser photocoagulation, photocoagulation is no longer recommended as the initial treatment of subfoveal neovascularization. More recently, infrared lasers used at a low-power setting have been investigated as a technique to photocoagulate subfoveal lesions.

Age-related Macular Degeneration

Age-Related Macular Degeneration (AMD) is a painless, insidious process. In its earliest stages, it is characterized by minimal visual impairment and the presence of large drusen and other pigmentary abnormalities on ophthalmoscopic examination. As AMD progresses, two distinctively different forms of degeneration may be observed. The first, called the atrophic or areolar or dry form, evolves slowly. Atrophic AMD is the most common form of degeneration and is often a precursor of the second form, the more devastating exudative neovascular form, also referred to as disciform or wet degeneration. The wet form is distinguished from the atrophic form by serous or hemorrhagic detachment of the retinal pigment epithelium and the development of CNV, sometimes called neovascular membranes. Risk of developing severe irreversible loss of vision is greatly increased by the presence of CNV. The pattern of CNV, as revealed by fluorescein or indocyanine angiography, is further categorized as classic or occult. For example, 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, either due to the opacity of coexisting subretinal hemorrhage or, especially in CNV associated with AMD, by a tendency for epithelial cells to proliferate and partially or completely surround the new vessels. Interestingly, lesions consisting only of classic CNV carry a worse visual prognosis than those made up of only occult CNV, suggesting that the proliferative response that obscures new vessels may also favorably alter the clinical course of AMD.

A 2000 TEC Assessment offered the following observations and conclusions:

- Two multicenter, double-masked, randomized placebo-controlled trials including 402 patients reported that, at 1 year of follow-up, fewer patients treated with PDT experienced a clinically significant loss of visual acuity compared to those treated with placebo: 38.8% compared to 53.6%, respectively ($p < 0.001$).
- Subgroup analysis suggests that the treatment effect is predominantly experienced by patients with AMD characterized by at least 50% classic CNV.
- There were inadequate data to permit scientific conclusions regarding other etiologies of CNV.

A 2003 Cochrane review (Wormald et al.) concluded that PDT is effective in preventing visual loss in classic and occult CNV due to AMD. An updated Cochrane review in 2007 by the same authors evaluated results of 1,022 patients from 3 randomized controlled trials (RCT)s, which included the TAP and VIP trials described below. Meta-analysis showed a 24-month risk ratio of losing 6 or more lines of visual acuity of 0.62 compared to the control group. The authors concluded that PDT is probably effective in treating CNV due to AMD, although there is doubt about the size of the effect. In a 2004 meta-analysis of the safety of PDT, Azab and colleagues (2004) analyzed data from the 24-month TAP A and B and VIP trials, totaling 948 patients with AMD. The authors concluded that the safety profile of verteporfin therapy was not statistically different from placebo.

In 2001, Bressler NM published the 2-year results of the pivotal randomized trial Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP). Beneficial outcomes regarding visual acuity and contrast sensitivity noted after 12 months were sustained through 24 months. At the end of 2 years, 53% of the treatment group, as compared to 38% of the placebo group, lost fewer than 15 letters. The average number of applications of verteporfin treatment in the second year (2.2) was lower than that required during the first year (Wormald et al., 2003; Wormald et al., 2007). Subgroup analysis compared results between those patients with predominantly classic CNV (> 50% of lesional area) compared to minimally classic CNV (< 50%). For patients with minimally classic disease, no statistically significant differences in visual acuity were noted. Several additional reports from the TAP trial have been published (Blumenkranz et al., 2002; Bressler et al., 2002; Rubin and Bressler, 2002). These reports demonstrated positive outcomes with the use of PDT 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 study. Of 402 verteporfin-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 and 122 (38%) discontinued prematurely, 3 (1%) were noncompliant. Yearly treatment rates declined from 3.5 treatments in the first year to 0.1 in the fifth year; subjects 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 published in 2001 is another randomized study that primarily focused on efficacy of PDT in patients with occult but no classic lesions who were presumed to have progressive disease due to visual or anatomic deterioration within the previous 3 months. Of the 339 patients enrolled in the trial, 76% had occult disease; the remainder had early classic CNV with good visual acuity. Similar to other randomized trials, 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 had lost vision (55% versus 68%, respectively; $p = 0.032$). These results contrast with those of the TAP trial, although the patient populations are slightly different. The TAP trial 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.

In 2008, Schmidt-Erfurth and Sacu conducted a multicenter clinical trial to compare efficacy and safety of a more intense regimen versus a standard one for retreatment of neovascular AMD during the early period of verteporfin therapy. Patients (n = 231) with predominantly classic CNV secondary to AMD were included. During the first 6 months of verteporfin therapy, patients were randomly assigned 1:1 to retreatment every 2 months (group A) or 3 months (group B). After 6 months, both groups underwent retreatment every 3 months for as long as CNV activity was documented. At all follow-up through 24 months, mean best-corrected visual acuities (BCVA) were similar for groups A and B; mean numbers of PDT treatments were similar for both groups (4.07 vs. 4.36, respectively); a lower proportion (51.9% vs. 56.7%) of patients in group A had lost at least 3 lines of vision at 24 months; and groups A and B had similar increases in mean lesion size from baseline to 24 months. Overall, outcomes regarding

visual benefit, lesion anatomic features, and number of retreatments after 6 months, were similar for patients receiving more intense or standard early therapy.

