Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/17/2018

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), pathologic myopia, presumed ocular histoplasmosis, chronic central serous chorioretinopathy (CSC) or choroidal hemangioma 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 VPDT as monotherapy for all other ophthalmologic disorders to be **investigational.***

Based on review of available data, the Company considers 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 CNV associated with AMD, pathologic myopia, presumed ocular histoplasmosis, chronic CSC, choroidal hemangioma, or for other ophthalmologic disorders to be **investigational.***

Policy Guidelines

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

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

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Background/Overview

VISION LOSS

Severe vision loss can occur with ocular neovascularization, the growth of abnormal blood vessels in the retina or choroid. Neovascularization occurs in a number of ocular diseases, including AMD.

Age-Related Macular Degeneration

AMD is a degenerative disease of the retina that results in loss of central vision. Two distinctive forms, known as dry and wet degeneration, may be observed. The dry form (also known atrophic or areolar) is more common and is often a precursor of the wet form (also known as exudative neovascular or disciform). The wet form is more devastating and characterized by serous or hemorrhagic detachment of the retinal pigment epithelium and development of CNV, which greatly increases the risk of developing severe irreversible loss of vision. CNV is categorized as classic or occult. Classic CNV appears as an initial lacy pattern of hyperfluorescence followed by more irregular patterns as the dye leaks into the subretinal space. Occult CNV lacks the characteristic angiographic pattern. Classic CNV carries a worse prognosis for vision than occult CNV, suggesting that the proliferative response that obscures new vessels may also favorably alter the clinical course of AMD.

Pathologic Myopia

Pathologic myopia refers to an abnormal elongation of the eye associated with severe near-sightedness. It generally occurs among people older than 30 years of age and can result in a progressive, severe loss of vision, frequently related to the development of CNV. 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.

Presumed Ocular Histoplasmosis

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

Central Serous Chorioretinopathy

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 the progressive decline of visual acuity. CSC has been treated with medication and laser photocoagulation, but these treatments have limited efficacy. Multiple definitions have been used in the literature to classify CSC as acute or chronic based cutoff time points (e.g., persistent fluid for <3, 4 or 6 months) or less frequently based on the timing of treatment. For example, acute CSC defined as the first attempted treatment to improve visual acuity, and chronic CSC is defined as being refractory to treatment. Further, multiple VPDT

strategies that use either reduced-dose or half-fluency have been evaluated for the treatment of CSC because full-dose VPDT used in AMD has shown a potentially higher risk of developing choroidal ischemia and retinal atrophic changes.

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

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

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

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

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

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

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
In 2000, verteporfin (Visudyne®‡; Novartis), an intravenous photodynamic therapy (PDT) 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 PDT 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 PDT with verteporfin 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 [ocular photodynamic therapy] with verteporfin for indications such as "pathologic myopia or the presumed histoplasmosis syndrome" may be "eligible for coverage through individual contractor discretion."

Rationale/Source

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice. The following is a summary of the key literature to date.

AGE-RELATED MACULAR DEGENERATION
The use of VPDT in CNV has decreased substantially with the availability of anti-VEGF therapy. Subsequent to FDA approval of VPDT in 2000, the 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 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 with 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 TEC Assessment (2000) concluded that fewer patients treated using VPDT compared with 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 with 38% of the placebo arm lost fewer than 15 letters. Further, an average number of VPDT treatments required was lower in the second year (2.2) compared with the first year (3.4). 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. Kaiser (2006) reported on 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 Cochrane review (2003) concluded that VPDT was effective at preventing vision loss in classic and occult CNV due to AMD. In a meta-analysis of the safety of VPDT, Azab et al (2004) 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 (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.

The result of a multicenter RCT (2008) 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 in overall outcomes for visual acuity or anatomic lesion features.

