KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
Photodynamic Therapy (PDT)

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	Ocular Photodynamic Therapy (OPT) (80.2)
Local Coverage Determinations (LCD)	None
Local Coverage Article	Ocular Photodynamic Therapy (OPT) with Verteporfin (A52769) RETIRED
Kaiser Permanente Medical Policy	Due to the absence of an active NCD, LCD, or other coverage guidance related to non-ocular conditions, Kaiser Permanente has chosen to use their own Clinical Review Criteria for medical necessity determinations**. For all non-ocular conditions, use the Non-Medicare criteria below**.

For Non-Medicare Members

Service	Criteria Used
PDT with Visudyne for Pathologic Myopia PDT for Advanced Esophageal Cancer and Barrett's Esophageal Disease PDT for Age-Related Wet Macular Degeneration PDT for Actinic Keratosis	Medical necessity review no longer required
Photodynamic Laser Therapy for Tracheobronchial Cancer	Covered when the patient has obstructive tracheobronchial cancer as a palliative treatment.
PDT for Brain Tumors PDT for Rosacea	There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Photodynamic therapy (PDT) is a cancer treatment that destroys cancer cells selectively by an interaction between absorbed light and a retained photosensitizer. It is a two-part treatment using a photosensitizing drug, and red non-thermal laser light. The photosensitizing agent is a light activated chemical that selectively concentrates in malignant tissue. This agent is usually injected intravenously, and two days later it is activated by exposing the tissue to a laser light energy of a specific wavelength. For Photofrin, the FDA approved

Back to Top

photosensitizer, the wavelength of light used for activation is 630 nm. The photosensitizer will absorb the light energy and produce toxic oxygen radicals that destroy the tumor and result in its necrosis in about 24 to 48 hours. The depth of penetration and tumor necrosis after PDT is limited to approximately 5-10 mm. This shallow depth of light penetration in the tumor provides a safety factor against perforation, but on the other hand it is a limiting factor to the effectiveness of the therapy for deeper tumors.

Photodynamic therapy is an outpatient procedure, performed with the patient sedated. It can be used together with other treatments and can be repeated several times. It does not require anesthesia or pre-dilation of the esophagus.

The side effect most commonly associated with PDT is photosensitivity. This is usually manifested as sunburn or periorbital edema. Patients are advised to avoid direct light for at least 4 weeks, after the treatment.

Evidence and Source Documents

Photodynamic Therapy (PDT) for Advanced Esophageal Cancer and Barrett's Esophageal Disease
Photodynamic Therapy for Brain Tumors
Photodynamic Laser Therapy for Tracheobronchial Cancer
Photodynamic Therapy with Visudyne for Pathologic Myopia
Visudyne with Photodynamic Therapy for Age-Related Wet Macular Degeneration

Medical Technology Assessment Committee (MTAC)

Photodynamic Therapy (PDT) for Advanced Esophageal Cancer and Barrett's Esophageal Disease

