Medical Policy

Description

Photodynamic therapy (PDT), also called phototherapy, photoradiation therapy, photosensitizing therapy, or photochemotherapy, is an ablative treatment consisting of administration of a photosensitizing agent and subsequent exposure of tumor cells to a light source of a specific wavelength to induce cellular damage. After administration of the photosensitizing agent, the target tissue is exposed to light using a variety of laser techniques. For example, a laser fiber may be placed through the channel of the endoscope, or a specialized modified diffuser may be placed via fluoroscopic guidance. Tumor selectivity in treatment occurs through a combination of selective retention of photosensitizing agent and selective delivery of light.

Photodynamic therapy (PDT) has been investigated for use in a wide variety of tumors, including esophageal cancer, cholangiocarcinoma, prostate, bladder, lung, breast, brain (where it is administered intraoperatively), skin, and head and neck cancers. Barrett's esophagus has also been treated with PDT.

Barrett's Esophagus

The esophagus is normally lined by squamous epithelium. Barrett's esophagus is a condition in which the normal squamous epithelium is replaced by specialized columnar-type epithelium known as intestinal metaplasia in response to irritation and injury caused by gastroesophageal reflux disease (GERD). Barrett's esophagus occurs in the distal esophagus, may be of any length, focal or circumferential, and can be visualized by the endoscopist as being a different color than the background squamous mucosa. Confirmation of Barrett's esophagus requires biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia.
Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and patients with Barrett’s esophagus are at a 40-fold increased risk for developing this disease compared to the general population. Esophageal adenocarcinoma is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, which results in the phenotypic expression of histologic features of low-grade dysplasia to high-grade dysplasia to carcinoma. Most patients with nondysplastic Barrett’s esophagus do not progress past nondysplasia. Nondysplastic Barrett’s esophagus progresses to high-grade dysplasia at a rate of 0.9% per patient, per year. (1) Progression of low-grade to high-grade dysplasia has been reported as 6–28%. (2) Once high-grade dysplasia is present, the risk of developing adenocarcinoma is 2–10% per patient, per year, and approximately 40% of patients diagnosed with high-grade dysplasia by biopsy are found to have associated carcinoma in the resection specimen.

Several different photosensitizing agents have been used: porfimer sodium (Photofrin®), administered intravenously 48 hours before light exposure, and 5-aminolevulinic acid (5-ALA), administered orally 4 to 6 hours before the procedure. ALA is metabolized to protoporphyrin IX, which is preferentially taken up by the mucosa. Clearance of porfimer occurs in a variety of normal tissues over 40–72 hours, but tumors retain porfimer for a longer period. Treatment of Barrett's esophagus may be enhanced by the use of balloons containing a cylindrical diffusing fiber. The balloon is designed to compress the mucosal folds of the esophagus, thus increasing the likelihood that the entire Barrett's mucosa is exposed to light. All patients who receive porfimer become photosensitive and must avoid exposure of skin and eyes to direct sunlight or bright indoor light for 30 days.

The indications of the U.S. Food and Drug Administration (FDA) label for porfimer sodium as of January 23, 2010 are as follows:

- Palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy
- Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial non-small cell lung cancer (NSCLC)
- Treatment of microinvasive endobronchial NSCLC in patients for whom surgery and radiotherapy are not indicated
- Treatment of high-grade dysplasia in Barrett’s esophagus

As of February 22, 2012, oral 5-ALA has not yet received FDA approval for any indication. Topical 5-ALA as used for treatment of actinic keratoses is addressed in a separate policy.

This policy addresses only the non-dermatologic oncology applications of PDT and does not address its use in dermatologic applications such as actinic keratoses and superficial basal cell cancer or age-related macular degeneration. In addition, PDT should not be confused with extracorporeal photopheresis, which involves withdrawing blood from the patient, irradiating it with ultraviolet light, and then returning the blood to the patient. Extracorporeal photopheresis is addressed in a separate policy.
Policy

One or more courses of photodynamic therapy may be considered **medically necessary** for the following oncologic applications:

- palliative treatment of obstructing esophageal cancer
- palliative treatment of obstructing endobronchial lesions
- treatment of early-stage non-small cell lung cancer in patients who are ineligible for surgery and radiation therapy
- treatment of high-grade dysplasia in Barrett’s esophagus

Other oncologic applications of photodynamic therapy are **investigational** including, but not limited to, other malignancies and Barrett’s esophagus without associated high-grade dysplasia.

