9.03.08 Photodynamic Therapy for Choroidal Neovascularization

Summary
Photodynamic therapy (PDT) is a treatment modality designed to selectively occlude ocular choroidal neovascular tissue. The therapy is a 2-step process, consisting initially of an injection of the photosensitizer verteporfin, followed 15 minutes later by laser treatment to the targeted sites of neovascularization in the retina. The laser treatment selectively damages the vascular endothelium. Patients may be re-treated if leakage from choroidal neovascularization (CNV) persists.

The evidence for PDT in individuals who have CNV due to age-related macular degeneration (AMD), pathologic myopia, presumed ocular histoplasmosis, chronic central serous chorioretinopathy (CSC), or choroidal hemangioma includes randomized controlled trials (RCTs), nonrandomized comparative trials, and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The RCT evidence supports the efficacy of PDT in reducing visual loss and decreasing retinal thickness. Comparative studies of PDT versus anti-vascular endothelial growth factor (anti-VEGF) medications have reported that anti-VEGF medications are as good as, and possibly superior to, PDT for reducing visual loss. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for PDT in individuals who have CNV due to polypoidal choroidal vasculopathy, angiod streaks, or inflammatory chorioretinal disease includes RCTs, nonrandomized comparative trials, and case series. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. RCT evidence is limited for these conditions, and most published studies are case series. The case series have reported improved visual acuity following treatment, but this study design lacks sufficient methodologic rigor to allow conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PDT in combination with anti-VEGF medications in individuals who have CNV of any etiology (eg, AMD, chronic CSC, choroidal hemangioma, pathologic myopia, presumed ocular histoplasmosis, choroidal vasculopathy, angiod streaks, inflammatory chorioretinal disease) includes RCTs, nonrandomized comparative studies, and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. RCTs of combination therapy have reported that PDT can decrease the number of anti-VEGF injections needed, but PDT is not associated with improved visual acuity compared to anti-VEGF alone. Some studies have reported that the change in visual acuity after PDT is noninferior, but others have found that it is inferior to anti-VEGF alone. Further research is needed to better determine the tradeoff between fewer anti-VEGF injections and possible reduction in visual acuity. The evidence is insufficient to determine the effects of the technology on health outcomes.
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**FDA REGULATORY STATUS**

In 2000, verteporfin (Visudyne®; Novartis), an intravenous photodynamic therapy agent, was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process for the treatment of predominantly classic subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration, pathologic myopia, and presumed ocular histoplasmosis. The label notes that there is insufficient evidence for verteporfin use in predominately occult subfoveal CNV, and it is contraindicated in patients with porphyria.

**POLICY STATEMENT**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

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

Photodynamic therapy is considered investigational, as monotherapy for other ophthalmologic disorders, including CNV secondary to central serous chorioretinopathy.

Photodynamic therapy is considered investigational when used in combination with one or more of the anti-vascular endothelial growth factor therapies (anti-VEGF), i.e., pegaptanib (Macugen®), ranibizumab (Lucentis®), bevacizumab (Avastin®), aflibercept (Eylea™) as a treatment as a treatment of CNV associated with age-related macular degeneration, chronic serous chorioretinopathy, choroidal hemangioma, pathologic myopia, presumed ocular histoplasmosis, or for other ophthalmologic disorders, including CNV secondary to central serous chorioretinopathy.

**POLICY GUIDELINES**

The U.S. Food and Drug Administration (FDA) labeling for verteporfin indicates that the physician should re-evaluate the patient every 3 months and, if choroidal neovascular leakage is detected on fluorescein angiography, therapy should be repeated. However, the total number of treatments is not addressed by the FDA. Evidence defining when treatment should stop is not available, but expert opinion (convened by Novartis, Visudyne manufacturer) suggested stopping “when the situation is judged to be ‘futile’” (Verteporfin Roundtable Participants 2005). FDA labeling states “safety and efficacy of Visudyne beyond 2 years have not been demonstrated.”