BACKGROUND

Esophageal carcinoma is the seventh most common malignancy worldwide. Its incidence is increasing rapidly in the western world mainly due to adenocarcinoma of the lower third of the esophagus and gastro-esophageal junction, which usually arises from areas of Barrett's metaplasia (Lee 2001). Approximately 13,100 new cases of adenocarcinoma were diagnosed in the United States in 2002. The overall survival rate from esophageal cancer is 5-10% (Litle 2003). Most patients present with dysphagia, which usually occurs at an advanced stage of the disease. At that time, the lumen of the esophagus is often reduced by at least 50% of its diameter among most of the patients. Radical esophageal resection is still considered the therapeutic gold standard in patients with high-grade dysplasia or early cancer. For those not legible for surgical resection, treatment is palliative to reduce the esophageal obstruction and reduce the dysphagia. Different forms of palliative treatment include external beam radiation therapy, brachytherapy, pneumatic dilatation, esophageal stenting, Nd: YAG laser, and photodynamic (PDT) therapy. Some of these therapies e.g. external radiation therapy may take several weeks to relieve the dysphagia, others like esophageal bypass have a longer recovery time, and still others are associated with severe side effects as stricture, perforation, reflux, fistula formation and others. PDT is a two-part treatment using a photosensitizing drug, and red non-thermal laser light (green light has been used in some studies). The photosensitizing agent is a light- activated chemical that is selectively retained in tumor cells, and interstitial tissue of the tumor. (McCaughan, 1996). This agent is usually injected intravenously, and two days later it is activated by exposing the tissue to a laser light energy of a specific wavelength. For Photofrin, the FDA approved photosensitizer, the wavelength of light used for activation is 630 nm. The photosensitizer will absorb the light energy and produce toxic oxygen radicals that destroy the tumor and result in its necrosis in about 24 to 48 hours. The depth of penetration and tumor necrosis after PDT is limited to approximately 5-10 mm. This shallow depth of light penetration in the tumor provides a safety factor against perforation, but on the other hand it is a limiting factor to the effectiveness of the therapy for deeper tumors. Photodynamic therapy is an outpatient procedure, performed with the patient sedated. It can be used together with other treatments and can be repeated several times. It does not require anesthesia or pre-dilation of the esophagus. Sensitivity of the patient body tissues to light always occurs once the agent is injected, and the patients should avoid direct light for at least four weeks. An important adverse effect of PDT is the potential formation of esophageal strictures due to fibrosis and scarring during the healing process. Barrett's esophagus is a condition where the squamous epithelium of the lower esophagus is substituted by specialized columnar mucosa. It is estimated to affect 700,000 adults in the United States (FDA 2003) and is believed to occur as a response to esophageal reflux of gastric contents especially gastric acid. Barrett's esophagus is regarded as a premalignant condition and is the most important risk factor for the development of adenocarcinoma (Spechler 2002). Non-dysplastic metaplasia can progress to low-grade dysplasia, high-grade dysplasia, and finally to invasive cancer (Conio 2005). Several investigators reported that the relative risk of the adenocarcinoma depends on several negative prognostic factors among which are metaplasia extension, length of the involved segment, dysplasia grading, and timing of diagnosis (Pagoni 2003). Esophageal adenocarcinoma is often diagnosed at an advanced stage of the disease, and thus has a poor prognosis with 5-year survival rates below 20% (Enzinger 2003). The increased availability of endoscopy and

 Back to Top

awareness of Barrett's esophagus and its associated cancer risk have led to the increased detection of the condition in premalignant or early malignant stages. Partial or total esophagogastrectomy are considered the therapeutic gold standard in patients with high-grade dysplasia or early cancer. Surgical resection may however, be associated with high morbidity and mortality rates especially in low-volume surgical centers (Birkmeyer 2002). Moreover, some patients may be unfit for surgery. Other possible strategies have been proposed to destroy Barrett's mucosa. Among these techniques are photodynamic therapy (PDT), ablation therapy with Nd-YAG laser, Argon Plasma Coagulation (APC), and endoscopic mucosal resection (EMR). The objective of all these treatments is the complete destruction of the abnormal mucosa to reduce the cancer risk. The ideal treatment would destroy columnar metaplasia and achieve regeneration of the squamous epithelium. PDT is a two-part treatment using a photosensitizing drug and red non-thermal laser light (green light has been used in some studies). The photosensitizing agent is a light- activated chemical that selectively concentrates in malignant tissue. This agent is usually injected intravenously, and two days later it is activated by exposing the tissue to a laser light energy of a specific wavelength. The photosensitizer will absorb the light energy and produce toxic oxygen radicals that destroy the esophageal mucosa in about 24 to 48 hours. Photodynamic therapy is an outpatient procedure, performed with the patient sedated. It can be used together with other treatments and may be repeated several times. It does not require anesthesia or pre-dilation of the esophagus. Sensitivity of the patient body tissues to light always occurs once the agent is injected, and the patients should avoid direct sunlight or any bright light for at least four weeks. An important adverse effect of PDT is the potential formation of esophageal strictures due to fibrosis and scarring during the healing process. Porfimer sodium (photofrin) was approved by the FDA in December 1995, to use in PDT for the palliation of patients with completely obstructing esophageal cancer, or patients with partially obstructing esophageal cancer who cannot be satisfactorily treated with Nd:YAG laser therapy. More recently, in August 2003 it was also approved for the ablation of precancerous lesions in Barrett's esophagus patients who do not undergo esophagectomy (FDA 2003).