Photodynamic Therapy Compared to Anti-VEGF Therapies

A 2008 Cochrane review evaluated anti-VEGF therapies for neovascular AMD (Vedula & Krzystolik, 2011). Five RCTs on pegaptanib and ranibizumab were included in the review; all were conducted by pharmaceutical companies. The trials compared pegaptanib or ranibizumab versus sham, ranibizumab versus PDT, and ranibizumab plus PDT versus PDT alone (PDT trials are described in more detail below). Fewer patients treated with pegaptanib lost 15 or more letters of visual acuity at 1-year follow-up compared to sham (pooled relative risk [RR]: 0.71). In a trial of ranibizumab versus sham, RR for loss of 15 or more letters visual acuity at 1 year was 0.14 in favor of ranibizumab. The pooled RR for gain of 15 or more letters of visual acuity at 1 year was 5.81 for ranibizumab versus sham, 6.79 for ranibizumab versus verteporfin PDT, and 4.44 for ranibizumab plus verteporfin PDT versus verteporfin PDT.

Ranibizumab was compared in 2006 with PDT in a multicenter, double-blind study (423 patients) by the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration (ANCHOR) study group (Brown, et al., 2006). Patients with subfoveal CNV and a predominantly classic lesion (n = 423) were randomized in a 1:1:1 ratio to receive 0.3 mg (n = 137) or 0.5 mg (n = 139) of intravitreal ranibizumab plus sham verteporfin or sham injections plus active verteporfin (n = 142) monthly. Patients were to receive monthly injections for 2 years in the study eye. Only 1 eye per patient was chosen as the study eye, and only the study eye received ranibizumab with sham PDT or sham injection with active PDT. Following 12 monthly treatments, patient groups treated with ranibizumab (0.3 or 0.5 mg) and sham verteporfin had 94% to 96% of subjects lose fewer than 15 letters. The patient group treated with monthly sham injection and active verteporfin therapy (average 2.8 times over the year) had 64% of subjects lose fewer than 15 letters. Visual acuity improved by more than 15 letters in 36% and 40% of the ranibizumab groups (average dose-dependent gain of 8.5 and 11.3 letters), in comparison with 5.6% of subjects in the verteporfin group (average loss of 9.5 letters). Intraocular inflammation occurred in 10.2% and 15% of ranibizumab-treated patients, with presumed endophthalmitis in 1.4% and serious uveitis in 0.7% of patients treated with the highest dose.

In 2009, Brown et al. evaluated the 2-year results of the Phase III multicenter, manufacturer-funded ANCHOR trial. The primary, intent-to-treat (ITT) efficacy analysis was at 12 months, with continued measurements to month 24. Key measures included the following: the percentage losing greater than 15 letters from baseline visual acuity score (month 12 primary efficacy outcome measure); percentage gaining equal to or greater than 15 letters from baseline; and mean change over time in visual acuity score and fluorescein angiography-assessed lesion characteristics. Adverse events were monitored. Of 423 patients, at least 77% in each group completed the 2-year study. Consistent with results at month 12, at month 24, the visual acuity benefit from ranibizumab was statistically significant and felt to be clinically meaningful; 89.9% to 90.0% of ranibizumab-treated patients had lost less than 15 letters from baseline versus 65.7% of PDT patients; and 34% to 41.0% had gained 15 or more letters versus 6.3% of the PDT group. Changes in lesion anatomic characteristics on fluorescein angiography also favored ranibizumab. There was a trend for an increased incidence of cataract in the ranibizumab groups compared

with the PDT group, which was statistically significant at the 0.5-mg dose. There were no statistically significant differences among the 3 treatment groups in the rates of serious nonocular adverse events. In this 2-year study, ranibizumab provided greater clinical benefit than verteporfin PDT in patients with age-related macular degeneration with new-onset, predominantly classic CNV. Rates of serious adverse events were low.

Bressler et al. (2009) reported a sub-analysis of the patient-reported outcomes from the ANCHOR trial. The National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) was administered at baseline and at 1, 2, 3, 6, 9, 12, 18, and 24 months. The primary outcome measure was mean change from baseline in NEI VFQ-25 scores at 12 months. At 12 months, patients treated with ranibizumab had mean improvements in NEI VFQ-25 composite scores of 5.9 (range: 3.6 to 8.3) for the 0.3-mg dose group and 8.1 (range: 5.3 to 10.8) points for the 0.5-mg dose group; patients treated with PDT had a mean improvement of 2.2 points (range: -0.3 to 4.7). At each dose through 24 months, patients treated with ranibizumab were more likely to improve in most subscales, including the prespecified subscales (near activities, distance activities, and vision-specific dependency). The authors concluded that "... patients treated with ranibizumab were more likely to report clinically meaningful improvements in visual function through 24 months compared with those treated with verteporfin PDT."

Photodynamic Therapy in Combination Therapies for AMD

Combining PDT with angiostatic agents, either concurrently or sequentially, has a biological basis and is under active investigation. Angiostatic agents block some stage in the pathway leading to new blood vessel formation (angiogenesis). Drugs currently under study target various parts of the angiogenic pathway: messenger RNA; VEGFs; endothelial cell proliferation, migration, and proteolysis. The angiostatic agents being studied in trials include pegaptanib, ranibizumab, bevacizumab, anecortave acetate, squalamine, vatalanib, and triamcinolone acetonide. In contrast to palliative treatments for CNV (e.g., thermal photocoagulation and PDT), they are potentially disease modifying by inhibiting the development of newly formed vessels.

PDT in Combination with VEGF Antagonists

A 2005 TEC Special Report found a number of trials in progress combining an angiostatic agent with photodynamic therapy. For example, in the pegaptanib trial, PDT was administered at physician discretion, but an analysis was not provided that examined possible synergistic effects (Gragoudas et al., 2004).