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

**RATIONALE**

Randomized, controlled trials (RCTs) are crucial in determining the efficacy of PDT treatment and comprise the bulk of the evidence on which the efficacy of this treatment can be evaluated. Where RCTs are lacking, non-randomized comparative studies provide some evidence for efficacy but are limited by potential selection bias, as patients may be preferentially selected for one treatment over another by disease severity or other clinical factors. Uncontrolled trials and case series offer little useful evidence on the efficacy of PDT.
Literature Review

Age-related Macular Degeneration (AMD)

A 2000 Technical Evaluation Center (TEC) Assessment (1) 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 photodynamic therapy (PDT) experienced a clinically significant loss of visual acuity compared to those treated with placebo: 38.8% compared to 53.6% (p<0.001).
- Subgroup analysis suggests that the treatment effect is predominantly experienced by patients with AMD characterized by at least 50% classic choroidal neovascularization (CNV).
- There were inadequate data to permit scientific conclusions regarding other etiologies of CNV.

Systematic reviews. A 2003 Cochrane review concluded that PDT is effective in preventing visual loss in classic and occult CNV due to AMD. (2) An updated Cochrane review in 2007 evaluated results from 3 randomized controlled trials (RCTs) (total of 1,022 patients), which included the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) and the Verteporfin in Photodynamic Therapy (VIP) trials described below. (3) 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 photodynamic therapy, Azab and colleagues analyzed data from the 24-month TAP A and B and VIP trials, totaling 948 patients with AMD. (4) The authors concluded that the safety profile of verteporfin therapy was not statistically different from placebo.

TAP trial. In 2001, the 2-year results of the pivotal randomized trial Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) were published. (5) 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 (3, 4). 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. (6-8) 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. (9) 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.

VIP trial. The Verteporfin in Photodynamic Therapy (VIP) trial 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. (10) 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% vs. 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.

**Early Retreatment Study Group trial.** 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. (11) 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); 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**

**Systematic reviews.** A 2008 Cochrane review evaluated anti-vascular endothelial growth factor (anti-VEGF) therapies for neovascular AMD. (12) 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.

**ANCHOR trial.** Ranibizumab was compared 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 in 2006. (13) Patients with subfoveal choroidal neovascularization and a predominantly classic lesion (n=423) were randomized in a 1:1:1 ratio to receive 0.3mg (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. (14) 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 three 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. reported a sub-analysis of the patient-reported outcomes from the ANCHOR trial in 2009. (15) 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 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**

Angiostatic agents being studied in trials include pegaptanib, ranibizumab, bevacizumab, anecortave acetate, squalamine, vatalanib, and triamcinolone.

**PDT in Combination with VEGF Antagonists**

**Systematic reviews.**

A systematic review of anti-VEGF injections for treating wet AMD was published in 2015, including a section comparing anti-VEGF monotherapy with anti-VEGF combination therapy with PDT. (16) The 4 RCTs included compared monotherapy with combination therapy, 3 of which are discussed later in this review (DENALI, (17) MONT BLANC, (18) Williams et al (19)). In combined analysis, there was a significant difference in BCVA of 2.74 letters (95% CI, 0.26 to 5.21, p=0.03) in favor of the monotherapy group (note that the conclusions of the systematic review indicate that the difference favored the combination group, which is incorrect). There were no differences between groups on central retinal thickness or lesion size. The authors did not report combined analysis of the number of anti-VEGF injections performed in each group.

In a 2010 editorial, Kaiser reported an ongoing clinical program (SUMMIT) investigating whether treatment with combination PDT and ranibizumab is safe and effective compared with monotherapy.(20) The SUMMIT program is intended to combine results from a North American trial (DENALI, N=321) and a European trial (MONT BLANC, N=255), however, no results of this program have been published. A 2005 TEC Special Report found a number of trials in progress combining an angiostatic agent with PDT. (21) For example, in the pegaptanib trial, PDT was administered at physician discretion, but analysis examining possible synergistic effects was not provided. (21)
DENALI trial. DENALI was a multicenter, double-blind, randomized Phase IIIb trial 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). (17) 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 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 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 trial. 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. (18) 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.