02/06/2000: MTAC REVIEW
Photodynamic Therapy for the Treatment of Advanced Esophageal Cancer
Evidence Conclusion: Photodynamic therapy when compared to Nd:YAG thermal ablation for palliation of dysphagia from advanced esophageal cancer provides equivalent improvement in dysphagia, improved objective tumor response as measured by esophageal lumen diameter (ARR of 12% at one month in "complete response + partial response" P <0.05), and increased mild to moderate complications including sunburn in 19% of patients treated with PDT. Perforations from laser treatments or associated dilatations occurred in 1% of patients following PDT and 7% of patients following Nd:YAG treatment. (p<0.05) Termination of laser sessions due to adverse events occurred in 3% of patients receiving PDT and 19% receiving Nd:YAG. While this is an RCT, the high dropout rate and lack of blinding limit our ability to understand the difference in clinically important outcomes between Nd:YAG thermal ablation and PDT.
Articles: Articles were sorted on the basis of study type. Case series and cohort studies were not selected. Two randomized controlled trials were selected for review. One randomized controlled trial was selected (study by Heier SK et al. *Gastroenterology.* 1995; 109:63-72) was excluded because of small study size: N=44; 20 in PDT group, 22 in Nd:YAG group). An evidence table was created for the best available evidence (Lightdale CJ, et al. *Gastrointestinal Endoscopy.* 1995; 42:507-12.) Reference**:** Lightdale CJ, Heier SK, Marcon NE, et al. Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd: YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointestinal Endoscopy.* 1995; 42:507-12. See Evidence Table.

The use of photodynamic therapy in treatment of esophageal cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*

02/11/2004: MTAC REVIEW
Photodynamic Therapy for the Treatment of Advanced Esophageal Cancer
Evidence Conclusion: Barrett's esophagus: Ackroyd's study was a small RCT with valid methodology. It is randomized, controlled, double blind, and with sufficient power to detect the difference in the treatment response between the two groups despite the small sample size. The trial however compared PDT to placebo and not to an alternative treatment. The photosensitizer used was ALA not the commonly used porphyrin-based agent, and the laser light used was the green light, not the red light described in the literature. Effect of the treatment on survival was not studied. Overall, the results of the trial show that patients treated with PDT showed significantly more macroscopic and microscopic evidence of regression and reduction in Barrett's area, compared to those who received a placebo treatment. The response to treatment observed was maintained for the follow-up duration of 24 months. The other study reviewed (Overholt 2003) was a case series with long-term follow-up. The study, like all case series, has potential threats to its internal validity, and lacks a comparison or control group. Its results show that PDT was associated with a success rate (no dysplasia with or without Barrett's) ranging from 44.4% for
 Back to Top