In a 2010 editorial, Kaiser reported an ongoing clinical program (SUMMIT) that is investigating whether treatment with combination PDT and ranibizumab is safe and effective compared to monotherapy. The SUMMIT clinical program will combine results from a North American trial (DENALI, n = 321) and a European trial (MONT BLANC, n = 255). Both are 12-month, randomized, controlled, double-blinded multicenter trials that evaluate the efficacy and safety of combination treatment with ranibizumab and PDT compared to ranibizumab monotherapy in patients with CNV secondary to AMD. Results from the DENALI and MONT BLANC trials were reported in 2012 (Kaiser PK, 2012; Larsen et al., 2012).

DENALI was a multicenter, double-blind, randomized Phase IIIb trial (Kaiser et al., 2012) that tested whether ranibizumab in combination with either standard fluence PDT (n = 104), or

reduced fluence PDT (n=105) was noninferior to ranibizumab given monthly (n = 112). The 2 combination-therapy groups received ranibizumab monthly for the first 3 months, followed by retreatment with PDT or ranibizumab as needed (*pro re nata*; PRN) based on specified retreatment criteria at monthly monitoring. The ranibizumab monotherapy group received sham PDT, and patients in the combination groups who did not require ranibizumab at the monthly follow-up visit received sham intravitreal injections. The 2 main outcome measures were the change in BCVA from baseline and the proportion of patients in the combination therapy groups with a treatment-free interval of 3 months or longer. A ranibizumab-free interval of 3 months or longer was achieved in most of the patients in the standard (92.6%) and reduced (83.5%) fluence combination groups. Patients in the monotherapy arm received an average of 10.5 injections, while patients in the standard and reduced fluence combination groups received an average of 5.1 and 5.7 injections. About 20% of patients in the combination groups did not receive any ranibizumab retreatments after the loading phase up until month 11. However, the mean BCVA change at 12 months was + 5.3 and + 4.4 letters for standard and reduced fluence PDT, respectively, compared with + 8.1 letters for the ranibizumab monotherapy group, and non-inferiority of visual outcomes was not demonstrated. Mean central retinal thickness, measured at a central reading center, was reduced more in the ranibizumab monotherapy group (172.2 microns) compared to the reduced fluence (140.9 microns) group. Florescein leakage was higher in the combination therapy groups (standard fluence: 58.2%, p = 0.008; reduced fluence: 54.5%, p = 0.075) compared with the ranibizumab monotherapy group (41.8%).

MONT BLANC was a multicenter, double-blind, randomized noninferiority trial that compared combination PDT/ranibizumab versus PRN ranibizumab monotherapy (with sham PDT) in 255 patients with CNV related to AMD (Larsen et al., 2012). Both groups received 3 consecutive monthly injections followed by PRN retreatments (active or sham) based on specified retreatment criteria. As with the DENALI trial, the 2 main outcome measures were the change in BCVA from baseline and the proportion of patients in the combination therapy group with a treatment-free interval of 3 months or longer. 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 and 92% monotherapy), and the change in BCVA with combination therapy (+ 2.5 letters) was found to be noninferior to ranibizumab monotherapy (+ 4.4 letters). On average, patients received 4.8 ranibizumab injections in the combination group compared with 5.1 injections in the monotherapy group over 12 months. Decreases in mean central retinal thickness were similar in the combination (115.3 microns) and monotherapy (107.7 microns) groups. This well-conducted study found that PDT did not reduce the number of ranibizumab injections when ranibizumab was administered PRN.

The FOCUS study group reported first- and second-year results of a blinded Phase I/II multicenter, RCT of ranibizumab (0.5 mg) combined with PDT (Heier et al., 2006; Antoszyk et al., 2008). Patients with subfoveal CNV secondary to AMD were randomized in a 2:1 ratio to ranibizumab (n = 106) or sham (n = 56) injection (initially 7 days) following verteporfin photodynamic therapy. PDT was repeated only if fluorescein angiography revealed persistent or recurrent leakage from CNV at evaluation visits (3-month intervals). A higher than expected rate of serious intraocular inflammation occurred in the first patients, and the 2 treatments were subsequently scheduled no closer than 21 days apart. Intent-to-treat 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 PDT-alone group. Twenty-nine percent of patients in the ranibizumab group received additional PDT (average of 0.4 treatment), compared with 93% of patients in the photodynamic therapy-alone group (average of 3 treatments). Visual acuity improved by 15 or more letters in 25% of patients treated with ranibizumab (plus PDT as needed) compared with 7% of the patients treated with PDT alone. Endophthalmitis or intraocular inflammation was observed in 16 (15%) patients treated with ranibizumab. The majority of adverse events (9%) reported for the photodynamic therapy-alone group was AMD-related (i.e., CNV, macular degeneration, retinal hemorrhage).

A small RCT by Lim et al. (2012) was published that randomized 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy (PCV) to bevacizumab monotherapy or bevacizumab in combination with PDT. 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. The total number of bevacizumab injections was not reduced when PDT was given.

A randomized, open-label assessor-blinded trial (n = 165) from Croatia with short-term (3-month) follow-up reported similar results with bevacizumab and PDT (Lazic & Gabric, 2007). The frequency of treatment was described only as “standard procedures.” Twenty-two of 52 (42%) patients improved by greater than 0.2 logarithm of the minimum angle of resolution (LogMAR) following combined treatment, compared with 1 (2%) patient treated with bevacizumab alone and none treated with PDT alone. Adverse events (21%) in the bevacizumab groups (alone or combined) were frequent and included 3 pigment epithelial tears, 12 posterior vitreous detachments, and 7 cataract progressions.

