Policy

I. Aetna considers photodynamic therapy (PDT) with light-activated verteporfin (Visudyne) medically necessary for treatment of subfoveal choroidal neovascularization (CNV) lesions caused by age-related macular degeneration (AMD), chronic (greater than 4 months) central serous chorioretinopathy, ocular histoplasmosis, or pathological myopia (see Appendix for selection criteria).

Note: Most individuals treated with verteporfin will need to be re-treated every 3 months. All individuals having a re-treatment will need to have a fluorescein angiogram or ocular coherence tomography (OCT) performed prior to each treatment. Re-treatment is necessary if fluorescein angiograms or OCT show any signs of recurrence or persistence of leakage.

II. Aetna considers Visudyne PDT experimental and investigational for the treatment of the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established:

- Alopecia areata
- Angioid streaks
- Angiomatous lesions secondary to systemic diseases
- Astelangiectasia
- Basal cell carcinoma
- Choroidal metastasis
- CNV associated with macular dystrophy or secondary to choroiditis and retino-choroiditis
- Diseases without CNV (e.g., choroidal osteoma, choroidal hemangioma, choroidal melanoma, and retinal hamartoma)
- Idiopathic CNV
- Neovascular glaucoma
- Pancreatic cancer
- Parafoveal CNV (occult CNV lesions with no classic component)
- Polypoidal choroidal vasculopathy
- Retinal angiomatous proliferation
- Retinal capillary hemangioma
- Retinoblastoma
- Rubeosis iridis.

See also CPB 0701 - Vascular Endothelial Growth Factor Inhibitors for Ocular Indications.

Background

Verteporfin (Visudyne) is a light-activated drug used in photodynamic therapy (PDT). Once verteporfin is activated by light in the presence of oxygen, highly reactive, short-lived reactive oxygen radicals are generated. Light activation of verteporfin results in local damage to neovascular endothelium, resulting in vessel occlusion.

Because of photodynamic therapy's potential for selective tissue injury, it offers advantages over conventional laser treatments. Photodynamic therapy's potential to selectively affect choroidal neovascularization (CNV) is attributable to preferential localization of the photosensitizer dye to the CNV complex and irradiation of the complex with light levels far lower than required for thermal injury.

Photodynamic therapy with verteporfin has been shown in 2 randomized controlled studies (RCTs) involving 609 patients to be effective for patients with CNV secondary to age-related macular degeneration (so-called "wet AMD"), the type of late age-related macular degeneration that is the most frequent cause of visual loss to the level of legal blindness or worse. In clinical studies, patients with predominantly classic CNV (CNV with distinct, subretinal neovascular membranes) showed clinically significant results; in comparison, among patients demonstrating less than 50 % classic CNV at the initial visit, there was no improvement in outcome compared to placebo treatment. After 12 months, 67 %of patients treated with verteporfin lost less than 3 lines of visual acuity, compared to 40 % of patients treated with placebo (sham treatment). Patients with predominantly classic (as opposed to occult) CNV lesions exhibited the greatest benefit, with 77 % of verteporfin-treated patients versus 27 % of placebo-treated patients losing less than 3 lines of visual acuity at 12 months.

A multi-center RCT conducted in Europe showed significant benefit of PDT with verteporfin for patients with predominantly occult CNV lesions. In this study, 258 of the 339 patients included in this study had occult CNV. After 2 years, 45 % of verteporfin-treated patients with occult CNV lost less than 15 letters (equivalent to approximately 3 lines), compared with 32 % of placebo-treated patients.
The evidence of effectiveness of verteporfin for pathologic myopia is based on a RCT involving 120 patients. After 1 year of treatment, 86% of verteporfin-treated patients lost less than 3 lines of visual acuity, compared to 67% of patients receiving placebo (sham) treatment. After 2 years, a difference persisted between groups in favor of the verteporfin-treated group (79% for verteporfin patients compared to 72% for placebo patients), but the difference was not statistically significant.

Food and Drug Administration's approval of verteporfin for presumed ocular histoplasmosis is based on a non-randomized open-label study involving 26 patients. Verteporfin-treated patients demonstrated a reduction in the number of episodes of severe visual acuity loss (greater than 6 lines of loss) compared with historical control data.

A recent update of a consensus guideline on the use of Visudyne for choroidal neovascularization due to AMD and other causes (Verteporfin Roundtable Participants, 2005) stated that additional courses of treatment should be considered as often as every 3 months (+/- 2 weeks) if fluorescein leakage from CNV is noted at that time. Moreover, additional courses of treatment could be deferred if the biomicroscopic and fluorescein angiographic appearances of the lesion are unchanged and show minimal fluorescein leakage, especially when there is no subretinal fluid or fluorescein leakage from CNV underlying the center of the foveal avascular zone. An analysis by the Centers for Medicare & Medicaid Services (CMS, 2013) found optical coherence tomography (OCT) as an appropriate alternative to FA to assess treatment response.

Visudyne has also been studied for the treatment of central serous chorioretinopathy (CSC). Central serous chorioretinopathy is an idiopathic disease in which a serous detachment of the neurosensory retina occurs over an area of leakage from the choriocapillaris through the retinal pigment epithelium. Photodynamic therapy is known to have a direct effect on the choroidal circulation but was limited by potential adverse effects, such as macular ischemia. In a pilot study (n = 20 eyes), Yannuzzi et al (2003) reported that indocyanine green angiography-guided PDT with verteporfin seems to aid in the resolution of exudative detachments in patients with chronic CSC. This treatment was associated with a rapid reduction in subretinal fluid and improvement in visual acuity. Although the follow-up time and number of patients in this pilot study were limited, the encouraging results and lack of complications suggest that further study is indicated. In a case reports study (n = 9), Ober et al (2005) stated that the treatment of acute CSC with PDT may result in prompt resolution of neurosensory detachment and fluorescein leakage, which can be associated with rapidly improved vision. Although this case series is limited in follow-up and number of patients, the encouraging results and lack of visually significant complications suggest that further investigation is warranted.