cases with early stage carcinoma to 92.9% for cases with low-grade hyperplasia. PDT was not compared to an alternative treatment. In addition, it was supplemented with Nd: YAG laser photoablation and continuous use of omeprazole, which may be responsible in part for the treatment success. Advanced esophageal cancer: Only case series data were available. The dysphagia scores seem to significantly improve after PDT treatment in the two-series reviewed. There are no studies comparing the PDT with other treatments, so the relative effectiveness cannot be determined. Moreover, the case series studies are subject to selection and observation bias. A RCT (Lightdale, et al, 1995) with 218 patients randomized to receive either PDT or Nd:YAG was reviewed for MTAC in February 2000. It was not blinded, and had a high dropout rate, and did not provide sufficient evidence to determine the effect of the PDT on the treatment of esophageal cancer.
Conclusion: There is some weak evidence from one small RCT that PDT using ALA photosensitizer has more than a placebo effect on the regression of Barrett's area. There is insufficient evidence on the effect of PDT in the palliative treatment of advanced, and/ or inoperable esophageal cancer.
Articles: Barrett's esophagus: The search revealed 125 articles. The majority were reviews and tutorials. There was one RCT comparing the procedure to placebo, two others small RCTs comparing different methods for performing PDT, and several case series or case reports. The RCT and the case series with a relatively large sample size, and long-term follow-up were selected for critical appraisal. Ackroyd R, Brown JN, Davis MF, et al. Photodynamic therapy for dysplastic Barrett's oesophagus: a prospective, double blind, randomized, placebo-controlled trial. *Gut* 2000; 47:612-617. See Evidence Table. Overholt BF, Panjehpour M, Halberg D, et al. Photodynamic therapy for Barrett's oesophagus with dysplasia and/or early stage carcinoma: Long-term results. *Gastrointest Endosc* 2003; 58:183-188. See Evidence Table. Advanced esophageal cancer: The search on esophageal cancer in general revealed 94 articles, and that on advanced esophageal cancer revealed 21 articles the great majority of which were review articles. There were no RCTs comparing PTD to other modes of treatment. There were three case series with more than 50 patients each. One of these series compared PDT given in addition to radiotherapy. The other two were critically appraised. Luketich JD, Christie Na, Buenavantura PO, et al. Endoscopic photodynamic therapy for obstructive esophageal cancer. *Surg Endosc* 2000; 14:653-657. See Evidence Table. Moghissi K, Dixon K, Thorpe JA, et al. The role of photodynamic therapy (PDT) in inoperable oesophageal cancer. *Eur J Cardiothorac Surg* 2000; 17:95-100. See Evidence Table.

The use of photodynamic therapy in treatment of esophageal cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

06/06/2005: MTAC REVIEW
Photodynamic Therapy in Treatment of Barrett's Disease
Evidence Conclusion: Kelty et al's RCT compared photodynamic therapy (PDT) and argon plasma coagulation (APC) for the ablation of Barrett's esophagus. The outcomes were the number of treatments required to achieve ablation, and the complete macroscopic reversal of the columnar epithelium. All patients had a biopsy proven Barrett's epithelium, but none had any evidence of dysplasia. Thirty-four patients were randomized to each treatment group and followed for up to two years (range 6-24, median 12 months). 50% of the patients in the PDT group showed complete response to PDT, and 50% had only a partial regression. The APC therapy had significantly better outcomes with a complete response rate of 97%. Hage et al's trial was a smaller study (N=40) that also compared PDT with APC, and the primary outcome was the endoscopic reduction of the Barrett's esophagus surface. All patients had no or a low-grade dysplasia. They were randomized to receive APC therapy, single illumination (PDT 100), or a fractionated illumination (PDT 20+100), and followed for up to two years. The results of the trial show that patients who received a single illumination of PDT had a significantly lower rate of Barrett's esophagus surface reduction when compared to the PDT 20+100 group or the APC group (51%, 86% and 93% respectively). The difference between the latter two groups was insignificant. The two studies used 5-aminolevulonic acid (5-ALA); a more recent sensitizing agent and not the FDA approved photofrin (porfimer sodium). Both trials had generally valid methodology. However, they had relatively small sample sizes, and the follow-up duration of 2 years might be insufficient to study the effect of the therapy on reducing the risk of cancer. The outcome in these trials was the effect of the therapy on the reversal of the columnar epithelium and not on patient survival. Moreover, all study subjects had no or low-grade dysplasia, which might limit generalization of the results. The 2004 MTAC review only found weak evidence from one small RCT that PDT using ALA photosensitizer had more than a placebo effect on the regression of Barrett's area. The therapy failed the committee evaluation criteria. In conclusion, the studies reviewed provide some evidence that PDT may achieves complete clearance of Barrett's epithelium in at least 50% of the patients with no or low-grade dysplasia. They do not provide evidence on the effect of the therapy on higher-grade dysplasia, or its impact on cancer risk, and patient survival. Larger trials with long-term follow-up may be needed to establish these effects.
Articles: The search revealed 26 articles. The majority were review articles or opinion pieces. There were two randomized controlled trials and two case series. The two RCTs were selected for critical appraisal: Kelty CJ, Ackroyd R, Brown JN, et al. Endoscopic ablation of Barrett's esophagus: a randomized controlled trial of
 Back to Top