FOCUS trial. 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 photodynamic therapy. (23,24) 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 two 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).

In addition to the above trials, several smaller randomized trials have been published. In 2015, Semeraro et al published an RCT of 75 patients with treatment-naive exudative CNV due to AMD. (25) Patients were randomized into 3 groups: ranibizumab monotherapy, ranibizumab combined with reduced-fluence verteporfin PDT, and ranibizumab combined with ketorolac eye drops. At the 12-month follow-up, BCVA (SD) was superior in the ranibizumab plus ketorolac group (-0.25 [0.60] logMAR), compared with ranibizumab monotherapy (-0.14 [0.52] logMAR) or ranibizumab combined with PDT (-0.10 [0.30] logMAR). Change in mean (SD) central retinal thickness was also superior in the ranibizumab plus ketorolac group (-141 [21] µm) compared with the ranibizumab monotherapy group (-125 [15] µm) and the ranibizumab plus PDT group (-130 [15] µm).

In a multicenter, unmasked trial, Williams et al (2012) randomized 60 patients to ranibizumab with half-fluence PDT or ranibizumab alone. (19) The difference between groups in the number of injections did not differ significantly. BCVA improved by 9.9 letters in the ranibizumab group and by 2.6 letters in the combined treatment group. This difference did not differ significantly. A similar number of patients gained 15 or more letters (33% monotherapy vs 31% combination therapy). A small RCT by Lim et al (2012) included 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy who were randomized to bevacizumab monotherapy or bevacizumab in combination with PDT. (26) 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 PDT was given. A randomized, open-label assessor-blinded trial from Croatia with short-term (3-month) follow-up evaluated combined treatment with bevacizumab and PDT (N=165 eyes). (27) At 3-month follow-up, 22 (42%) of 52 patients improved by more than 0.2 logMAR (logarithm of the minimum angle of resolution) following combined treatment, compared with 1 (2%) patient treated with bevacizumab alone and none treated with PDT alone.

**PDT in Combination with Corticosteroids**

**The RETINA trial.** 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. (28) The triamcinolone group also had a larger proportion of subjects with elevated, although managed, intraocular pressure (18 vs. 4, respectively).

**Piermarocchi et al.** conducted a prospective randomized study in Italy to evaluate the long-term effect of intravitreal triamcinolone acetonide (IVT) treatment combined with PDT versus PDT alone for neovascular AMD. (29) 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 best-corrected visual acuity (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 that "...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."
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**Triple therapy**

*Triple therapy* (PDT, intravitreal dexamethasone and intravitreal bevacizumab) for AMD has been reported. (30) 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.

**Section Summary: Age-Related Macular Degeneration**

PDT monotherapy is an established treatment for CNV secondary to AMD, with evidence from multiple RCTs supporting benefit compared with placebo. Although PDT is established as superior to no treatment, recent comparative trials showed anti-VEGF therapy to be superior to PDT. For combination therapy, the literature to date includes 2 high-quality randomized trials, several smaller RCTs, and a meta-analysis of the existing trials. This evidence does not demonstrate an improvement in BCVA with combination therapy compared with anti-VEGF monotherapy. Combination therapy may lead to a reduction in the number of intravitreal injections needed, but this is not consistently reported across studies. Combination therapy with PDT and corticosteroids shows no improvement in outcomes or reduction in the number of intravitreal injections. Comparative trials are needed to evaluate the efficacy of triple therapy with intravitreal steroids, anti-VEGF agents, and PDT.

**Pathologic Myopia**

PDT has also been investigated in patients with CNV related to pathologic myopia.

**PDT in Comparison with 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 to receive PDT or placebo. (31) 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 intent-to-treat 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 treatment for at least 1 year. Results were not reported separately for those with predominantly classic CNV versus occult CNV.