A pilot open-label, non-randomized trial assigned 40 eyes of 30 patients to combination therapy (single session of PDT) or ranibizumab monotherapy (Bashshur et al., 2011). Follow-up treatment consisted only of as-needed ranibizumab, and patients in the monotherapy group received a mean of 6 injections compared to a mean of 3 injections in the combination therapy group. At 12 months, only 1 eye in the combination group lost 15 letters or more of visual acuity. Five eyes (25%) in the ranibizumab monotherapy group and 2 eyes (10%) in the combination therapy group gained at least 15 letters. There was a mean gain of 12 letters for the monotherapy compared to a 3.2 letter gain for combination therapy. These differences were not statistically significant in this small study.

Kaiser et al. (2009) conducted a retrospective case series database (registry) analysis to assess outcomes for patients with CNV due to AMD treated with combination therapy of verteporfin PDT and bevacizumab. Patients (n = 1,196) with CNV due to AMD who received one or more combination treatment of 1.25 mg intravitreal bevacizumab within 14 days of verteporfin PDT were included in the analysis. Physicians from 45 clinical centers entered patient data at baseline and follow-up examinations, including subsequent treatments. The primary outcome measure was change from baseline in visual acuity and retreatment rates of any therapy after the initial combination treatment. As noted by the authors, RCTs are needed.

In 2010, Rudnisky et al. reported a retrospective comparison of 236 eyes that received combined treatment with bevacizumab and PDT versus 139 eyes treated with bevacizumab alone. Treatment assignment and retreatment were made by the treating retina specialist and the patient.

Patients were seen at approximately 3-month intervals. Bevacizumab injections were repeated if subretinal or intraretinal fluid was present on clinical examination and/or optical coherence tomography (OCT), or if vision was reduced in comparison to their previous visit. Combination treatment was performed at the discretion of the treating ophthalmologist. At an average follow-up of 410 or 417 days for the monotherapy and combined-treatment groups, there was no significant difference in outcomes. The monotherapy eyes received 3.3 injections of bevacizumab and gained 5 letters; the combination therapy eyes received 3.1 injections and gained 4.8 letters. The mean time between bevacizumab injections was 73.6 days for the monotherapy group versus 71.0 days for the combination group. This retrospective study suggests that long-term visual outcomes are not improved with the addition of PDT to bevacizumab, nor are fewer injections needed.

PDT in Combination with Corticosteroids

Intravitreal triamcinolone acetonide was one of the first pharmacologic compounds evaluated for the treatment of choroidal neovascularization secondary to AMD. The most important effects of this treatment consist of the stabilization of the blood-retinal barrier and the down-regulation of inflammation. Triamcinolone acetonide also has anti-angiogenic and anti-fibrotic properties and remains active for months after intravitreal injection.

The Retinologists Evaluating Triamcinolone In Neovascular AMD (The RETINA Study), a multicenter double-blind RCT with 100 subjects with CNV related to AMD found that combination therapy with PDT and triamcinolone resulted in no significant difference in the primary outcome of visual acuity at 1 year compared to PDT with sham injection but that subjects receiving triamcinolone required fewer retreatments (1.28 vs. 1.94, respectively) to control lesion leakage/activity (Maberley D, 2009). The triamcinolone group also had a larger proportion of subjects with elevated, although managed, intraocular pressure (18 vs. 4, respectively).

A second prospective randomized study in Italy by Piernarocchi et al. (2008) evaluated combination therapy with corticosteroids and PDT. In this trial, the long-term effect of intravitreal triamcinolone acetonide (IVT) treatment combined with PDT was compared with PDT alone for neovascular AMD. Eighty-four patients were enrolled to receive PDT (n = 41) or IVT treatment followed by PDT (n = 43) within approximately a 7- to 15-day interval. All patients were naive to treatment. At baseline and each follow-up visit at 3, 6, 12, and 24 months, measurement of BCVA, fluorescein angiography, indocyanine green angiography, and OCT were performed. Mean changes in visual acuity and retreatment rate were considered as primary outcome indicators. Mean visual acuity increased at 1 month of follow-up but decreased progressively by the 24-month point in both groups ($p = 0.74$). The retreatment rate was significantly lower in the combined therapy group. Choroidal hypoperfusion/nonperfusion and areas with decreased/absent fundus autofluorescence within the PDT spot area were significantly greater with combined therapy. The authors concluded: “Combination IVT treatment with PDT seemed to be more effective for managing neovascular age-related macular degeneration, but long-term analysis failed to demonstrate functional benefits.”

Triple Therapy

Triple therapy (PDT, intravitreal dexamethasone and intravitreal bevacizumab) for AMD has been reported (Ehmann & Garcia, 2010). Thirty-two eyes of 30 patients received reduced-fluence PDT followed immediately by intravitreal dexamethasone. At 1 and 7 weeks after PDT and dexamethasone, patients received a bevacizumab injection. At 13 weeks after PDT, patients were evaluated with OCT and fluorescein angiography, with additional triple therapy treatment cycles as needed for visible leakage or increased foveal thickness with vision loss. At 12-month follow-up, the mean number of treatment cycles was 1.4 and the mean number of bevacizumab injections was 2.8. Visual acuity improved from 0.74 LogMAR to 0.53 LogMAR. Foveal thickness decreased from 328 to 216 microns. Ninety-four percent of patients lost fewer than 3 lines, 31% gained more than 3 lines, and 6% lost more than 3 lines. Comparative trials are needed to evaluate the efficacy of triple therapy.

Notably, several industry-sponsored trials and completed studies of combined photodynamic and pharmacologic therapies for the treatment of CNV are listed at the government clinical trials online site as completed, but results have not been published at this time.

In summary, PDT monotherapy is an established treatment for CNV secondary to AMD, with evidence from multiple RCTs supporting benefit compared to placebo. Although PDT is established as superior to no treatment, recent comparative trials show anti-VEGF therapy to be superior to PDT. For combination therapy, the literature to date, which includes 2 high-quality randomized trials, shows no improvement in outcomes or reduction in the number of intravitreal injections with combined PDT and anti-VEGF therapy, nor with a combination of PDT and corticosteroids. Thus, combination therapy is considered investigational.