photodynamic therapy vs. argon plasma coagulation. *Aliment Pharmacol Ther* 2004; 20:1289-1296. See Evidence Table. Hage M, Siersema PD, van Dekken H, et al. 5-Aminolevulinic acid photodynamic therapy versus argon plasma coagulation for ablation of Barrett's oesophagus: a randomized trial. *Gut* 2004; 53:785-790. See Evidence Table.

The use of photodynamic therapy in treatment of Barrett's disease does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Photodynamic Therapy for Brain Tumors

BACKGROUND

Photodynamic therapy (PDT) refers to the use of photosensitizing agents to treat tumors. The only FDA-approved photosensitizing agent is porfimer sodium (Photofrin). The PDT process involves the infusion of photosensitizing agents intravenously that are selectively retained within tumor cells. The photosensitizing agents are activated by exposure to light and cause oxidative damage to tumor tissues in which the drug has been retained.

The use of PDT to treat cerebral gliomas (brain tumors) was first investigated in 1972 using hematoporphyrin activated by white light on glioma cells in vitro and in rat tumors. Animal models have demonstrated the selective uptake of photosensitizers into cerebral gliomas. The first examination of PDT to treat human gliomas was reported by Perria in 1980. The ideal dose of photosensitizer and light for cerebral tumors has yet to be determined (Popovic). Other treatments for cerebral gliomas include surgical resection, postoperative whole-brain irradiation and chemotherapy. The effectiveness of these treatments is limited by inadequate local control of disease. It is hoped that PDT can improve local disease control and increase survival (Rosenthal).

02/13/2002: MTAC REVIEW

Photodynamic Therapy for Brain Tumors

Evidence Conclusion: There is insufficient evidence to determine the effect of PDT on health outcomes for patients with brain tumors. Much of the research appears to focus on developing the best methods for applying PDT to the treatment of brain tumors. Few clinical data are available. Popovic reported on a series of 120 patients; few methodological details were given, and the intervention may not have been consistent. They found that the median survival among 38 patients with glioblastoma multiforme was 24 months; in a historical control group subject to selection bias, median survival in patients with a similar diagnosis was 8 months.
Articles: The search yielded 69 articles, most of which were review articles, laboratory studies, dealt with technical aspects of the procedures or addressed other, similar treatments. There were no randomized controlled trials or meta-analyses. There were several small case series, many of which did not report clinical outcomes. A recent review article with some case series data was reviewed: Popovic EA, Kaye AH, Hill JS. Photodynamic therapy of brain tumors. J of Clin Laser Med & Surg 1996; 14: 251-261. See Evidence Table.

The use of photodynamic therapy in the treatment of brain tumors does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Photodynamic Laser Therapy for Tracheobronchial Cancer

BACKGROUND

Lung cancer is the leading cause of cancer deaths. It usually originates from bronchial cells, and grows in the bronchial lumen or peribronchially, thus, the term bronchial cancer is used synonymously with lung cancer. Resectional surgery is considered the treatment of choice, and the therapy with potential cure or long survival. However, the majority of patients diagnosed with lung cancer are at an advances stage, and only 15-20% are surgical candidates at the time of diagnosis (Fry, 1996). There are several methods used for palliative treatment for bronchial obstruction including Nd: YAG laser therapy, brachytherapy, electrocautery, balloon dilatation, stent insertion, and photodynamic therapy (PDT). PDT is a cancer treatment that destroys cancer cells selectively by an interaction between absorbed light and a retained photosensitizer. It is a two-part treatment using a photosensitizing drug, and red non-thermal laser light. The photosensitizing agent is a light activated chemical that selectively concentrates in malignant tissue. This agent is usually injected intravenously, and two days later it is activated by exposing the tissue to a laser light energy of a specific wavelength. For Photofrin, the FDA approved photosensitizer, the wavelength of light used for activation is 630 nm. The photosensitizer will absorb the light energy and produce toxic oxygen radicals that destroy the tumor and result in its necrosis in about 24 to 48 hours. The depth of penetration and tumor necrosis after PDT is limited to approximately 5-10 mm. This shallow depth of light penetration in the tumor provides a safety factor against perforation, but on the other hand it is a limiting factor to the effectiveness of the therapy for deeper tumors. Of the potential advantages of the procedure is that may be technically easier and potentially safer than other procedures, and that it is repeatable and appears to be compatible with other treatments. The procedure does not require general anesthesia, and