Policy Guidelines

The following CPT codes may be used to describe endoscopic photodynamic therapy:

96570: Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drugs; first 30 minutes. (List separately in addition to code for endoscopy or bronchoscopy.)

96571: as above, but each additional 15 minutes.

As noted in the CPT code description, the procedure will be coded in conjunction with an esophagoscopy or bronchoscopy, which may be coded as follows:

43228; Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), not amenable to removal by hot biopsy forceps, bipolar cautery, or snare technique.

31641: Bronchoscopy; with destruction of tumor or relief of stenosis by any method other than excision.

Claims may also be identified by the use of HCPCS code J9600, describing the drug porfimer sodium.
Rationale

Evidence for photodynamic therapy (PDT) for oncologic applications identified through literature searches conducted for development of this policy and for regular updates through January 2012 is summarized below. Much of the recent literature from outside the U.S. reports experience with photosensitizing agents that have not been cleared for use in the U.S.

Fayter and others produced a systematic review of PDT in the treatment of pre-cancerous skin conditions, Barrett’s esophagus, and cancers of the biliary tract, brain, head and neck, lung, esophagus and skin published in 2010 for the Health Technology Assessment (HTA) program of the United Kingdom’s National Institute for Health Research (NIHR). (1) The review included literature published through June 2009 and included 88 trials. The authors note a number of limitations in the body of evidence including that there were few well-conducted, adequately powered randomized controlled trials (RCTs), and methodologic limitations and gaps in the evidence base make drawing firm conclusions difficult. The authors’ conclusions are summarized as follows: for Barrett’s esophagus, PDT in addition to omeprazole appeared to be more effective than omeprazole alone at long-term ablation of high-grade dysplasia and slowing/preventing progression to cancer. No firm conclusions could be drawn for esophageal cancer. Further research into the role of PDT in lung cancer is needed. For cholangiocarcinoma, PDT may improve survival when compared with stenting alone. There was limited evidence on PDT for brain cancer and cancers of the head and neck. A wide variety of photosensitizers were used and, overall, no serious adverse effects were linked to PDT.

Obstructing Esophageal Tumors

When used for palliative treatment, relevant outcomes include short-term resolution of symptoms, such as dysphagia or improvement in swallowing. Long-term outcomes, such as disease-free survival (DFS), may not be relevant in the palliative setting. The product insert for porfimer sodium (Photofrin) describes a multicenter, single-arm study of the use of PDT in 17 patients with obstructing esophageal cancer. (2) Patients received from 1 to 3 monthly treatments of PDT. Of the 17 treated patients, 11 (65%) received clinically important benefit from PDT, defined as complete tumor response, normal swallowing, or improvement in dysphagia. Endoscopic debridement of the esophagus may be required after the PDT. At that time, the residual tumor can also be retreated.

McCann and colleagues, in 2011, reported on a systematic review of traditional non-endoscopic and endoscopic treatments for early esophageal cancer, including 26 PDT studies. (3) The reviewers noted the lack of evidence from large, randomized trials and found the quality of evidence available overall was generally low. While the evidence did demonstrate that endoscopic techniques reduced morbidity and mortality compared to esophagectomy, outcomes from endoscopic treatments were similar, and no single endoscopic technique could be identified as a recommended treatment approach. The review focused on tumor response and recurrence and disease-specific and overall survival and did not examine quality-of-life outcomes.

In 2011, Rupinski and colleagues reported on a randomized study of 93 patients with inoperable cancer of the esophagus or esophageal junction to compare argon plasma coagulation (APC) alone to PDT with APC or high-dose rate brachytherapy (HDR) with APC. (4) Both combination therapies were more effective than APC alone in median time to recurrence of dysphagia (65,
59, and 35 days for HDR with APC, PDT with APC, and APC alone, respectively). Overall survival was not significantly different between groups. However, complications occurred more often in the PDT with APC and APC alone groups than the HDR with APC group.