Lai et al (2006) assessed the short-term safety of an enhanced PDT protocol with half-dose verteporfin for treating chronic CSC. A total of 20 eyes of 18 patients with symptomatic chronic CSC underwent PDT using 3 mg/m2 verteporfin. Verteporfin was infused over 8 minutes followed by indocyanine green angiography guided laser application 2 minutes later. Serial optical coherence tomography (OCT) and multi-focal electroretinography (mfERG) recordings were
performed before PDT, at 4 days, 2 weeks, and 1 month after PDT. The best corrected visual acuity (BCVA), OCT central retinal thickness, and mean mfERG response amplitudes and peak latencies were compared longitudinally. Subgroup analysis was further performed for eyes with or without pigment epithelial detachment (PED). At 1 month after PDT, the median BCVA improved from 20/40 to 20/30 (p = 0.001). The mean central retinal thickness also reduced from 276 micron to 158 micron (p < 0.001) and 17 (85 %) eyes had complete resolution of serous retinal detachment and/or PED. MfERG showed no significant changes in the mean N1 and P1 response amplitude and latency for all eyes. Subgroup analysis showed that eyes without PED had a significant increase in the mean central mFERG P1 response amplitude with reduction in P1 peak latency at 1 month post-PDT. For eyes with PED, transient reduction in the mean central P1 response amplitude was observed at 4 days post-PDT. The authors concluded that the modified safety enhanced PDT protocol with half-dose verteporfin appeared to be a beneficial treatment option for patients with chronic CSC, especially in eyes without serous PED. They stated that further controlled study is needed to demonstrate the long-term safety and effectiveness of this treatment option. Moreover, a practice guideline on PDT for CNV due to AMD and other causes (Verteporfin Roundtable Participants, 2005) did not list CSR as an indication for Visudyne.

Spaide et al (2005) examined the 12-month results of a group of patients treated with combined PDT with verteporfin and intra-vitreal triamcinolone acetonide for CNV secondary to AMD. A total of 26 eyes of 26 patients with CNV secondary to AMD were included in the study -- 13 with CNV, without restriction to type, were not treated with prior PDT (newly treated group); and 13 with prior PDT therapy who experienced visual loss while being treated with PDT alone comprised the remainder (prior PDT group). Patients with CNV were treated with PDT, immediately followed by an intra-vitreal injection of 4 mg of triamcinolone acetonide. Visual acuity was measured by Early Treatment Diabetic Retinopathy Study protocol refraction. Need for re-treatment was based on fluorescein angiographic evidence of leakage at 3-month follow-up intervals. Main outcome measures were visual acuity and re-treatment rate. In the newly treated group, the mean acuity change was an improvement of 2.5 lines (last observation carried forward [LOCF], +2.4 lines; p = 0.011, Wilcoxon signed ranks test, as compared with baseline acuity) for patients completing the 12-month follow-up. In the prior PDT group, the mean change was an improvement of +0.44 lines (LOCF, +0.31 lines; p = 0.53). Re-treatment rates were 1.24 for the newly treated group and 1.2 for the prior PDT group over the first year. Ten patients (38.5 %) developed an intra-ocular pressure of greater than 24 mm Hg during follow-up, a threshold used to institute pressure reduction therapy. No patient developed endophthalmitis. The authors concluded that although the number of patients in this pilot study was limited, the improvement of acuity and the reduced treatment frequency in these patients suggested that combination therapy with PDT and intra-vitreal triamcinolone acetonide, particularly when used as first-line therapy, merits further investigation. Elevated intra-ocular pressure seems to be the most frequent early side effect of the treatment.

Ergun et al (2006) examined the effectiveness of PDT with verteporfin and intra-vitreal triamcinolone acetonide in the treatment of neovascular AMD. A total of 60 eyes of 56 patients with neovascular AMD were treated with PDT with verteporfin
followed by an intra-vitreal injection of 4 mg triamcinolone acetonide. The main outcome measures were visual acuity, re-treatment frequency with PDT (and triamcinolone), and frequency of side effects. Mean follow-up was 15.9 months (range of 12 to 30 months, median 15 months). Twenty-three (38.3 %) of 60 eyes had a stable result at 12 months' follow-up (i.e., loss/gain less than 3 lines) and 34 (56.7 %) of 60 had a loss of 3 lines or more. Three patients (5 %) had an improvement of 3 lines or more. Lesion type, patient age, and lesion size had no influence on the outcome, but baseline visual acuity had a statistically significant effect ($p = 0.006$). The median number of PDT-intra-vitreal triamcinolone acetonide treatments was one. One-third (20 of 60) of all eyes had an increase in intra-ocular pressure that required therapy. There were no cases of endophthalmitis, but 13 patients (21.6 %) developed severe cataract that required surgery. The authors concluded that the combination of PDT and intra-vitreal triamcinolone acetonide requires careful consideration as a treatment option for neovascular AMD. In the present study, this treatment combination did not prevent a considerable decrease in visual acuity.

Augustin and Schmidt-Erfurth (2006) reported that pilot studies as well as large case series suggested that a combination of PDT and intra-vitreal triamcinolone acetonide has the potential to improve visual outcomes and reduce the need for additional PDT treatments. They noted that randomized, prospective clinical trials are underway to confirm the safety and effectiveness of this novel treatment modality.

Mennel and colleagues (2007) noted that PDT has been performed in several other ocular pathologies with some remarkable results, however, with most reports being case reports and small case series without statistical significance. These extended applications include CNV secondary to choroiditis and retino-choroiditis, angioid streaks, central serous chorioretinopathy, retinal angiomatous proliferation, parafoveal telangiectasia or CNV associated with macular dystrophy and idiopathic CNV, as well as diseases without CNV, such as choroidal hemangioma, retinal hamartoma, choroidal melanoma, chronic central serous chorioretinopathy, angiomatous lesions secondary to systemic diseases, rubeosis iridis or neovascular glaucoma. With the introduction of anti-vascular endothelial growth factor (VEGF) therapy, the role of PDT will certainly change.