 Back to Top

only requires a prolonged bronchoscopy. The side effect most commonly associated with PDT is photosensitivity. This is usually manifested as sunburn or periorbital oedema. Patients are advised to avoid direct light for at least 4 weeks, after the treatment. The risk of serious bronchial hemorrhage, which may be fatal is another important complication associated with the PDT therapy used for treating tumors invading bronchial walls, and big vessels. Other complications include cough, dyspnea, bronchitis, and pneumonia. PDT is approved by the FDA for the palliation of airway obstruction caused by malignant tumors in patients with advanced obstructive endobronchial disease, and as an alternative to surgery in selected patient with early-stage lung cancer. PDT use in the treatment of tracheobronchial cancer was reviewed by MTAC in February 2002 and failed the committee evaluation criteria.

02/11/2004: MTAC REVIEW
Photodynamic Laser Therapy for Tracheobronchial Cancer
Evidence Conclusion: There is insufficient new evidence to determine the effectiveness of photodynamic therapy in the treatment of tracheobronchial cancer.
Articles: The search yielded 25 articles. The majority were reviews and tutorials. There was a small longitudinal study (32 patients) on all bronchoscopic treatments of occult lung cancer, another retrospective study on all palliative measures for malignant airways including 8 patients receiving PDT treatment or stents, and a small trial with 16 patients comparing 2 photosensitizers used in PDT for the treatment of malignant bronchial stenosis. None of the studies was critically appraised.

The use of photodynamic therapy in the treatment of bronchial cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

02/13/2002: MTAC REVIEW
Photodynamic Laser Therapy for Tracheobronchial Cancer
Evidence Conclusion: Early-stage lung cancer: Only case series data were available. A large proportion of the patients studied appear to have complete remission following PDT (approximately 80%); there are no studies comparing remission rates with other treatments, so the relative effectiveness cannot be determined. The case series reports are subject to selection and observation bias. The long-term effectiveness is difficult to determine because patients were permitted to have other treatments after PDT. Advanced lung cancer: The highest grade of evidence was an RCT. Diaz-Jimenez compared Nd-YAG to PDT in 31 patients. They found that patients who received PDT had a median of 12 days longer before treatment failure for any reason (50 vs. 38 days) and survived for a mean of 170 days longer (265 vs. 95 days) than the group receiving Nd-YAG. Because this is a small RCT, selection bias is likely. A greater proportion of patients assigned to the Nd-YAG group had advanced lung cancer that could at least partially explain the shorter time to treatment failure and shorter survival time. The existing evidence is insufficient to determine the effect of PDT on advanced lung cancer.
Articles: The search yielded 57 articles, many of which were review articles, opinion piece, dealt with technical aspects of the procedures or addressed other, similar treatments. Early-stage lung cancer: There were no randomized controlled trials (RCTs) or meta-analyses. The highest grade of evidence available was case series. The two largest case series were critically appraised: Furuse K, Fukoka M, Kato H, Horai T, Kubota K, Kodamo N et al. A prospective Phase II study on photodynamic therapy with photofrin II for centrally located early-stage lung cancer. J Clin Oncol 1993; 11: 1 852-57. See Evidence Table. Kato H, Okunaka T, Shimatani H. Photodynamic therapy for early stage bronchogenic carcinoma. J Clin Laser Med & Surg 1995; 14: 235-238. See Evidence Table Advanced lung cancer: There were two RCTs. The remaining empirical articles were case series. One RCT had included only 11 patients and did not compare outcomes in the two randomized groups in analysis. One RCT was critically appraised: Diaz-Jimenez JP, Martinez-Ballerin JE, Llunell A, Farrero E, Rodriguez A, Castro MJ. Efficacy and safety of photodynamic therapy versus Nd-YAG laser resection in NSCLC with airway obstruction. Eur Respir J 1999; 14: 800-805. See Evidence Table.