In a retrospective study from China, 90 patients with esophageal cancer underwent photofrin PDT (n=27), PDT combined with chemotherapy (n=33), or chemotherapy alone (n=30) from 2004 to 2007. (5) Rates of symptomatic palliation (85.2%, 93.9%, and 60.0%, respectively) were not significantly different. The differences in median survival rate at 2 years were statistically significant (29.6%, 54.5%, and 16.7%, respectively) (p=0.046).

**Obstructing Endobronchial Tumors**

Similar to obstructing esophageal tumors, short-term outcomes are also relevant for PDT as a treatment of endobronchial tumors. Laser ablation is commonly used to treat endobronchial lesions, and, thus, the relative efficacy of PDT and laser ablation is also relevant. The product insert cites 2 studies totaling 211 patients with obstructing endobronchial tumors who were randomized to receive PDT or Nd:YAG laser therapy. (2) The response rates (i.e., the sum or complete response (CR) and partial response (PR) rates) for the 2 treatments were similar at 1 week (59% PDT, 58% laser therapy) with a slight increase in response rates for PDT at 6 weeks (60% PDT, 41% laser therapy). Clinical improvement, as evidenced by improvements in dyspnea, cough, and hemoptysis, were similar in the 2 groups at 1 week (25–29%); however, at 1 month or later, 40% of patients treated with PDT reported clinical improvement compared to 27% treated with laser therapy. Due to missing data in the studies, statistical comparisons were not performed.

In another small, published, randomized study comparing PDT and Nd:YAG laser therapy in patients with airway obstruction, Diaz-Jimenez and colleagues reported that the 2 techniques had similar effectiveness over a 24-month period. (6) The authors noted a better immediate response rate associated with laser therapy and suggested that laser therapy may be particularly appropriate for those requiring rapid relief of symptoms. Results of a larger case series of 100 patients with unresectable lesions also report that PDT is associated with successful palliation. (7)

Similar to treatment of obstructing esophageal lesions, repeat endoscopy may be required for tumor debridement, at which time repeat PDT may be performed to treat residual tumor.

**Early-Stage Lung Cancer**

It is anticipated that only a minimal number of patients with non-obstructing lung cancer will be appropriate candidates for PDT. Of the 178,000 new cases of lung cancer annually, only 15% are detected with early-stage lung cancer. Of these, approximately 60% are treated with surgery, and another 25% are treated with radiation therapy. Candidates for PDT are limited to those patients who cannot tolerate surgery or radiation therapy, most commonly due to underlying emphysema, other respiratory disease, or prior radiation therapy. In this primary treatment setting, long-term outcomes such as response rates and DFS are important. The product insert for porfimer sodium (Photofrin) also refers to 3 case series totaling 62 patients with microinvasive lung cancer. (2) The complete tumor response rate, biopsy-proved, at least 3 months after treatment was 50%, median time to tumor recurrence was more than 2.7 years, median survival was 2.9 years, and disease-specific survival was 4.1 years. (1) In another case series of 95 early-stage lung cancers, the CR rate was 83.2%. (8)
The labeled indication suggests that PDT for early-stage lung cancer should be limited to those who are not candidates for either surgery or radiation therapy. However, Cortese and colleagues reported on a case series of 21 patients with early-stage squamous cell cancer of the lung who were offered PDT as an alternative to surgery. (9) Patients were followed up closely with repeat endoscopy and surgical resection if cancer persisted after no more than 2 courses of PDT. A total of 9 patients (43%) had a CR at a mean follow-up of 68 months (range 24–116 months) and thus were spared surgical treatment.

It should be noted that Nd:YAG laser therapy, electrocautery, and endobronchial brachytherapy are also considered treatment options for early-stage lung cancer. However, unlike obstructing endobronchial lesions, no controlled studies have compared the safety and efficacy of these techniques.