In a prospective, multi-center, non-randomized clinical trial, Boixadera and co-workers (2009) evaluated PDT for symptomatic circumscribed choroidal hemangioma (CCH). A total of 31 eyes of 31 patients with posterior pole CCH and symptoms caused by exudation into the macular area were included in this study. Photodynamic therapy was administered by Zeiss laser. Intravenous verteporfin at 6 mg/m$^2$ body surface was given before treatment, and light emitted at 689 nm for photosensitization. The treatment spot diameter was calculated on early-phase frames of pre-treatment indocyanine green angiography. Fifteen minutes after starting the verteporfin infusion, the laser beam was applied to the retina at radiant exposure 50 J/cm$^2$ and exposure time 83 seconds. One to 4 treatments were applied at 12-week intervals over 1 year. Standardized evaluation was performed before and at 4-week intervals after each treatment, and at 3, 6, 9, and 12 months. All patients were followed for greater than or equal to 12 months. The primary outcome measure was the absence of exudative retinal detachment at the 12-month follow-up visit on ophthalmoscopy, fluorescein angiography, and optical
coherence tomography. Secondary measures were the visual acuity outcome, with best-corrected visual acuity determined by the Early Treatment for Diabetic Retinopathy Study chart, tumor thickness decrease on B-scan ultrasonography, and adverse events. Among the total, 82.8% of patients required 1, 13.8% required 2, and 3.4% needed 3 PDTs to eliminate exudative retinal detachment. Visual acuity increased from a mean of 20/60 to 20/35 ($p < 0.001$); 69% of patients demonstrated visual recovery ($p < 0.001$). Cystoid macular edema regressed in all cases and exudative macular detachment disappeared in all but 2 cases. The CCH thickness decreased in all cases from a mean of 3.0 to 1.7 mm, with the most intense effect seen after 4 weeks of treatment ($p < 0.001$). Visual fields showed resolution of central scotomas. There were no severe adverse events. The authors concluded that combining PDT with the standard AMD protocol is an effective treatment for CCH in terms of resolution of exudative subretinal fluid and recovery of visual acuity. Moreover, the authors also stated that "because recurrence has been observed long after treatment, a lengthier follow-up period is required to assess the risk of late recurrence and the long-term visual prognosis in these patients”.

Kaiser (2007) discussed the rationale for combining anti-angiogenic treatment with Visudyne PDT in the management of CNV due to AMD and evaluated available evidence for the therapeutic benefits of such approaches. Treatments for CNV due to AMD can be directed at either the vascular component of CNV or the angiogenic component that leads to the development of the condition. Verteporfin targets the vascular component, whereas anti-angiogenic agents (such as pegaptanib and ranibizumab) target key mediators of the angiogenic cascade. The different mechanisms of action of these approaches offer the potential for additive or synergistic effects with combination therapy. In addition, anti-angiogenic agents might counteract up-regulation of angiogenic factors (including VEGF) that occur after verteporfin PDT. Results from pre-clinical and clinical studies of the combination of ranibizumab or pegaptanib with verteporfin warrant continued investigation. The author concluded that the use of anti-angiogenic agents in combination with verteporfin may have the potential to improve visual outcomes and reduce the number of treatments in eyes with CNV due to AMD, and requires further evaluation in randomized, controlled clinical trials.

In a recent review on verteporfin combination regimens in the treatment of neovascular AMD, Shah and colleagues (2009) concluded that a rationale exists for investigating combination approaches to target different processes in CNV pathogenesis, which may optimize treatment benefits in neovascular AMD.

Cruess and associates (2009) noted that PDT with verteporfin has been used less comprehensively in the treatment of exudative AMD, and specifically of CNV, since the advent of anti-angiogenic therapies. Recently, there has been a renewed interest in PDT as an adjunct to these and other agents in the treatment of neovascular AMD. In light of this new development and the European Medicines Evaluation Agency's (EMEA) recent labeling decision to rescind approval for the use of PDT in occult CNV lesions; these investigators reviewed the evidence supporting its clinical application. Photodynamic therapy provided the first pharmacological treatment for patients suffering from subfoveal CNV, the major cause of severe vision loss in AMD. Key clinical trials evaluating the safety and effectiveness of PDT have examined patients with all lesion subtypes, with the
primary labeled indication (i.e., lesions containing a classic component of greater than or equal to 50 %) deriving from the results of the Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) Study. The subsequent TAP Study Group post-hoc categorization of lesions as predominantly classic is open to question, however, as it appears that the overall effectiveness in this group only may have reflected the especially strong response in 100 % classic lesions. Based on a subgroup analysis of the verteporfin in Photodynamic Therapy Study, the indication for PDT subsequently was expanded in some jurisdictions, including that of the EMEA, to include occult lesions with no classic component. However, the subsequent Visudyne in Occult Study found no benefit in 100 % occult lesions, resulting in the EMEA rescinding its approval for this indication.

Kaiser (2009) examined if verteporfin PDT can safely reduce the risk of vision loss in patients with subfoveal occult with no classic CNV due to AMD. Eligible patients were greater than or equal to 50 years of age with lesion size less than or equal to 6 disc areas and best-corrected vision 20/40 to 20/200. A total of 364 patients with occult with no classic CNV were randomly assigned 2:1 to verteporfin PDT (n = 244) or placebo (n = 120). The primary outcome measures were loss of greater than or equal to 15 and greater than or equal to 30 letters of visual acuity (VA) from baseline at 12 and 24 months. A total of 37 % and 47 % of verteporfin-treated patients versus 45 % and 53 % of placebo recipients lost greater than or equal to 15 letters of VA at month 12 and month 24, respectively; 16 % and 23 % of verteporfin-treated patients versus 17 % and 25 % of placebo recipients lost greater than or equal to 30 letters at month 12 and month 24, respectively. These differences were not statistically significant. Four (1.6 %) verteporfin-treated patients and 1 placebo patient (who received verteporfin in error) experienced an acute severe VA decrease; all 5 patients recovered some degree of vision. No unexpected ocular or systemic adverse events were identified. The authors concluded that verteporfin PDT in the treatment of occult with no classic CNV was safe and well-tolerated. The differences between the 2 groups in the primary efficacy variables were not significant. Baseline characteristics and patient selection methods may have contributed to the small treatment effect.

Akaza et al (2007) examined the effectiveness of PDT with verteporfin for polypoidal choroidal vasculopathy (PCV). Photodynamic therapy was performed in 35 patients (35 eyes) with PCV. These researchers evaluated the number of treatments and compared VA, ophthalmological findings, and changes in polypoidal lesions and branching vascular networks by measuring lesion diameters using Heidelberg retina angiography before PDT, and then every 3 months for 1 year after PDT. The mean annual number of treatment sessions was 2.2; VA was improved or maintained in 80 % of the patients. Retinal pigment epithelium detachment, retinal detachment, hemorrhage, and/or exudates disappeared in 69 %, and leakage resolved in 74 % of the patients. Polypoidal lesions disappeared completely on indocyanine green angiography in 83 % of the patients. All branching vascular networks persisted. Polypoidal lesions had recurred at the termini of the remaining branching vascular networks at 9 months after the first PDT in 2 eyes and at 12 months in 1 eye. The authors concluded that PDT with verteporfin for PCV appears to improve or maintain VA for the first post-treatment year. Approximately 70 % of PCV cases showed improved ophthalmoscopic findings. However, as polypoidal lesions recur after PDT in
some cases, further study is needed to confirm the long-term effectiveness of PDT for PCV.