The use of photodynamic therapy in the treatment of bronchial cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

Photodynamic Therapy with Visudyne for Pathologic Myopia
BACKGROUND
Choroidal neovascularization (CNV) in patients with pathologic myopia is a condition in which there is an abnormal growth of blood vessels under the retina due to an elongation of the back of the eye associated with severe myopia. This condition can result in a progressive and serious loss of vision. There have not been effective treatments for this disease. Photodynamic therapy using Visudyne (verteporfin for injection) involves intravenous injection of verteporfin, a light activated or “photosensitive” drug. After infusion, verteporfin is activated by illumination with laser light shone into the patient’s eye from a slit lamp of a microscope. The
 Back to Top

wavelength used corresponds to the wavelength at which peak absorption occurs but is not so strong as to cause thermal damage. The light is directed to the area of neovascularization and damage to the retina is minimized. In April 2000, the FDA approved Visudyne for the treatment of the wet form of age-related macular degeneration. In August 2001, photodynamic therapy with Visudyne was additionally approved for the treatment of subfoveal choroidal neovascularization (CNV) due to pathologic myopia. Visudyne for age-related macular degeneration was found to meet MTAC review criteria in June 2000.

02/13/2002: MTAC REVIEW
Photodynamic Therapy with Visudyne for Pathologic Myopia
Evidence Conclusion: One well done randomized controlled trial (VIP study group) was reviewed. This study provides evidence that photodynamic therapy with verteporfin is effective at decreasing vision loss 12 months after treatment. 28% of patients in the verteporfin group compared to 56% in the placebo group had at least an eight-letter loss at 12 months, the study's primary outcome ($p<0.01$, NNT=4). This finding is likely to be clinically as well as statistically significant. The treatment appears to be safe. Ideally, the findings would be replicated in other studies and there would be longer-term follow-up. 24-month follow-up data will be available from the VIP study.
Articles: The search yielded 26 articles, many of which were review articles, opinion pieces, dealt with technical aspects of the procedures or addressed other, similar treatments. There was 1 randomized controlled trial (n=120) with and 1 case series (n=13). The case series included patients with choroidal neovascularization due to several conditions, e.g. pathologic myopia, ocular histoplasmosis syndrome, angiod streaks and idiopathic causes. *The RCT was critically appraised:* Verteporfin in photodynamic therapy (VIP) study group. Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin: 1-year results of a randomized clinical trial: VIP report no. 1. Ophthalmol 2001; 108: 841-52. See Evidence Table

The use of photodynamic therapy in the treatment of pathologic myopia passed the *Kaiser Permanente Medical Technology Assessment Criteria*.

Visudyne with Photodynamic Therapy for Age-Related Wet Macular Degeneration
BACKGROUND
Age-related macular degeneration (AMD) is the most common and most severe cause of vision loss in the U.S. and many developed countries. With increasing life expectancy, the prevalence of AMD (currently about 25%) in people aged 65 years and older will increase significantly, with an enormous social and financial cost. In spite of the significance of this problem, AMD's pathogenesis remains unclear and is essentially untreatable.
AMD is characterized by two forms: the "dry" and more severe "wet" form. The latter accounts for 15% of all AMD cases, but is responsible for 90% of the severe vision loss associated with this condition. Visual acuity loss usually results from choroidal neovascularization (CNV), the ingrowth of new vessels from the choriocapillaris. These new vessels are accompanied by fibrous tissue that can destroy central visual function over months to years. Standard treatment of CNV has been with a thermal laser. The drawback of this laser is that in addition to destroying the CNV it destroys the surrounding retinal tissue with immediate vision loss. Photodynamic Therapy (PDT) utilizing verteporfin (Visudyne; CIBA Vision Corp, Duluth, GA) is a new technology which completed Phase III clinical trials last year and was recently recommended for FDA approval by the Ophthalmic Drugs Subcommittee of the FDA. Verteporfin therapy involves an intravenous administration of verteporfin, a light activated drug. Laser light at the specific wavelength absorbed by Visudyne is then directed to the area of neovascularization and causes preferential closure of these vessels while sparing the overlying retina.
The articles described below evaluate PDT as a treatment for choroidal neovascularization (CNV), the type of late AMD that is the most frequent cause of visual loss.