Pathologic Myopia

Pathologic Myopia (PM) refers to an abnormal elongation of the eye associated with severe near-sightedness. It generally occurs among people over 30 years of age and can result in a progressive, severe loss of vision, frequently related to the development of CNV. Photodynamic therapy has also been investigated in patients with CNV related to pathologic myopia as a comparison with a 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 PDT or placebo. Patients received an average of 3.4 PDT treatments over the course of 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. Visual acuity, contrast sensitivity, and fluorescein angiographic outcomes were better in the PDT eyes than in the placebo-treated eyes at every follow-up examination through 12 months. At month 12, PDT-treated eyes lost fewer than 8 letters on a standard eye chart in 72% of patients versus 44% who were receiving placebo. Improvement of at least 5 letters was observed in 32% of PDT-treated eyes in comparison with 15% of placebo-treated eyes. Fluorescein angiography showed progression of the classic CNV in 36% of PDT-treated eyes compared with 54% of the placebo-treated group. The authors concluded that verteporfin therapy increases the chance of stabilizing or improving vision compared to placebo treatment for at least 1 year. Results were not reported separately for those with predominantly classic CNV versus occult CNV.

El Matri et al. (2011) reported a retrospective comparison of PDT in comparison with VEGF antagonists for myopic CNV in 2011. Eighty eyes of 80 patients with myopic CNV were treated with standard PDT (2005-2007, n = 40) or bevacizumab (2008-2009, n = 40). Retreatment was given every 3 months in the PDT group and every 4 weeks in the bevacizumab group as needed; patients received a mean of 1.8 bevacizumab injections and 1.55 PDT treatments during 12 months. At baseline, BCVA was 0.9 LogMAR (20/159 Snellen equivalent) in the bevacizumab group and 0.88 LogMAR (20/152 Snellen equivalent) in the PDT group. At 3, 6, and 12 month follow-up, mean LogMAR BCVA was significantly better in the bevacizumab group (0.5-0.6 LogMAR) in comparison with the PDT group (0.85-0.86 LogMAR). The BCVAs improved by 3 lines or more in 70% of eyes in the bevacizumab group and 22.5% of the PDT group. Mean central retinal thickness was similar at baseline (421 versus 393) and significantly lower in the bevacizumab group compared to the PDT group at 3 (328 versus 393 microns), 6 (300 versus 370 microns), and 12 (305.5 versus 352 microns) months. Chorioretinal atrophy developed in 6 eyes (15%) treated with bevacizumab and in 24 eyes (60%) treated with PDT. Although limited by the retrospective nature of the comparison, these results are strongly suggestive of the superiority of anti-VEGF treatment over PDT for myopic CNV.

Bevacizumab monotherapy (n = 17) was compared to combination treatment of bevacizumab with PDT (n = 6) in a retrospective analysis of patients with CNV secondary to causes other than AMD; about half of the patients had myopic CNV (Chen et al., 2011). Most of the observed differences between the groups did not reach statistical significance, likely due to the small sample size. For example, the mean change in visual acuity at 12-month follow-up was 1.7 lines in the monotherapy group compared with 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. There was a trend for the combination group to receive fewer reinjections (2.6 versus 4.8, $p = 0.11$). Subgroup analysis for cases of myopic CNV showed no significant difference between groups in mean acuity gains (2.0 lines in the monotherapy group versus 2.3 lines in the combination therapy group) with fewer reinjections (2 versus 7.2, $p < 0.05$) needed in the combination group during the 12 months of follow-up. No serious ocular complications were observed. Prospective comparison with a larger number of patients is needed.

In summary, PDT has been shown in one RCT to be more effective than placebo for myopic CNV, and these findings have been corroborated in non-randomized studies. RCTs are needed to evaluate the efficacy and safety of combined PDT and anti-VEGF treatment in patients with myopic CNV.

Presumed Ocular Histoplasmosis

Presumed ocular histoplasmosis (POHS) may be the second most common cause of blindness in patients younger than 50 years of age in certain endemic areas (the Ohio and Mississippi River valleys in the United States). It is a condition 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 choroidal neovascular lesions, which may develop many years after chorioretinal scarring has taken place, affect the macula.

There are minimal published data regarding the use of PDT in patients with CNV related to POHS. The approval by the U.S. Food and Drug Administration (FDA) was based on an open-label safety study involving 26 patients with POHS. Visual acuity improved by an average of more than 1 line on a standard eye chart at 12 months (6.7 letters on a standard eye chart), with 28% of patients experiencing a visual acuity improvement of 3 lines (15 letters) or more. Visual acuity decreased by less than 3 lines of vision in 88% of patients during the same time period.

Central Serous Chorioretinopathy

Central serous chorioretinopathy (CSCR) 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. Although CSCR often resolves spontaneously in 3 to 4 months, chronic or recurrent CSCR can result in progressive decline of visual acuity. Central serous chorioretinopathy has been treated with medication

In 2010, Chan et al. published a systematic review of PDT for non-standard indications, which included 12 case series (119 eyes) on PDT for CSCR. In addition, 3 nonrandomized comparative studies and 2 small randomized controlled trials with reduced dose (verteporfin) and reduced fluence (laser) PDT have been identified.