In a prospective, interventional study, Gomi et al (2008) determined the prevalence of PCV in Japanese patients presumed to have AMD and compared 1-year outcomes after PDT between PCV and CBV secondary to AMD. A total of 93 consecutive patients (93 eyes) met the inclusion criteria: at least 50 years old, BCVA of 34 to 73 on the Early Treatment Diabetic Retinopathy Study (ETDRS) letter chart, a subfoveal lesion 5,400 mum or smaller in greatest linear dimension (GLD) on fluorescein angiography (FA), and eligibility for PDT. Indocyanine green angiography was performed in all subjects, and PCV and AMD were differentiated, treated with PDT, and the patients observed for 1 year. The GLD was determined by FA for AMD and by indocyanine green angiography for PCV, and the diameter of the laser spot size was chosen, with an extra 1,000 microm added to the GLD. Photodynamic therapy was repeated if leakage occurred on FA at 3-month follow-up visits. Main outcome measures were prevalence of PCV at baseline and visual and angiographic changes 1 year after PDT in PCV and AMD. Using indocyanine green angiography, 36 eyes (39 %) were diagnosed with PCV and 54 eyes (58 %) with CNV secondary to AMD. The median change in VA using the ETDRS letter score from baseline to 1 year was -7.0 in AMD eyes and +8.0 in PCV eyes (Mann-Whitney rank sum test; p < 0.001). The VA improved (greater than or equal to 15 letters) in AMD and PCV by 6 % and 25 %, respectively, and decreased (greater than or equal to 15 letters) by 31 % and 8 %, respectively. Fluorescein leakage stopped at 1 year in 86 % of PCV and 61 % of AMD eyes (p = 0.031). Polypoidal choroidal vasculopathy recurred in 2 PCV eyes (5.6 %), and a new PCV lesion developed in 1 PCV eye (2.8 %) and 2 AMD eyes (3.7 %) on indocyanine green angiography at 1 year. The authors concluded that the prevalence of PCV meeting the treatment criteria for PDT for presumed AMD is high in Japanese patients. Photodynamic therapy is more effective for PCV than for AMD, which may explain the good results in Japanese patients. They stated that further study should assess the long-term clinical results because PCV lesions might occur or new lesions might develop.

Yamashita et al (2010) reported 1-year results of reduced-fluence PDT for PCV in Japanese patients. In the present study, 28 treatment-naïve eyes of 28 consecutive patients underwent PDT with a reduced laser fluence of 25 J/cm(2). Patients were followed-up at 1 week and 3, 6, 9, and 12 months after PDT. Choroidal perfusion changes were evaluated by indocyanine green angiography and leakage from PCV lesions and exudative changes by fluorescein angiography and OCT. Treatment safety was assessed according to VA and adverse events. The BCVA obtained by Landolt ring tests was converted into the logarithm of the minimal angle of resolution (logMAR). At baseline, the mean logMAR BCVA was 0.45 (geometric mean: 7/20). At 12 months, the mean logMAR BCVA significantly improved to 0.29 (geometric mean: 10/20) (p = 0.0001). The logMAR BCVA was stable or improved by greater than or equal to 0.2 in 26 eyes (93 %) at 1-year follow-up. In 10 eyes with VA better than 20/40 at baseline, the mean logMAR BCVA was significantly improved compared with baseline at 12 months. Although 16 of 28 eyes (57 %) showed mild-to-moderate non-perfusion of choriocapillaris in early indocyanine green angiography at 1 week, 27 eyes (96 %) showed recovery to pre-treatment levels at 3 months. Mean number of treatment sessions during the 12 months was 1.3. No severe side effects related to treatment were
encountered. The authors concluded that reduced-fluence PDT is an effective treatment for PCV and could improve vision even in eyes with VA better than 20/40. Moreover, they stated that the limitations of this study included small sample size and the lack of control; further studies with longer follow-up periods are needed to assess treatment safety and effectiveness.

Chan and colleagues (2010) stated that verteporfin PDT is approved for the treatment of predominantly classic subfoveal CNV due to AMD, as well as for subfoveal CNV due to pathologic myopia and ocular histoplasmosis syndrome. Verteporfin PDT addresses the underlying pathology of ocular vascular disorders through its angio-occlusive mechanism of action, which reduces both VA loss as well as the underlying leakage associated with lesions. Verteporfin PDT has also been associated with encouraging treatment outcomes in case studies involving patients with choroidal vascular disorders (e.g., angiod streaks, central serous chorioretinopathy, choroidal hemangioma, inflammatory CNV, and PCV, i.e., conditions currently considered as non-standard indications of verteporfin PDT). In many studies, outcomes were better than expected based on the natural courses of each of these conditions. Although the anti-VEGF therapies, ranibizumab and pegaptanib, have been approved for CNV due to AMD, their role in these other choroidal vascular disorders remains to be established. The authors concluded that the complex pathogenesis of CNV provides a rationale for investigating combination approaches comprising verteporfin PDT and anti-VEGF therapies. They stated that randomized controlled studies are needed to confirm the preliminary results of verteporfin PDT as a monotherapy or in combination with anti-VEGF therapies in the treatment of a variety of choroidal vascular conditions.

In a prospective, consecutive, 2-centered, non-comparative, interventional case series, Blasi et al (2010) evaluated the long-term efficacy of verteporfin PDT as the primary treatment for symptomatic CCH (n = 25). All patients had recent onset of visual symptoms and evidence of exudative macular changes on FA and optical OCT. Verteporfin 6 mg/m(2) body surface area was administered intravenously over a 10-minute interval. Five minutes after infusion, a 689-nm laser was applied with a light dose of 50 J/cm(2) for the first 3 patients and a light dose of 100 J/cm (2) for all the other patients. Re-treatments were performed in case of persistent exudation found on OCT. Evaluation of BCVA using ETDRS criteria, FA, indocyanine green angiography (ICGA), OCT, and ultrasound were performed before PDT and on follow-up examinations. All patients were followed for at least 5 years. Primary outcome measures were changes in BCVA and foveal center thickness (FCT) between baseline and month 60. Secondary measures were tumor thickness decrease, absence of leakage on FA, and adverse events. Twenty-two patients received 1 PDT session at 100 J/cm(2), and no recurrences were detected. Three eyes, treated with 50 J/cm(2), received a second PDT session at 100 J/cm(2) 1 month after the first session. After a follow-up of 60 months, BCVA improved an average of 18.5 ETDRS letters (p < 0.001); BCVA improved by greater than or equal to 2 lines in 19 eyes (76 %). The FCT decreased from a mean of 386.20 microm to 179.2 microm, and OCT showed the complete resolution of macular exudation in all cases. All tumors responded with a reduction in size. No treatment-related adverse events or complications were identified. The authors concluded that 5-year results of PDT in treating symptomatic CCH support treatment with a light dose of 100 J/cm(2) after slow intravenous infusion of verteporfin to stabilize or improve visual acuity and
resolution of macular exudation. They also stated that RCTs with lon follow-up periods are needed to determine the precise timing of treatment and to compare the different PDT.