06/14/2000: MTAC REVIEW
Visudyne with Photodynamic Therapy for Age-Related Wet Macular Degeneration
Evidence Conclusion: The prospect of verteporfin (Visudyne) as a new therapy for subfoveal wet AMD is very promising, in light of the fact AMD is an important public health problem with no currently available treatment that spares destruction of the fovea itself. However, the efficacy and safety of verteporfin cannot be fully determined from the limited evidence provided by these two studies, which were conducted by the same investigators. The findings from the case series are threatened by small sample size and possible observation and selection biases. The findings from both studies are threatened by short length of follow-up, concerns about the generalizability of the findings, and the fact that the investigators would benefit financially from FDA approval of the drug. Further studies, preferably blinded, randomized controlled trials, such as the Verteporfin in Photodynamic Therapy (VIP) Trial (to be completed this Fall), will provide further evidence regarding whether photodynamic therapy with verteporfin can safely and effectively reduce the risk of vision loss in patients with age-related macular degeneration.
 Back to Top

Articles: Miller JW, Schmidt-Erfurth U. Sickenberg M; Piurnaras CJ et al. Photodynamic Therapy with verteporfin for Choroidal Neovascularization caused by age-related Macular Degeneration. *Archives of Ophthalmology 1999; 117:1167-1173.* See Evidence Table. TAP Study Group. Photodynamic Therapy of subfoveal choroidal neovascularization in age-related Macular Degeneration. *Archives of Ophthalmology 1999; 117:1329-1345.* See Evidence Table.

The use of Visudyne with Photodynamic Therapy in the treatment of Age-related Macular Degeneration does meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Applicable Codes

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

Verteporfin

CPT® or HCPC Codes	Description
J3396	Injection, verteporfin, 0.1 mg

Photodynamic Therapy

CPT® or HCPC Codes	Description
96567	Photodynamic therapy by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitive drug(s), per day
96570	Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drug(s); first 30 minutes (List separately in addition to code for endoscopy or bronchoscopy procedures of lung and gastrointestinal tract)
96571	Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drug(s); each additional 15 minutes (List separately in addition to code for endoscopy or bronchoscopy procedures of lung and gastrointestinal tract)
96573	Photodynamic therapy by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day
96574	Debridement of premalignant hyperkeratotic lesion(s) (ie, targeted curettage, abrasion) followed with photodynamic therapy by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.

Date Created	Date Reviewed	Date Last Revised
12/1998	04/06/2010 MDCRPC, 02/10/2011 MDCRPC, 12/06/2011 MDCRPC, 10/02/2012 MDCRPC, 8/06/2013 MPC, 11/05/2013 MPC, 09/02/2014MPC, 07/07/2015MPC, 05/03/2016MPC, 03/07/2017MPC, 01/09/2018MPC, 12/04/2018MPC, 12/03/2019MPC, 12/01/2020MPC,12/07/2021MPC,12/06/2022MPC	09/03/2019

MDCRPC Medical Director Clinical Review and Policy Committee
MPC Medical Policy Committee

Revision History	Description
06/02/2015	Added Actinic Keratosis

 Back to Top

10/11/2016	Added Medicare coverage article A52769
09/03/2019	MPC approved to add PDT for Rosacea to the non-covered list

Back to Top