Section Summary: VPDT vs Placebo
The evidence for the efficacy of VPDT includes multiple RCTs that have established its superiority over 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 a decreased need for monthly VEGF injection and increased the durability of response while maintaining visual acuity. The open-label, phase 2 PROTECT study (2006) 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 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 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 (2012) that tested the noninferiority of ranibizumab plus VPDT vs 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 regarding 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 vs 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, 0.04; 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 (2015) of anti-VEGF injections for treating wet AMD compared anti-VEGF monotherapy with 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 this systematic review indicated that the difference favored the combination group, which is incorrect). There were no differences between groups on the central retinal thickness or lesion size. Reviewers did not report a 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. Semeraro et al (2015) published an RCT evaluating 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) assessed 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy who were randomized to bevacizumab monotherapy or 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 randomized, open-label assessor-blinded trial (2007)

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 a favorable effect on visual acuity and anatomic outcomes. Lee and Lee (2016) reported on 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 with 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 the 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 (2014) randomized 84 treatment-naive patients who had 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 therapy compared with anti-VEGF monotherapy. Comparative trials are needed to evaluate the efficacy of this triple therapy.

PATHOLOGIC MYOPIA
The initial evidence on pathologic myopia was based primarily on retrospective studies and clinician experience. RADIANCE, a multicenter RCT (2014) compared intravitreal ranibizumab with 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 2:1 to 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 loss at 12 months by intention-to-treat analysis. At month 12, 58 (72%) of patients who received VPDT lost fewer than 8 letters on a standard eye chart and 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 the progression of classic CNV in 36% of VPDT-treated eyes compared with 54% of the placebo group. Trialists 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 significant 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 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 the 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 Plus Anti-VEGF Therapy
The evidence for the efficacy of VPDT plus anti-VEGF therapy includes a small RCT and a retrospective study. This evidence does not demonstrate improvements in BCVA. Comparative trials are needed to evaluate the efficacy of this combination therapy vs relevant comparators.

PRESUMED OCULAR HISTOPLASMOSIS
There are few published data on the use of VPDT to treat patients with CNV related to ocular histoplasmosis. The FDA approval of VPDT for ocular histoplasmosis 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 fewer than 3 lines in 88% of patients during the same period from a historical control. Ramaiya et al (2013) reported on 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 were 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 and 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, a 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 a small prospective single-arm study and an RCT. Lack of a control arm in the single-arm study and 50% loss to follow-up in the RCT preclude a 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
A Cochrane review with network meta-analysis (2015) evaluated various treatments for CSC that included both acute and chronic CSC. Only RCTs were included. Pairwise (direct) comparison for VPDT included anti-VEGF vs VPDT, anti-VEGF plus 50% VPDT vs 50% VPDT alone, 50% VPDT vs observation or sham treatment, and 30% VPDT vs 50% VPDT vs VPDT. (Percentages refer to the dose of verteporfin used.) The primary outcome was visual acuity at 12 months. Low-quality evidence from a 2008 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 with sham treatment. Moderate-quality evidence from 2 studies suggested that 30% VPDT results in a small improvement in vision compared with VPDT (MD = -0.16 logMAR; 95% CI, -0.22 to -0.10 logMAR) and compared with 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 and VPDT or anti-VEGF plus 50% VPDT and 50% VPDT alone, or 50% VPDT and observation or sham treatment.

Acute CSC
Chan et al (2008) conducted a double-masked, placebo-controlled trial of 63 patients who were randomized 2:1 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 the 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.

Zhao et al (2015) reported on a double-masked, randomized, noninferiority trial with 131 patients that compared a 50% with 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. 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 and 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.

Salehi et al (2015), in their network meta-analysis which included a total of 25 studies (total N=1098 patients; 1098 eyes), judged these studies to be at low risk of bias in most domains with the exception of attrition bias (6% of the 30% VPDT group vs 13% of the 50% VPDT group) and selective outcomes reporting (primary and secondary outcomes were designated differently on the trial registry entry and the published report). The 30% dose did not achieve noninferiority.