**PDT in Comparison with VEGF Antagonists.**

El Matri et al. reported a retrospective comparison of PDT versus bevacizumab for myopic CNV in 2011. (31) 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, best corrected visual acuity (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). BCVA 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 vs. 393) and significantly lower in the bevacizumab group compared to the PDT group at 3 (328 vs. 393 microns), 6 (300 vs. 370 microns), and 12 (305.5 vs. 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.

**PDT in Combination with VEGF Antagonists:**

**Bevacizumab Monotherapy.**

Chenet al (2003) compared 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. (33) 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 vs. 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 vs. 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.

**Section Summary Pathologic Myopia**

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**

There are minimal published data regarding the use of PDT in patients with CNV related to ocular histoplasmosis. The approval by the U.S. Food and Drug Administration (FDA) was based on an open-label safety study involving 26 patients with ocular histoplasmosis. 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 period.

**Central Serous Chorioretinopathy**

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 central serous chorioretinopathy. (34) In addition, 3 nonrandomized comparative studies and 2 small randomized controlled trials with reduced dose (verteporfin) and reduced fluence (laser) PDT have been identified.

A Cochrane systematic review on the treatment of CSC, both acute and chronic, was published in 2015. (35) For PDT monotherapy, there was 1 low-quality trial of patients with acute CSC comparing PDT to no treatment using a sham control. There was a small improvement in visual acuity for the PDT group (mean difference, -0.10 logMAR; 95% CI, -0.18 to -0.02). There was also a decrease in recurrence of CSC (risk ratio, 0.10; 95% CI, 0.01 to 0.81) and a trend toward a lower risk of persistent CSC (risk ratio, 0.12; 95% CI, 0.01 to 1.02). Two low-quality trials compared anti-VEGF agents with PDT and reported
no difference in BCVA at 1 year. There was a trend toward less recurrence and less persistent CSC in the PDT group, but these results were inconsistent across trials.

**Acute Central Serous Chorioretinopathy**
Chan et al (2008) conducted a randomized, double-masked, placebo-controlled trial of reduced-dose verteporfin PDT versus placebo for acute central serous chorioretinopathy. (36) Reduced-dose verteporfin was tested because full-dose PDT had to adverse effects, including CNV. A total of 63 patients were randomized in a 2:1 ratio to half-dose verteporfin or placebo before laser treatment. Thirty-nine patients in the verteporfin group completed the trial while 19 in the placebo group did. The primary outcome measure—the proportion of eyes with absence of subretinal fluid at the macula at 12 months—was observed in 95% (n=37) of eyes in the verteporfin group and 58% (n=11) of eyes in the placebo group. Mean central foveal thickness in the verteporfin group was lower than in the placebo group at 12 months (161 μm vs 278 μm). At 3 months after treatment, 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, mean logMAR remained statistically better in the PDT group than in the placebo group (-0.05 vs 0.05; p=0.008); however, because this is equivalent to visual acuity of 20/18 versus 20/22, this result was not a clinically meaningful difference. Mean increase of BCVA was 1.8 lines in the verteporfin compared with 0.6 lines in the placebo group; a difference of 2 lines is considered clinically meaningful. No ocular or systemic adverse event was encountered.

In 2015, Zhao et al reported a double-masked, randomized, noninferiority trial with 131 patients that compared a 50% versus a 30% dose of verteporfin PDT for acute (<6 months) central serous chorioretinopathy. (37) The 2 primary outcome measures were the proportion of eyes with complete absorption of subretinal fluid and the proportion of eyes with complete disappearance of fluorescein leakage at 6 and 12 months. The 30% dose did not achieve noninferiority. At 12 months, the proportion of eyes with complete absorption of retinal fluid was 75.4% in the 30% dose and 94.6% in the half-dose group (p=0.004). Complete disappearance of fluorescein leakage at 12 months was observed in 68.9% of the 30%-dose group versus 92.9% of the half-dose group (p=0.001). Visual acuity, a secondary outcome measure, improved from 20/32 to 20/20 in both groups, with a mean difference between the groups 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, although of high methodologic quality, does not provide sufficient evidence of a functional benefit that would outweigh the potential risk of treatment with PDT for acute central serous chorioretinopathy.