**Barrett’s Esophagus with High-Grade Dysplasia**

The FDA-labeled indication for treatment of high-grade dysplasia is based on a multicenter, partially blinded, study that randomized 199 patients to receive porfimer sodium (Photofrin) plus omeprazole or omeprazole alone. (2) Initially, 485 patients with high-grade dysplasia were screened for the trial; 49% were subsequently excluded because high-grade dysplasia was not confirmed on further evaluation. As noted in the package insert, the high patient exclusion rate re-enforces the recommendation by the American College of Gastroenterology that the diagnosis of dysplasia in Barrett’s esophagus be confirmed by an expert gastrointestinal pathologist. (10) Patients randomized to the treatment group received up to 3 courses of PDT separated by 90 days. The primary efficacy endpoint was the CR rate at any one of the endoscopic assessment time points. Complete response was defined, at a minimum, as ablation of all areas of high-grade dysplasia but with some areas of low-grade dysplasia. A total of 76.8% of patients in the treatment group achieved a CR compared to 38.6% in the control group. At the end of 24 months of follow-up, patients in the treatment group had an 83% chance of being cancer-free compared to a 54% chance in the control group.

Five-year follow-up of subjects in the RCT of PDT with porfimer sodium (Photofrin) in Barrett’s high-grade dysplasia conducted for the FDA approval process was reported by Overholt et al. in 2007. (11) Patients with Barrett’s esophagus and high-grade dysplasia (HGD) were randomized to PDT plus omeprazole or omeprazole only. Sixty-one patients were enrolled in the long-term phase of the trial, 48 PDT plus omeprazole group and 13 in the omeprazole only group. Endoscopy with mucosal assessment and biopsies was performed at the first visit and every 3 months until 4 consecutive quarterly biopsy results were negative for HGD and then biannually until 60 months after randomization or until treatment failure. At 5 years, PDT plus omeprazole was significantly more effective than omeprazole alone in eliminating HGD (77% [106/138] vs. 39% [27/70], respectively; p<0.0001). Patients in the PDT group were about half as likely to progress to cancer as those in the omeprazole alone group (21/138 [15%] vs. 20/70 [29%], respectively; p=0.027), with a significantly longer time to progression to cancer favoring PDT. The small number of subjects available for long-term follow-up is a limitation of this study.

Badreddine and colleagues performed a retrospective analysis of a cohort of Barrett’s esophagus patients seen at a specialized Barrett’s esophagus clinic in the U.S. to identify risk factors for recurrence of dysplasia after ablative treatment including PDT. (12) Three-hundred sixty-three patients underwent PDT with or without endoscopic mucosal resection. Forty patients were lost to follow-up, 46 had residual dysplasia, and 12 had no dysplasia at baseline. Indications for ablation were low-grade dysplasia in 53 patients, high-grade dysplasia in 152
patients, and intramucosal cancer in 56 patients. Median follow-up was 36 months. Recurrence occurred in 45 patients, and median time to recurrence was 17 months. Significant predictors of recurrence on the multivariate model were older age, presence of residual nondysplastic Barrett’s, and a history of smoking. The authors note that the possibility of missing prevalent dysplasia despite aggressive surveillance is a limitation in the study.

Pech and colleagues, in a study from Germany, report long-term (i.e., 5-year) outcomes of endoscopic treatment of high-grade intraepithelial neoplasia and mucosal adenocarcinoma in patients with Barrett’s esophagus. (13) Patients were excluded if staging examinations did not confirm the suspected diagnosis of Barrett’s carcinoma or high-grade intraepithelial neoplasia or if they showed more advanced tumor stage (greater than T1), lymph-node involvement, or metastasis. Patients with localized neoplasia were offered endoscopic resection; those with lesions that were not clearly localized, those with superficial subtle multifocal neoplasia, and patients with no neoplasia found in esophageal biopsies were treated with 5-aminolevulinic acid (5-ALA) PDT. (Note: Oral ALA does not have FDA approval.) Fifty-five patients received only PDT, and 13 had endoscopic resection and PDT. A complete response was achieved in 98.5% of the patients, and CR was achieved in 17% during median follow-up of 37 months.