In a retrospective case-series study, Butler and colleagues (2012) described the safety and efficacy of very minimal fluence PDT for chronic central serous chorioretinopathy (CCSC). A total of 5 patients with CCSC were included in this study; 2 had previously failed alternative therapies, and 1 was taking concomitant corticosteroids. Patients were treated with very minimal fluence PDT (12 J/cm(2), 150 mW/cm(2), for 80 seconds). Median follow-up time after PDT was 100 days (range of 51 to 154). All patients experienced an improvement in visual acuity and symptoms, as well as complete resolution of sub-retinal fluid. The authors concluded that very minimal fluence PDT appears to be a safe and effective treatment for CCSC. They stated that based on these preliminary findings, a randomized controlled trial is warranted.

Alcubierre et al (2012) evaluated safety and effectiveness of low-fluence PDT (LFPDT) with verteporfin in patients affected with CCSC, in terms of VA and macular morphology measured with OCT. A retrospective, non-randomized and interventionist analysis was performed on 16 eyes in 15 patients with CCSC treated with LFPDT. Best corrected visual acuity with ETDRS optotypes and central foveal thickness (CFT) in OCT were evaluated as outcome measures. The mean follow-up was 10.8 months. The mean BCVA improved from 58.12 to 68.68 ETDRS letters, and CFT decreased from 280.5 to 172.18 microns, with sub-retinal fluid resolution in 14 eyes (87.5 %), 2 of them after a second LFTPD. No complications related to treatment were recorded. The authors concluded that LFPDT with verteporfin can be useful in CCSC to stabilize or improve BCVA, reabsorb sub-retinal fluid and reduce CFT. They stated that randomized studies with a longer follow-up are needed to assure the role of this treatment and to optimize parameters for higher safety and effectiveness in CCSC patients.

Boni and colleagues (2012) stated that in persistent CSC resolution of detachment can be achieved by PDT. These investigators evaluated the effectiveness of half-dose verteporfin compared to full-dose verteporfin. In 2009, the standard PDT regimen for CSC in the authors’ clinic was changed from full-dose to half-dose verteporfin. After a retrospective analysis, 11 cases of half-dose PDT with documented course in 11 patients were presented. A comparison was performed with a control group of 11 consecutive patients with documented course who had received full-dose PDT before 2009. Prior to PDT, there were no statistically significant differences between the groups concerning age, CFT, thickness of detachment, BCVA (EDTRS) and size of spot. Six weeks after PDT, a significant reduction of foveal thickness and detachment was detected in both groups, as well as a significant increase in BCVA. No statistically significant differences in outcome could be found between the 2 groups (Mann-Whitney U-test, p < 0.05). The authors concluded that PDT with half-dose verteporfin seems to be an effective and safe treatment for persistent CSC. These findings showed comparable results after half-dose and after full-dose PDT.

In a retrospective, consecutive case-series study, Jirarattanasopa et al (2012) evaluated the 1-year results of half-dose PDT with verteporfin in chronic or recurrent CSC. A total of 27 eyes of 27 patients with chronic symptomatic CSC or
recurrent CSC underwent PDT with half-dose (3 mg/m²) verteporfin. The demographic data such as age, side, gender, spot sizes of laser PDT were recorded. The primary outcomes were the BCVA, CFT using the OCT and complication were recorded as secondary outcome at baseline, month 1, 3, 6, and 12 post-PDT. At 12 months after half-dose PDT, the mean logMAR BCVA improved from 0.32 to 0.18 (p = 0.001), the mean CFT decreased from 375.52 microm to 186.52 microm (p < 0.001). The results also showed significant improvement of logMAR BCVA and decreased CFT after 1 month (0.32 to 0.22, p = 0.003 and 375.52 microm to 175.41 microm, p < 0.001) and maintained the results until 1-year follow-up. Twenty-five eyes (92.6 %) showed complete resolution of subretinal fluid at 1 month, 27 patients (100 %) showed complete resolution at 3 month and all sustained the complete resolution until the last visit. No serious complications were recorded during and after the treatment. The authors concluded that the half-dose PDT in area of fluorescein leakage is one of the effective treatment options for chronic or recurrent CSC, especially in patients who cannot undergo focal laser photocoagulation. The treatment sustained the good visual results and has no serious complications up to 1-year.

In a retrospective case-series study, Li et al (2012) evaluated the effect of spectral HRA + OCT-guided PDT with half-dose verteporfin in the treatment of chronic or recurrent CSC. A total of 20 eyes of 18 patients with chronic or recurrent CSC were included. Photodynamic therapy was applied with half-dose verteporfin (3 mg/m²(2)) on the site of active area shown on spectral HRA + OCT (defined as focal or diffuse retinal pigment epithelial leakage, choroidal hyperpermeability, or pigment epithelial detachment located within the neurosensory detachment), and patients were observed to determine the anatomic and functional outcomes. Statistical analysis was performed using SAS (version 9.2). A “p” value of 0.05 was considered statistically significant. Comparisons of pre- and post-treatment BCVA and CFT were performed using a paired-t test. The relationship between BCVA and CFT post-treatment was analyzed by linear correlation analysis. Comparisons of the BCVA of eyes with and without the integrity of photoreceptor IS-OS and/or external limiting membrane at the last follow-up visit were performed using 2 sample t-test. The median CSC duration was 4.5 months (ranged 1 month to 2 years). The median follow-up period after PDT was 8 months (ranged 6 to 20 months). The mean BCVA before PDT was 0.35 ± 0.16 (ranged 0.05 to 0.6), at 3 months after PDT was 0.72 ± 0.32 (ranged 0.1 to 1.5) and at the last follow-up visit was 0.78 ± 0.29 (ranged 0.3 to 1.5) (t = 6.444, 6.883, p < 0.05). Fifteen eyes (75.0 %) had improved vision, and 5 eyes (25.0 %) had stable vision. The mean CFT was reduced from (369.0 ± 120.9) µm before PDT to (193.3 ± 30.6) µm 1 month after PDT, (194.9 ± 28.3) µm 3 month after PDT and (190.6 ± 33.7) µm at the last follow-up visit (t = -6.836, -6.826, -7.316; p < 0.05). At the last follow-up visit BCVA was not correlated with CFT (r = 0.166, p > 0.05), but BCVA of the eyes with the integrity of photoreceptor IS-OS and/or external limiting membrane was better than that of without (t = -3.53, p < 0.05). Subretinal fluid disappeared in all eyes 1 month after PDT and there was no recurrence during the follow-up. The authors concluded that spectral HRA + OCT-guided PDT with half-dose of verteporfin seems effective and safe for the treatment of chronic or recurrent CSC.