**Chronic Central Serous Chorioretinopathy**
Ma et al (2014) conducted a systematic review of PDT for central serous chorioretinopathy. (38) Included were 9 studies with a total of 319 patients (range, 16-67 patients). Six studies were prospective comparisons and 3 were randomized. Only 2 studies masked treatments. Meta-analysis found that PDT was more effective than laser photocoagulation and anti-VEGF medications in resolving subretinal fluid (p<0.01) and more rapid than anti-VEGF medications in decreasing central macular thickness (p<0.01). There was no significant difference between treatments for improving BCVA. Both half-dose and half-fluence PDT were effective for improving BCVA, decreasing central macular thickness, and resolving subretinal thickness compared with placebo.

Comparative treatment studies in the systematic review included a small, unblinded, randomized trial of low-fluence PDT versus intravitreal bevacizumab in 22 patients with chronic central serous chorioretinopathy, (39) and a small randomized trial of 16 eyes with chronic or recurrent central serous chorioretinopathy comparing low-fluence PDT versus 3 monthly injections of ranibizumab. (40) Also included were a prospective, multicenter, investigator-masked study that compared half-fluence PDT with conventional PDT in 42 eyes (42 patients) with chronic central serous chorioretinopathy, (41) and a retrospective multicenter study of 60 patients with chronic central serous chorioretinopathy. (42)
Use of reduced-dose verteporfin PDT for chronic central serous chorioretinopathy also has been reported. Uetani et al (2012) compared half-dose versus one-third dose PDT in a small (N=16 eyes) prospective open-label trial. (43) At 3 months, all 10 (100%) eyes in the half-dose PDT group and 2 (33%) eyes 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) also reported on reduced-dose verteporfin for the treatment of chronic central serous chorioretinopathy in a prospective series of 48 patients. (44) Mean duration of central serous chorioretinopathy was 8.2 months (range, 3-40 months). At 12 months after PDT, mean BCVA improved from 0.31 to 0.15 logMAR, an improvement of 1.6 lines.

Section Summary: Central Serous Chorioretinopathy

Quality evidence on use of PDT for central serous chorioretinopathy is limited. The available evidence indicates substantial numbers of adverse events with standard PDT. Reduced-dose PDT may result in improved anatomic outcomes for acute central serous chorioretinopathy, but clinically significant improvements in visual acuity have not been shown for this self-limiting disease. For chronic central serous chorioretinopathy, recent comparative studies of reduced fluence and reduced dose PDT have suggested a beneficial effect of this treatment.

Polypoidal Choroidal Vasculopathy

Tang et al published a systematic review in 2015 evaluating treatment for polypoidal choroidal vasculopathy. (45) PDT alone was compared to ranibizumab alone and to combination ranibizumab plus PDT. This review included 3 RCTs and 6 retrospective comparative studies. For PDT alone versus ranibizumab alone, 2 RCTs reported the weighted mean difference in visual acuity was 0.06 logMAR (95% CI, -0.01 to 0.12) in favor of ranibizumab alone, but this difference was not statistically significant. For combination therapy versus PDT alone, a single RCT reported that there was a nonsignificant weighted mean difference of -0.08 (95% CI, -0.20 to 0.04) in favor of combination therapy. The 2010 systematic review by Chan et al included 30 studies on PDT in patients with polypoidal choroidal vasculopathy. (34) Chan et al found numerous case series reporting favorable anatomic and visual acuity outcomes for patients treated with PDT. Also reported was an ongoing manufacturer-sponsored RCT of PDT as monotherapy or combined with ranibizumab for treatment of polypoidal choroidal vasculopathy.