Chan et al. (2008) reported a randomized double-masked placebo controlled trial of reduced dose PDT for acute CSCR. Reduced dose verteporfin was examined due to adverse effects, including CNV, with full-dose PDT. A total of 63 patients were randomized in a 2:1 ratio to half-dose verteporfin or placebo prior to laser treatment. The primary outcome measure, the proportion of eyes with absence of subretinal fluid at the macula at 12 months, was observed in 94.9% of eyes in the verteporfin group compared with 57.9% of eyes in the placebo group. The mean central foveal thickness was lower compared to the placebo group at 12 months (161 versus 278 microns). At 3 months after treatment, the mean LogMAR of the PDT group was 0.00 (Snellen equivalent 20/20), whereas the placebo group improved to 0.08 (Snellen equivalent 20/24). At 12 months, the mean LogMAR remained statistically better in the PDT group compared with placebo (-0.05 versus 0.05); however, since this is equivalent to visual acuity of 20/18 versus 20/22, this would not be a clinically meaningful difference. The mean increase of BCVA was 1.8 lines compared to 0.6 lines for the placebo group, whereas a difference of 2 lines is considered to be clinically meaningful. No ocular or systemic adverse event was encountered.

Bae et al. (2011) compared low-fluence PDT versus 3 monthly injections of ranibizumab in a small randomized trial of 16 eyes with chronic or recurrent CSCR. Rescue with the opposite treatment was allowed after 3 months since a gold standard treatment for chronic CSCR had not been established. The main outcome measures were excess foveal thickness, resolution of subretinal fluid, choroidal perfusion, and BCVA. For both groups at baseline, the mean LogMAR was 0.34 (20/44 Snellen equivalent). The mean excess foveal thickness was significantly higher in the PDT group at baseline (74.1 versus 26.3 microns), but showed a greater reduction with treatment. Six eyes (75%) in the PDT group achieved complete resolution of subretinal fluid and reduction of choroidal hyperpermeability compared with 2 (25%) eyes in the ranibizumab group. At 3 months, there was a trend toward improvement in BCVA in the PDT group (from 0.30 to 0.18 LogMAR, $p = 0.075$), whereas the ranibizumab group had

significantly improved BCVA (from 0.38 to 0.18 LogMAR). There was a trend for a greater proportion of eyes needing rescue treatment in the ranibizumab group versus the PDT group (75% vs. 25%, p = 0.066). During the follow-up period, no systemic or ocular complications associated with treatment were observed. The main limitations of this study are its small size, lack of investigator blinding, and lack of an untreated control group.

Reibaldi et al. (2010) compared the efficacy of half-fluence PDT compared to conventional PDT in a prospective multicenter, investigator-masked comparative study of 42 eyes (42 patients) with chronic CSCR. It is not clear whether the group assignment was based on patient preference or investigator preference, although the groups were comparable at baseline. The primary outcome measures were the changes in BCVA and the proportion of eyes with complete resolution of subretinal fluid. Secondary outcome measures were the changes in mean central foveal thickness and the rate of eyes with post-PDT changes in choroidal perfusion. At 1 month follow-up, BCVA had improved to a similar extent in both the low-fluence group (from 0.46 to 0.28 LogMAR) and the conventional fluence group (from 0.43 to 0.27 LogMAR). Complete resolution of subretinal fluid was observed in 96% of the low-fluence group and 89% of the conventional PDT group (not significantly different). At 12 months' follow-up, BCVA continued to improve in the low-fluence group (0.16 LogMAR) but remained stable in the conventional fluence group (0.24 LogMAR). Complete subretinal fluid reabsorption was seen in 91% of low-fluence-treated eyes and 79% of conventional PDT-treated eyes (not significantly different). Moderate choriocapillaris hypoperfusion (an adverse effect) was seen in 0% of low-fluence-treated eyes and 44% of conventional PDT-treated eyes. One eye in the conventional PDT group developed CNV requiring further treatment. A strength of this study is the prospective 12-month follow-up after a single treatment. Limitations of this study are the nonrandomization and the lack of an untreated control group.

Shin et al. (2011) compared outcomes from low-fluence PDT to conventional PDT in a retrospective multicenter study of 60 patients with chronic central serous chorioretinopathy (34 eyes treated with low-fluence PDT and 33 eyes treated with conventional PDT). All eyes treated at one center received conventional PDT and all consecutive eyes treated at another center between 2006 and 2009 received low-fluence PDT. Follow-up examinations were done at 1 and 3 months after PDT and as needed thereafter, with a mean follow-up period of 12.6 months (range, 6-33 months) for the low-fluence PDT group and 13.4 months (range, 5-25 months) for the conventional PDT group. Treatment success without recurrence was achieved in 94.1% of eyes treated with low-fluence PDT and 100% of eyes treated with conventional PDT (not significantly different). Improvement with treatment in both groups was noted with no significant difference in final BCVA between the 2 groups (0.17 versus 0.21 LogMAR) at the final follow-up. Choriocapillaris nonperfusion was significantly more severe in the conventional PDT group.

Use of reduced dose verteporfin PDT has also been reported. Uetani et al. (2012) compared half-dose versus one-third dose PDT for CSCR in a small (n = 16) prospective open-label trial. Patients were assessed at baseline and at 4 days, 1 month, and 3 months after PDT. At 3 months, all 10 eyes (100%) in the half-dose PDT group and 2 eyes (33%) in the one-third dose PDT group had complete resolution of subretinal fluid. Patients in the half-dose PDT group gained an

average of 5.4 letters while patients in the one-third-dose group gained 1.7 letters (not significantly different).

Chan et al. (2008) have also reported reduced dose of verteporfin for the treatment of chronic CSCR in a prospective series of 48 patients. The mean duration of CSCR was 8.2 months (range, 3-40 months). At 12 months after PDT, the mean BCVA improved from 0.31 to 0.15 LogMAR, an improvement of 1.6 lines.