Lim et al (2013) examined the effectiveness of half-fluence PDT depending on the degree of hyper-fluorescence based on ICGA for treatment of chronic CSC (CCSC). These researchers conducted a prospective study of 30 eyes of 30
patients with CCSC. Half-fluence PDT (25 J/cm\(^2\) for 83 s) with ICGA guidance was applied to the area of choroidal hyperpermeability. The baseline middle-phase ICGA findings were classified as intense or weak hyper-fluorescence depending on the degree of hyperpermeability from choriocapillaris. Changes in mean BCVA, resolution of subretinal fluid, recurrence rate, and complications were compared between the 2 groups. The baseline ICGA findings showed intense hyper-fluorescence in 16 eyes (53.3 %) and weak hyper-fluorescence in 14 eyes (46.7 %). Subretinal fluid showed complete resolution in both the groups 1 month after a single application of half-fluence PDT. Recurrence of subretinal fluid was observed in 1 of 14 eyes (7.1 %) with weak hyper-fluorescence and in no eyes (0 %) with intense hyper-fluorescence. No statistically significant difference in the rate of recurrence was observed between the 2 groups. The authors concluded that half-fluence PDT appears to be an effective and safe treatment option for patients with CCSC regardless of the degree of hyper-fluorescence based on ICGA. According to these findings, choroidal hyperpermeability, rather than dysfunction of retinal pigment epithelium, might be more important as primary pathogenesis of CCSC.

Karakus et al (2013) evaluated the safety and effectiveness of PDT with half-dose verteporfin in patients with CCSC and retinal functional changes, by functional acuity contrast test (FACT). In this study, 27 eyes of 24 patients with CCSC were treated with PDT with half-dose verteporfin. Best-corrected visual acuity, CFT and resolution of subretinal fluid on OCT, and leakage on FA and ICGA were assessed. Contrast sensitivity test was performed at baseline and at 12 months for investigating retinal functional changes. The mean follow-up period was 25.33 ± 11.08 months. The mean age was 43.7 ± 8.6 years. Seventeen patients were male (70.8 %) and 7 patients were female (29.2 %). Post-PDT at 1st, 3rd, 6th, 12th month and at last follow-up, BCVA were significantly improved compared with the baseline BCVA (p < 0.001), and CFT post-PDT were significantly thinner than the baseline measurement (p < 0.001). There was significant difference between pre- and post-PDT 12th month contrast sensitivities at all 5 different spatial frequency channels (p < 0.01). The authors concluded that the half-dose PDT is safe and effective in treating CCSC with anatomical and functional success. The measurement of contrast sensitivity by FACT can be useful for evaluating the functional effectiveness of half-dose PDT for CCSC.

Ohkuma et al (2013) evaluated the effectiveness of reduced-fluence PDT (RFPDT) for CSC. This retrospective medical record review of consecutive CSC patients treated with RFPDT (full-dose verteporfin and laser fluence of 25 J/cm\(^2\)) examined 22 eyes of 21 patients (20 males and 1 female). All patients were followed-up for 1 year. Best-corrected visual acuity, complete resolution of subretinal fluid (CR of SRF), CRT, the outer nuclear layer (ONL) thickness, and the photoreceptor inner and outer segments (IS/OS) line determined by OCT imaging were evaluated at baseline, 1, 3, 6, 9, and 12 months after initial RFPDT. A single RFPDT session was performed in all cases during a 12-month period. Complete resolution of SRF was identified in all patients; BCVA significantly improved between 3 and 12 months (p < 0.05). The CRT significantly decreased between 1 and 12 months. A significantly thicker ONL was observed at 1 month, and 17 eyes (77.2 %) showed recovery of the continuous foveal IS/OS line. Outer nuclear layer thickness was correlated with BCVA at 12 months (p < 0.01). Stepwise analysis indicated that pre-treatment BCVA (p < 0.01) and ONL thickness
(p < 0.01) were significant predictive factors for BCVA at 12 months. Neither ocular nor systemic adverse effects were observed during the follow-up period. The authors concluded that RFPDT appears to be an effective treatment for CSC. Outer nuclear layer thickness is an important visual predictive factor of RFPDT for CSC.

Smretschnig et al (2013) evaluated the results of ICGA-guided verteporfin (Visudyne) PDT with half-fluence rate in the treatment of CCSC. A retrospective review was conducted of 20 eyes of 19 consecutive patients with subfoveal fluid cause by CCSC with choroidal hyperpermeability on ICGA and symptoms of at least 6 months. Indocyanine green angiography-guided verteporfin (6 mg/m) PDT with half-fluence rate (25 J/cm) was performed; ICGA findings were classified as intense, intermediate, or minimal hyper-fluorescence depending on the degree of choroidal hyperpermeability. The resolution of the subretinal fluid and recurrence rates were assessed in relation to the different degrees of choroidal hyper-fluorescence. Best-corrected visual acuity at baseline was 40 letters (± 13; n = 20) according to the ETDRS chart. At 12 months after PDT, the mean BCVA improved to 44 letters (p < 0.01). Pre-treatment CFT was 325 μm and decreased by a mean of 103 μm at month 12 control (p < 0.05). At month 1 after PDT, subretinal fluid in spectral-domain OCT was completely resolved in 100 % of eyes regardless to their degree of choroidal hyper-fluorescence. Two eyes of the intense hyper-fluorescence group and 1 eye of the intermediate hyper-fluorescence group developed recurrence of symptoms over 12 months and received another PDT with half-fluence rate within the 12-month control period. Treatment effect was not depending on the degree of choroidal hyperpermeability at baseline. No systemic side effects were observed during the 12-month follow-up. The authors concluded that ICGA-guided half-fluence PDT with verteporfin is effective in treating CCSC with choroidal hyperpermeability in ICGA, resulting in both visual improvement and reduction of CFT.