Prasad et al. report similar outcomes between 2 groups (nonrandomized) of patients who received either PDT (n=129) or surgery (n=70) for high-grade dysplasia in Barrett’s esophagus. (14)

Cholangiocarcinoma

There has been ongoing research interest in PDT as an adjunct to endoscopic management of cholangiocarcinoma, primarily as a palliative strategy. In addition, percutaneous biliary drainage is a frequent management strategy for cholangiocarcinoma, and PDT can thus be administered percutaneously. Several case series have reported positive results, as measured by quality-of-life studies. (15-17) Two small randomized studies have reported both palliative effects and an increase in median survival. For example, Ortner and colleagues conducted a trial of 39 patients with nonresectable cholangiocarcinoma who were randomized to receive either endoscopic stenting alone or in conjunction with PDT. (18) The median survival of the 20 patients in the PDT group was 493 days compared to 98 days in the 19 patients who underwent stenting alone. The trial was terminated prematurely due to the favorable results. Zoepf and colleagues randomized 32 patients with cholangiocarcinoma to stenting with and without PDT. (19) The median survival for the PDT group was 21 months compared to 7 months in the control group.

Gao and colleagues performed a systematic review of the literature on PDT for unresectable cholangiocarcinoma. (20) The authors reviewed 2 RCTs, 2 comparative trials with concurrent controls, 1 comparative trial with historical controls, and 15 case series. The 2 randomized trials were rated of moderate quality, and the other available studies were of low to moderate quality. The mean number of subjects was 27 (range: 1–184 subjects). Porfimer sodium (Photofrin) was the photosensitizer used in all but 2 of the included studies. The RCTs were discussed above.

In a retrospective study by Kahaleh et al., 19 patients were treated with endoscopic retrograde cholangiopancreatography (ERCP) with PDT and stents, and 29 patients treated with ERCP and stents alone at a U.S. center. (21) Most of the patients had Bismuth III and IV lesions; however, some had Bismuth I and II lesions. Some patients in each group received chemoradiation therapy. Mortality in the PDT/stent group at 3, 6, and 12 months was 0%, 16%, and 56% respectively, and 28%, 52%, and 82% in the stent-alone group. The difference was
statistically significant at 3 and 6 months. The authors note “it remains to be proved whether this effect is attributable to PDT or the number of ERCP sessions and a randomized multicenter study is required to confirm these data.”

In a comparative review with concurrent controls, Witzigmann et al. analyzed records of 184 patients treated over a 10-year period in Germany for hilar cholangiocarcinoma. (22) Sixty patients underwent resection (8 after neoadjuvant PDT), 68 had PDT and stenting, and 56 had stenting alone. Median survival was 12 months in the PDT and stenting patients versus 6.4 months in the stent-alone group (p<0.01). Patients who received PDT and stenting had lower serum bilirubin levels (p<0.05) and higher Karnofsky performance status (p<0.01).

In a 2008 editorial, Baron reviews the pros and cons of PDT for palliation of cholangiocarcinoma and the questions remaining about its role given the available options of chemoradiation, brachytherapy, and plastic and metal stents. (23) On the negative side, he notes that PDT is not available at all centers and requires expertise in endoscopy and PDT, and the fibers available in the U.S. are suboptimal for ERCP use; because of their stiffness, treatment is limited to the main hepatic ducts. The procedure is time-consuming. Post-treatment photosensitivity lasts for 4-6 weeks and may limit quality of life. In favor of PDT, it is reasonably well-tolerated, seems to be effective, and can be repeated without a ceiling dosage effect. It is the only treatment to date in which data suggest improved survival over plastic stent placement alone for advanced cholangiocarcinoma. Baron concludes that the answer to whether PDT should be used for palliation of cholangiocarcinoma is a “qualified yes” but that “further comparative trials are needed to determine the optimal regimen of palliation of obstructive jaundice in these patients.”