This ongoing study randomized 31 patients with AMD and 10 patients with polypoidal choroidal vasculopathy to bevacizumab monotherapy or bevacizumab in combination with PDT. (26) Bevacizumab was administered at 6-week intervals for the first 18 weeks, and then at 3-month intervals as needed. At 12 months, the monotherapy and combined treatment groups showed similar improvements in BCVA and central foveal thickness. Patients with polypoidal choroidal vasculopathy did not show significant improvement in BCVA (p=0.050) or central foveal thickness (p=0.088) when analyzed alone; however, the study was likely underpowered for this subset analysis.

EVEREST was a small, exploratory, multicenter double-blind randomized trial of PDT, ranibizumab, or combination treatment in 61 treatment-naïve Asian patients with polypoidal choroidal vasculopathy. (46) Patients in the PDT monotherapy group (angio-occlusive) received sham ranibizumab, and patients in the ranibizumab monotherapy group (angiogenic and antipermeability) received sham PDT. The primary end point, proportion of patients with complete regression of polyps at 6 months, showed PDT alone (71.4%) or in combination with ranibizumab (77.8%) to be superior to ranibizumab monotherapy (28.6%) in achieving complete polyp regression. The mean improvement in BCVA was generally similar for the 3 groups (7.5 letters for PDT, 10.9 for combined treatment, and 9.2 for ranibizumab alone). The
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proportion of patients gaining at least 15 letters was 19% in the PDT group, 21% in the combination group, and 33.3% in the ranibizumab monotherapy group. Interpretation of the visual acuity results is limited, as the study was not powered to assess differences in BCVA. There were no new safety findings.

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 polypoidal choroidal vasculopathy who were followed for 1 year after the primary PDT treatment. (47) 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 serious macular detachment at baseline were independent predictors of improvement in visual acuity.

Akaza et al. reported 3-year follow-up of 43 eyes treated with PDT for polypoidal choroidal vasculopathy. (48) Before the initial PDT, 40 eyes (93%) exhibited polypoidal choroidal vasculopathy 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.

Five-year follow-up was reported by Kang et al in 2013 for 42 eyes treated with PDT for polypoidal choroidal vasculopathy. (49) Patients received a mean of 2.21 PDT treatments over the course of the study, with additional intravitreal injections of anti-VEGF agents if exudative changes were observed. During follow-up, recurrence was observed in 78.6% of 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) at follow-up. Using a change of at least 0.3 logMAR as a threshold, BCVA improved in 33.3% of eyes, remained stable in 54.8%, and decreased in 11.9%. Interpretation of the efficacy of PDT in this study is limited, because all patients received combination treatment with intravitreal VEGF antagonists, and there were no comparison groups.

Kim and Yu conducted a retrospective review of 39 consecutive patients with polypoidal choroidal vasculopathy who received PDT monotherapy (before April 2007) or a combination of PDT and intravitreal bevacizumab (after April 2007). (50) 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. BCVA improved by 3.0 lines in the combined therapy group 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.

Section Summary: Polypoidal Choroidal Vasculopathy
The available evidence on efficacy of PDT for polypoidal choroidal vasculopathy consists of 2 small RCTs, a large number of case series and a retrospective comparative study. Controlled trials with a larger number of subjects and longer follow-up are needed to permit conclusions regarding the efficacy of PDT (monotherapy or combined) compared with anti-VEGF therapy.
Choroidal Hemangioma

The 2010 systematic review by Chan et al. included 11 case series on PDT in patients with choroidal hemangioma. (34) 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 choroidal hemangioma 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 choroidal hemangioma. (51) 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, best corrected visual acuity (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

The 2010 systematic review by Chan et al. included 8 case series on PDT in 148 patients with angioid streaks. (34) 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

The 2010 systematic review by Chan et al. included 15 case reports on PDT in 115 patients with inflammatory eye conditions. (34) 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.