Nicholson et al (2013) stated that recent technological advances -- new pathophysiological insights, new imaging techniques for diagnosis and management, and new treatments -- have led to an improved understanding of CSC. The primary role of the choroid has become more widely accepted with widespread use of ICGA. Optical coherence tomography, and particularly enhanced depth imaging OCT, demonstrated a thickened and engorged choroid. Adaptive optics, fundus autofluorescence, mfERG, micro-perimetry, and contrast sensitivity testing revealed that patients with even a mild course suffer previously undetected anatomic and functional loss. Although focal laser and PDT are the current standard of care for persistent subretinal fluid in CSC, they are not appropriate in all cases, and the optimal timing of intervention remains unclear.

In a retrospective, interventional case series study, Kaliki et al (2012) examined the effectiveness of PDT in the treatment of choroidal metastasis. A total of 9 tumors in 8 eyes of 8 patients were included in this study. Photodynamic therapy using verteporfin at a dose of 6 mg/m(2) body surface area and 689 nm diode laser at an intensity of 600 mW/cm(2) for 83 seconds (50 J/cm(2)) was employed. Main outcome measure was tumor control and BCVA. Nine choroidal metastases in 8 eyes were treated with 1 (8 tumors) or 2 (1 tumor) sessions of PDT. The mean tumor basal diameter was 7 mm (median of 7 mm [range of 2 to 13 mm]), and mean tumor thickness was 2.9 mm (median of 2.9 mm [range of 1.6 to 4.0
All 9 tumors were associated with shallow subretinal fluid. After PDT, complete control with resolution of subretinal fluid was achieved in 7 tumors (78%), with mean tumor thickness reduction of 39% (median of 43% [range of 6% to 61%]). Two tumors failed to respond to PDT, both requiring plaque radiotherapy. Improvement or stabilization of vision was achieved in 7 eyes. Photodynamic therapy-related complications included intra-retinal hemorrhage in 1 eye. The authors concluded that PDT can be an effective alternative for the treatment of choroidal metastasis. Moreover, they noted that additional studies with long-term results in a large cohort will assist in further defining the role and limitations of PDT for management of choroidal metastasis.

In a Health Technology Assessment on “Verteporfin photodynamic therapy for neovascular age-related macular degeneration”, Reeves and colleagues (2012) stated that “VPDT also has potential as monotherapy in the management of vascular malformations of the retina and choroid and with trials underway in neovascularisation due to myopia and polypoidal choroidopathy”.

Beardsley et al (2013) reported on the recurrence of serous retinal detachment following verteporfin PDT for CCH. A single-center chart review was performed for patients with CCH treated with Visudyne (verteporfin injection; QLT Ophthalmics, Menlo Park, CA) PDT. Initial and post-treatment VA, ultrasound and OCT were evaluated. A total of 4 patients who were treated with PDT for symptomatic serous retinal detachment secondary to CCH were managed for recurrent leakage and followed for an average of 47.5 months. Two patients required 3 re-treatments and 2 required 4 re-treatments for recurrent detachment. Average time to re-treatment was 23.4 months, with successive re-treatment intervals decreasing to 13 months, then 9.5 months, and finally 3.5 months. The authors concluded that Visudyne PDT is a successful initial treatment modality for CCH with serous retinal detachment; however, those patients who require multiple re-treatments may experience recurrent leakage at more frequent intervals.

Mitropoulos and colleagues (2014) presented a case of juxtapapillary retinal capillary hemangioma treated with PDT. A 69-year old woman with no previous ocular history presented with blurred vision and photopsias in the right eye 3 months ago. At presentation, her BCVA was 6/9 in the right eye and 6/6 in the left eye. The anterior segment was totally normal and intra-ocular pressure (IOP) was normal in both eyes as well. Dilated fundoscopy revealed a yellowish, well-circumscribed, elevated area with blood vessels, on the inferior margin of the right optic disc, as optic disc edema. Fluorescein angiography and ICGA confirmed the diagnosis of juxtapapillary retinal capillary hemangioma. The patient was treated with PDT with verteporfin (VP) and 3 months later her VA was 6/7.5 in the right eye, while the lesion was slightly smaller. These findings remained stable at the 1-year follow-up. The authors concluded that PDT offers promising anatomical and functional results for juxtapapillary retinal capillary hemangioma, providing VA improvement or even stabilization and restriction of enlargement of the lesion. These preliminary findings from a single case study need to be validated by well-designed studies.

Huggett and colleagues (2014) noted that patients with pancreatic cancer have a poor prognosis apart from the few suitable for surgery. Photodynamic therapy produces localized tissue necrosis but previous studies using the photosensitizer
meso-tetrahydroxyphenylchlorin (mTHPC) caused prolonged skin photosensitivity. This phase I/II study assessed a shorter acting photosensitizer, VP. A total of 15 inoperable patients with locally advanced cancers were sensitized with 0.4 mg kg\(^{-1}\) VP. After 60 to 90 mins, laser light (690 nm) was delivered via single (13 patients) or multiple (2 patients) fibers positioned percutaneously under computed tomography (CT) guidance, the light dose escalating (initially 5 J, doubling after each 3 patients) until 12 mm of necrosis was achieved consistently. In all, 12 mm lesions were seen consistently at 40 J, but with considerable variation in necrosis volume (mean volume of 3.5 cm\(^3\) at 40 J). Minor, self-limiting extra-pancreatic effects were seen in multi-fiber patients. No adverse interactions were seen in patients given chemotherapy or radiotherapy before or after PDT. After PDT, 1 patient underwent an R0 Whipple’s pancreaticoduodenectomy. The authors concluded that VP PDT-induced tumor necrosis in locally advanced pancreatic cancer is feasible and safe. It can be delivered with a much shorter drug light interval and with less photosensitivity than with older compounds. The findings of this safety/feasibility study need to be further evaluated in phase III clinical trials.