In summary, high-quality evidence on use of PDT for CSCR is limited. The available evidence indicates substantial numbers of adverse events with standard PDT. Reduced-dose PDT may result in improved anatomical outcomes for acute CSCR, but clinically significant improvements in visual acuity have not been shown for this self-limiting disease. For chronic CSCR, recent comparative studies of reduced fluence and reduced-dose PDT suggest a possible beneficial effect of this treatment.

Polypoidal Choroidal Vasculopathy

Polypoidal choroidal vasculopathy (PCV) arises primarily due to 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.

The systematic review by Chan et al. (2010) included 30 studies on PDT in patients with PCV. Chan et al. found numerous case series reporting favorable anatomical and visual acuity outcomes for patients treated with PDT. Also reported in the review was an ongoing manufacturer-sponsored RCT of PDT as monotherapy or combined with ranibizumab for treatment of PCV.

A study by Lim et al. (2012) randomized 31 patients with AMD and 10 patients with PCV to bevacizumab monotherapy or bevacizumab in combination with PDT. 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 PCV did not show significant improvement in BCVA ($p = 0.05037$) or central foveal thickness ($p = 0.0875$) when analyzed alone; however, the study is likely to be underpowered for this subset analysis.

Several non-randomized studies from Asia were reported in 2011. The largest was a prospective consecutive series of 220 eyes of 210 Japanese patients with PCV who were followed for 1 year after the primary PDT treatment (Hikichi et al., 2011). 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 eyes (93%) at 1-year follow-up. Average visual acuity improved by more than 0.3 LogMAR in 25% of eyes, remained stable in 65% of eyes, and decreased more than 0.3 LogMAR in 10% of eyes. Stepwise logistic regression analysis showed that younger age, smaller greatest linear dimension, better baseline visual acuity, less baseline hemorrhage, and the presence of a serous macular detachment at baseline were independent predictors of improvement in visual acuity.

Akaza et al. (2011) reported 3-year follow-up of 43 eyes treated with PDT for PCV. Before the initial PDT, 40 eyes (93%) exhibited PCV in the narrow sense, and 3 (7%) exhibited polypoidal CNV. The 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 of the 43 eyes (77%) at 3 years, although the 3 eyes with polypoidal CNV showed essentially no changes except for enlargement and recurrence. The authors concluded that long-term visual outcomes following PDT were not good due to the high frequency of recurrent polypoidal lesions, as well as enlargement and neovascular changes involving abnormal vascular networks.

Kim and Yu (2011) conducted a retrospective review of 39 consecutive patients with PCV who received PDT monotherapy (before April 2007) or a combination of PDT and intravitreal bevacizumab (after April 2007). During 12 months of follow-up, the patients in the monotherapy group (n = 19) received a mean of 1.89 PDTs, and patients in the combined therapy group (n = 20) received a mean of 1.30 PDTs and 2.90 bevacizumab injections. Improvement in BCVA by 3.0 lines in the combined therapy group was assessed compared with 1.6 lines in the PDT monotherapy group. Improvement in BCVA of 3 lines or more was achieved in 55.0% of patients in the combined therapy group versus 36.8% of patients in the monotherapy group.

In summary, the available evidence from case series is insufficient to permit conclusions regarding the efficacy of PDT for PCV. Controlled trials with longer follow-up are needed to evaluate the efficacy of PDT (monotherapy or combined) compared to anti-VEGF therapy.

Choroidal Hemangioma

Choroidal hemangioma (CH) 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 PDT in patients with circumscribed CH. PDT has been reported to induce complete and irreversible occlusion of the microvasculature, although this may require more than one treatment. Several case series demonstrated encouraging visual and anatomical outcomes in 150 patients with circumscribed CH who were treated with various PDT regimens.

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

Angioid Streaks

Angioid streaks (AS) are dehiscences in Bruch's membrane and occur in patients with some systemic diseases such as pseudoxanthoma elasticum, Paget's 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 PDT in 148 patients with angioid streaks. The authors concluded the PDT might limit or slow vision loss compared with the expected natural course of CNV due to angioid streaks, but one study showed a decrease in visual acuity following PDT, and others showed that substantial proportions of patients continued to lose visual acuity. Thus, further studies to assess its long-term safety and efficacy are warranted.

Inflammatory 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 on PDT in 115 patients with inflammatory eye conditions. Encouraging visual and anatomical outcomes have been reported with PDT 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 PDT on health outcomes for this indication. Therefore, PDT for inflammatory eye conditions is considered investigational.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In 2012, in response to requests by Blue Cross Blue Shield Association, input was received from 2 physician specialty societies and 2 academic medical centers. The input agreed that PDT monotherapy is medically necessary for AMD, PM, and POHS and also considered PDT monotherapy to be medically necessary for CSCR and CH. Input was mixed regarding the use of PDT for other ophthalmologic disorders. The input agreed that PDT in combination with VEGF antagonists is investigational for all ophthalmologic disorders.

Summary

The available published literature, together with clinical input, supports the use of PDT as monotherapy for the treatment of CNV associated with AMD, chronic CSCR, CH, PM, or POHS. Therefore, PDT may be considered medically necessary for these indications. Current evidence does not support the use of PDT in combination with anti-VEGF therapies or corticosteroids for the treatment of CNV associated with AMD or other ophthalmologic disorders.

Based on numerous case reports and case series, PDT is being used in an attempt to decrease CNV of many different etiologies. For example, PDT has been reported to slow down, but not prevent or reverse, the progression of disease of CNV associated with PCV, angioid streaks, and inflammatory chorioretinal disease. There is insufficient evidence to support the use of PDT as monotherapy or in combination therapy for these other ophthalmologic disorders. As a result, PDT is considered investigational for ophthalmologic disorders other than AMD, chronic CSCR, CH, PM, or POHS.