Section Summary: Acute CSC
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 CSC
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 with 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 CSC
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

Verteporfin Photodynamic Therapy
A systematic review by Chan et al (2010) included 30 studies assessing VPDT in patients with polypoidal choroidal vasculopathy. Reviewers 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 a weighted MD in visual acuity of 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 on 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 examination findings, 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 on 3-year follow-up of 43 eyes (43 patients) treated with VPDT for polypoidal choroidal vasculopathy. Before the initial VPDT, 40 (93%) eyes exhibited polypoidal choroidal vasculopathy in the narrow sense and 3 (7%) exhibited polypoidal CNV. 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 for 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 for Polypoidal Choroidal Vasculopathy
Available evidence on the efficacy of VPDT for polypoidal choroidal vasculopathy consists of several retrospective studies and a 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 (2015) published a systematic review that evaluated treatment for polypoidal choroidal vasculopathy. A single RCT, which compared VPDT with 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 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 improvements in BCVA (p=0.050) or central foveal thickness (p=0.088) when analyzed alone; however, the trial was likely underpowered for this subgroup 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 trial 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 on 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 for Polypoidal Choroidal Vasculopathy
Available evidence on the efficacy of VPDT for polypoidal choroidal vasculopathy consists of 2 small RCTs, a meta-analysis, and 2 retrospective studies. While results of 1 RCT reported no difference in visual acuity for patients treated with VPDT plus anti-VEGF therapy vs 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
The systematic review by Chan (2010) 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.

Blasi et al (2010) 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 the 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 a systematic review of 11 case series and a prospective study. This body of evidence has suggested a favorable effect of VPDT on various visual acuity and anatomic outcomes in patients with a 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
The systematic review by Chan (2010) included 8 case series on VPDT assessing 148 patients with angioid streaks. Reviewers concluded that 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.

Section Summary: Angioid Streaks
Available evidence on the efficacy of VPDT for angioid streaks consists of a systematic review of 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 systematic review by Chan (2010) included 15 case reports evaluating 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 with placebo or sham procedure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have CNV due to AMD who receive VPDT plus 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.

Pathologic Myopia
For individuals who have CNV due to pathologic myopia who receive VPDT, the evidence includes a 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 one year but not in the second year. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

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

Central Serous Chorioretinopathy
For individuals who have CNV due to acute 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 of 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 a meta-analysis of 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Prospective cohort studies have reported favorable anatomic and visual acuity outcomes for patients treated with VPDT. However, RCTs comparing VPDT with anti-VEGF therapies have reported no statistically significant differences in visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have CNV due to polypoidal choroidal vasculopathy who receive VPDT plus anti-VEGF therapy, the evidence includes 2 small RCTs, a 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 statistically significant differences in visual acuity outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

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

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

Inflammatory Chorioretinal Conditions
For individuals who have CNV due to inflammatory chorioretinal conditions who receive VPDT, the evidence includes a systematic review of case reports. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Methodologic limitations limit 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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Policy History

Original Effective Date: 06/05/2002
Current Effective Date: 10/17/2018

04/18/2002	Medical Policy Committee review
06/05/2002	Managed Care Advisory Council approval
06/24/2002	Format revision. No substance change to policy.
06/01/2004	Medical Director review
06/15/2004	Medical Policy Committee review
06/28/2004	Managed Care Advisory Council approval
05/03/2005	Medical Director review
05/17/2005	Medical Policy Committee review. Format revision. Patient selection criteria added.
05/23/2005	Managed Care Advisory Council approval
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
08/17/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
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); photocoagulation, 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

Photodynamic Therapy for Choroidal Neovascularization

Policy # 00097
Original Effective Date: 06/05/2002
Current Effective Date: 10/17/2018

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.
10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 10/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	67221, 67225
HCPCS	C9257, J0178, J2503, J2778, J3396
ICD-10 Diagnosis	B39.9 D18.09 H32 H35.30 H35.711-H35.719 H44.20-H44.23

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.