Summary of Evidence

The evidence for photodynamic therapy (PDT) in individuals who have CNV due to age-related macular degeneration (AMD), pathologic myopia, presumed ocular histoplasmosis, chronic central serous chorioretinopathy (CSC), or choroidal hemangioma includes randomized controlled trials (RCTs), nonrandomized comparative trials, and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The RCT evidence supports the efficacy of PDT in reducing visual loss and decreasing retinal thickness. Comparative studies of PDT versus antivascular endothelial growth factor (anti-VEGF) medications have reported that anti-VEGF medications are as good as, and possibly superior to, PDT for reducing visual loss. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for PDT in individuals who have CNV due to polypoidal choroidal vasculopathy, angioid streaks, or inflammatory chorioretinal disease includes RCTs, nonrandomized comparative trials, and
case series. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. RCT evidence is limited for these conditions, and most published studies are case series. The case series have reported improved visual acuity following treatment, but this study design lacks sufficient methodologic rigor to allow conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PDT in combination with anti-VEGF medications in individuals who have CNV of any etiology (eg, AMD, chronic CSC, choroidal hemangioma, pathologic myopia, presumed ocular histoplasmosis, choroidal vasculopathy, angioid streaks, inflammatory chorioretinal disease) includes RCTs, nonrandomized comparative studies, and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. RCTs of combination therapy have reported that PDT can decrease the number of anti-VEGF injections needed, but PDT is not associated with improved visual acuity compared to anti-VEGF alone. Some studies have reported that the change in visual acuity after PDT is noninferior, but others have found that it is inferior to anti-VEGF alone. Further research is needed to better determine the tradeoff between fewer anti-VEGF injections and possible reduction in visual acuity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Medicare National Coverage

Since July 2001, ocular PDT has been eligible for Medicare coverage in the treatment of patients with 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. On review in January 2004, Medicare found evidence to conclude that ocular PDT may be reasonable and necessary for patients with AMD with either occult or minimally classic CNV 4 disk areas or less in size with evidence of progression within the 3 months prior to initial treatment. (50) Medicare also reiterated use of ocular PDT with verteporfin for indications such as pathologic myopia or presumed histoplasmosis syndrome may be eligible for coverage through individual contractor discretion.

SUPPLEMENTAL INFORMATION

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

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<td>Terminated (planned analyses)</td>
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NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.
Practice Guidelines and Position Statements

American Academy of Ophthalmology

A 2015 Preferred Practice Patterns guideline on AMD from the American Academy of Ophthalmology describes PDT as a treatment option approved by the U.S. Food and Drug Administration for subfoveal lesions and predominantly classic CNV related to AMD. (52)

The 2015 update states that anti-VEGF therapies have become first-line therapy for treatment and stabilizing most cases of AMD. PDT is a less commonly used treatment for neovascular AMD; recommendations state that the following diagnoses are eligible for PDT treatment with verteporfin:

- Macular CNV, new or recurrent where the classic component is >50% of the lesion, and ≤5400 µm in greatest linear diameter
- Occult CNV may be considered for PDT with vision <20/50 or if the CNV is <4 MPS [macular photoagulation study] disc areas in size when the vision is >20/50
- Juxtafoveal CNV is an off-label indication for PDT but may be considered in select cases

National Institute for Health and Care Excellence

In September 2003, the U.K.’s National Institute for Health and Care Excellence (then the National Institute for Clinical Excellence) issued Technology Appraisal Guidance 68 on the use of PDT for AMD. (53) Guidance 1.1 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.”

Canadian Agency for Drugs and Technologies in Health

In 2008, the Canadian Agency for Drugs and Technologies in Health (CADTH) released a health technology assessment on management of neovascular AMD. (54) CADTH concluded that “…overall, 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…."

Medicare National Coverage

Since July 2001, ocular PDT has been eligible for Medicare coverage in the treatment of patients with 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. On review in January 2004, Medicare found evidence to conclude that ocular PDT may be reasonable and necessary for patients with AMD with either occult or minimally classic CNV 4 disk areas or less in size with evidence of progression within the 3 months prior to initial treatment. (55) Medicare also reiterated use of ocular PDT with verteporfin for indications such as pathologic myopia or presumed histoplasmosis syndrome may be eligible for coverage through individual contractor discretion.
REFERENCES


POLICY HISTORY

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