Practice Guidelines and Position Statements

In September 2003, the United Kingdom's National Institute for Clinical Excellence (NICE) issued Technology Appraisal Guidance 68, *Guidance on the use of photodynamic therapy for age-related macular degeneration*. The guidance states that:

> Photodynamic therapy (PDT) is recommended for the treatment of wet age-related macular degeneration for individuals who have a confirmed diagnosis of classic with no occult subfoveal choroidal neovascularization (CNV) (that is, whose lesions are composed of classic CNV with no evidence of an occult component) and best-corrected visual acuity 6/60 or better. PDT should be carried out only by retinal specialists with expertise in the use of this technology.

The 2008 Preferred Practice Patterns (practice guidelines) on PDT from the American Academy of Ophthalmology (AAO) are based on the TAP and VIP reports described here. The AAO recommends PDT with verteporfin for subfoveal CNV in which the classic component is greater than 50% of the lesion and the entire lesion is 5,400 microns or less in diameter. Occult subfoveal CNV may be considered for PDT under specified conditions (see AAO guidelines). While PDT was recommended for recurrent juxtafoveal CNV, evidence was considered insufficient to guide treatment recommendations for the primary use of PDT for juxtafoveal CNV. Combination therapy with VEGF inhibitors and PDT was not discussed. There was insufficient evidence to guide treatment recommendations for photodynamic therapy combined with pharmacologic therapy or for adjunctive use of intravitreal corticosteroids with verteporfin PDT

The AAO Preferred Practice Patterns (practice guidelines) reviewed the evidence on VEGF inhibitors and thermal laser photocoagulation surgery for CNV. The guidelines state that because of the loss of vision associated with laser photocoagulation (82% of treated patients end up with visual acuity worse than 20/200), photocoagulation is no longer the initial treatment for subfoveal CNV. The guidelines also indicate that VEGF inhibitors have demonstrated improved visual outcomes compared with other therapies and have become the first-line therapy for treating neovascular AMD.

The AAO also reviewed the evidence on thermal laser photocoagulation surgery for CNV from a randomized controlled multicenter study by the macular photocoagulation study group. The group reported a 5-year persistence/recurrence rate of 54% for extrafoveal CNV, a 4-5-year rate of 78% for juxtafoveal CNV, and a 3-year rate of 56% for subfoveal CNV. Introduction of a scotoma or enlargement of a pre-existing scotoma, with or without visual acuity loss, is an immediate and permanent effect of photocoagulation surgery. Because of the loss of vision associated with laser photocoagulation (82% of treated patients end up with visual acuity worse than 20/200), photocoagulation is no longer considered the initial treatment of subfoveal neovascularization.

In 2008, the Canadian Agency for Drugs and Technologies in Health (CADTH), released a Health Technology Assessment (HTA) titled *Management of Neovascular Age-related Macular Degeneration: Systematic Drug Class Review and Economic Evaluation.* The authors concluded: "The efficacy of anti-vascular endothelial growth factor (anti-VEGF) therapies over verteporfin

(V-PDT) is well supported by (randomized controlled trials [RCTs]). What remains unclear is whether combination therapy (and which combinations) are superior or equal to monotherapy."

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

Type	Number	Description
CPT	67221	Destruction of localized lesion of choroid (e.g., choroidal neovascularization); photodynamic therapy (includes intravenous infusion)
	67225	Destruction of localized lesion of choroid (e.g., choroidal neovascularization); photodynamic therapy, second eye, at single session (List separately in addition to code for primary eye treatment)
HCPC	J3396	Injection, verteporfin, 0. 1 mg
ICD9 Procedure	None	
ICD9 Diagnosis	All Diagnoses	
Place of Service	All Places of Service	

Tables

N/A

Definitions

Central Serous Chorioretinopathy - 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.

Choroidal Hemangioma - 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.

Choroidal Neovascularization - (CNV) is the creation of new blood vessels in the choroid layer of the eye .This is a common symptom of the degenerative maculopathy wet AMD (age-related macular degeneration).

Pathologic Myopia - An abnormal elongation of the eye associated with severe near-sightedness. It generally occurs among people over 30 years of age and can result in a progressive, severe loss of vision.

Presumed Ocular Histoplasmosis - A condition 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.

Polypoidal Choroidal Vasculopathy - Abnormal choroidal circulation, resulting in characteristic lesions comprising well-defined vascular networks of vessels ending in polyp-like structures.

Subfoveal - Beneath the fovea (the central, most important part of the macula for central vision).

Vascular Endothelial Growth Factor - Is a signal protein produced by cells that stimulates vasculogenesis and angiogenesis. It is part of the system that restores the oxygen supply to tissues when blood circulation is inadequate.

Index / Cross Reference of Related BSC Medical Policies

The following Medical Policies share diagnoses and/or are equivalent BSC Medical Policies:

- N/A

Key / Related Searchable Words

- Age-related Macular Degeneration
- Anti-VEGF Therapies
- Central Serous Chorioretinopathy
- Choroidal Neovascularization
- Myopia
- Ocular Histoplasmosis

- Photodynamic Therapy
- Polypoidal Choroidal Vasculopathy
- Visual Acuity

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Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
6/18/2000	BCBSA Medical Policy adoption	Medical Policy Committee

Effective Date	Action	Reason
7/1/2001	Administrative Review; no changes	Administrative Review
5/8/2002	Coding Update	Administrative Review
11/1/2005	Coding modified/updated: delete J3395; Added J3396	Administrative Review
10/1/2010	Policy title change from Photodynamic Therapy with Verteporfin for Age Related Macular Degeneration Policy revision with position change	Medical Policy Committee
6/28/2013	Policy revision with position change	Medical Policy Committee

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.

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