Furthermore, the National Comprehensive Cancer Network’s clinical practice guideline on “Pancreatic adenocarcinoma” (Version 1.2014) does not mention the use of verteporfin PDT as a therapeutic option.

Brodowska et al (2014) stated that VP is clinically used in PDT for neovascular macular degeneration. Recent studies indicated that VP may inhibit growth of hepatoma cells without photo-activation through inhibition of YAP-TEAD complex. These researchers examined the effects of VP without light activation on human retinoblastoma cell lines. Verteporfin but not vehicle control inhibited the growth, proliferation and viability of human retinoblastoma cell lines (Y79 and WERI) in a dose-dependent manner and was associated with down-regulation of YAP-TEAD associated downstream proto-oncogenes such as c-myc, axl, and surviving. In addition VP affected signals involved in cell migration and angiogenesis such as CTGF, cyr61, and VEGF-A but was not associated with significant effect on the mTOR/autophagy pathway. Of interest the pluripotency marker Oct4 were down-regulated by VP treatment. These findings indicated that the clinically used VP is a potent inhibitor of cell growth in retinoblastoma cells, disrupting YAP-TEAD signaling and pluripotential marker OCT4. The authors concluded that this study highlighted for the first time the role of the YAP-TEAD pathway in retinoblastoma and suggested that VP may be a useful adjuvant therapeutic tool in treating patients with retinoblastoma.

Appendix

Visudyne is covered for members meeting the following criteria:

I. The member has predominantly classic subfoveal CVN\(^1\) due to either:

    A. Age-related macular degeneration, or
    B. Pathologic myopia, or
    C. Presumed ocular histoplasmosis, or
    D. Chronic (greater than 4 months) central serous chorioretinopathy\(^2\); and
II. The member is not legally blind;³ and

III. The treatment spot size is less than or equal to 6.4 mm in diameter (according to the labeling, the maximum spot size in clinical trials was 6.4 mm).

Visudyne therapy has no proven value for members with the following conditions:

I. The member is legally blind, or

II. The member has predominantly occult subfoveal choroidal neovascularization (according to the labeling, there is insufficient evidence to indicate Visudyne for the treatment of predominantly occult subfoveal choroidal neovascularization), or

III. The member has porphyria (according to the labeling, Visudyne is contraindicated in persons with porphyria), or

IV. The member has moderate to severe hepatic impairment or biliary obstruction (according to the labeling, Visudyne therapy should be considered carefully in persons with moderate to severe hepatic impairment or biliary obstruction since there is no clinical experience with verteporfin in such persons).

Discontinuation Criteria:

Continued Visudyne is considered not medically necessary if:

I. The member has become legally blind, or

II. A loss in vision of greater than or equal to 4 lines on visual acuity exam within 1 week after treatment (according to the labeling, persons who experience severe decrease of vision of greater than or equal to 4 lines within 1 week after treatment should not be retreated, at least until their vision completely recovers to pretreatment levels), or

III. The CNV has been occluded as confirmed by fluorescein angiography (according to the labeling, the physician should reevaluate the patient every 3 months and if choroidal neovascular leakages detected on fluorescein angiography, therapy should be repeated), or

IV. The spot size to be treated has exceeded 6.4 mm.

¹ Predominantly Classic CNV: A lesion in which the classic component comprises 50 % or more of the area of the entire lesion. According to the labeling, persons with less than 50 % classic CNV were less likely to benefit from Visudyne therapy.

² Because most central serous chorioretinopathy resolves spontaneously, treatment is reserved for persons who fail to improve after 4 to 6 months (Kitzmann et al, 2009).

³ Legal blindness is defined in the U.S. as: Visual acuity of 20/200 or worse in the better eye with corrective lenses or visual field restriction to 20 degrees diameter or less (tunnel vision) in the better eye.
CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

**Photodynamic Therapy (PDT) with Light-Activated Verteporfin (Visudyne):**

67221  Destruction of localized lesion of choroid (e.g., choroidal neovascularization); photodynamic therapy (includes intravenous infusion)

+ 67225  photodynamic therapy, second eye, at single session (List separately in addition to code for primary eye treatment)

92235  Fluorescein angiography (includes multiframe imaging) with interpretation and report

HCPCS codes covered if selection criteria are met:

J3396  Injection, verteporfin, 0.1 mg [not covered in combination with intravitreal anti-angiogenic agents]

ICD-9 codes covered if selection criteria are met:

115.02  Infection by Histoplasma capsulatum, retinitis

115.12  Infection by Histoplasma duboisii, retinitis

115.92  Histoplasmosis, unspecified, retinitis

360.21  Progressive high (degenerative) myopia

362.16  Choroidal neovascularization

362.41  Central serous retinopathy [serous chorioretinopathy]

362.50 - 362.52  Macular degeneration (senile), unspecified, non-exudative and exudative

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

173.0 - 173.9  Malignant neoplasm of skin [basal cell carcinoma]

190.6  Malignant neoplasm of choroid [choroidal melanoma]

224.6  Benign neoplasm of choroid [choroidal osteoma]

228.09  Hemangioma of other sites [choroidal]

277.1  Disorders of porphyrin metabolism

362.15  Retinal telangiectasia [parafoveal]

362.29  Other nondiabetic proliferative retinopathy [retinal angiomatous proliferation]
363.20  Chorioretinitis, unspecified
363.43  Angioid streaks of choroid
363.8  Other disorders of choroid [polypoidal choroidal vasculopathy]
364.42  Rubeosis iridis
573.8  Other specified disorders of liver [hepatic impairment or biliary obstruction]
576.2  Obstruction of bile duct
704.01  Alopecia areata

**Ocular Coherence Tomography:**

CPT codes covered if selection criteria are met:

92133
92134

**ICD-9 codes covered if selection criteria are met:**

115.02  Infection by Histoplasma capsulatum, retinitis
115.12  Infection by Histoplasma duboisii, retinitis
115.92  Histoplasmosis, unspecified, retinitis
360.21  Progressive high (degenerative) myopia
362.16  Choroidal neovascularization
362.50 - 362.52  Macular degeneration (senile), unspecified, non-exudative and exudative

The above policy is based on the following references:


16. U.S. Department of Health and Human Services, Center for Medicare and Medicaid Services (CMS). Decision memo for ocular photodynamic therapy


89. Brodowska K, Moujahed A, Marmalidou A, et al. The clinically used photosensitizer Verteporfin (VP) inhibits YAP-TEAD and human