Gynecological Malignancies

A Phase II European trial with 20 patients of imiquimod and PDT for vulval intraepithelial neoplasia reported by Winters et al. demonstrated an overall response rate of 55% by intention-to-treat analysis. (24) Symptom response at 52 weeks was 65% asymptomatic versus 5% at baseline. The potential benefit of the treatment is its ability to treat multifocal disease. Results from this small trial need to be replicated in additional larger studies before changes are made to the policy statement.

Istomin and colleagues reported on 112 patients with morphologically proven cervical intraepithelial neoplasia grades II and III with at least 1-year follow-up after treatment with Photolon PDT. (25) Complete regression of neoplastic lesions was seen in 104 of the treated women. Of 88 patients infected with human papillomavirus (HPV) of highly oncogenic strains, 47 had complete eradication of the HPV infection 3 months after treatment.

Head and Neck Cancers

In a 2008 review, Biel reported his own experience with 276 patients treated with Photofrin PDT for early oral and laryngeal cancers over a period of nearly 16 years and summarized previously published small case series. (26) Of 115 patients in the author’s series with recurrent or primary carcinoma-in-situ (CIS), T1N0 and T2N0, there were 10 recurrences (5-year cure rate 100%) at mean follow-up of 91 months. Five-year cure rate for 113 patients with recurrent or primary CIS and T1N0 squamous cell carcinomas of the oral cavity was 100%, with 6 recurrences within 8 months of initial treatment salvaged with either repeat PDT or surgical resection. Two patients with T1 tongue tumors developed positive regional lymph nodes within 3 months of PDT, had conventional neck dissection, and had been free of disease for at least 5 years. In the 48 patients treated for superficial T2N0 and T3N0 squamous cell carcinomas of the oral cavity,
there were 5 recurrences, all salvaged with repeat PDT or surgical resection. Three-year cure rate was 100% (mean follow-up 56 months). Again, these data need to be replicated in larger, multicenter studies that include a comparison group.

In 2009, Wildeman and colleagues reviewed all of the available literature to determine the efficacy of PDT therapy for patients with recurrent nasopharyngeal carcinoma. (27) Of 5 studies, one was a series of 135 patients with reported CR in 76 cases and marked response in 47 cases after hematoporphyrin-derivative-mediated PDT; however, it was not clear if the patients had recurrent nasopharyngeal carcinoma or that PDT was primary treatment. The other 4 studies had 12 or fewer subjects.

A U.S. cancer center enrolled 30 patients in a trial to determine efficacy and safety of Photofrin PDT for primary or recurrent moderate to severe oral or laryngeal dysplasia, CIS, or T1NO carcinoma. (28) Twenty patients had a CR, one had a PR, and one had no response. Three patients with oral dysplasia with an initial CR experienced recurrence. All patients with no response or PR or recurrence after initial response underwent salvage treatment. No patient required airway intervention, and all complications resolved without permanent sequelae.

A retrospective review of Photofrin PDT of 30 patients with early-stage (TisT2N0M0) squamous cell carcinoma of oral cavity and oropharynx found that 24 patients demonstrated CR (follow-up 3-144 months). (29) Six patients who had PR with recurrence were subsequently treated with conventional therapy. Eleven of 24 patients were cancer disease-free at 2 years after PDT.

Mesothelioma

PDT for treatment of mesothelioma has also been discussed in recent reviews; however, studies identified in the review consisted of Phase one studies and animal studies. A study from Austria with 14 subjects involved intraoperative PDT under hyperbaric oxygenation. (30) No other studies using FDA-approved photosensitizers were identified.

Brain Cancer

Aziz and others describe using intraoperative Photofrin PDT in 14 metastatic brain cancers (7 originating in the lung and 7 from a variety of sources). (31) Of the patients with lung cancer metastases, 1 died of unrelated cause, and 6 were free of brain disease until their deaths. Two of the remaining patients (1 with metastatic bowel cancer and 1 with unknown primary) died of local brain recurrence. A review of the literature on PDT applications in brain tumors relied largely on unpublished data and was not reviewed for this policy. (32)

Ongoing Clinical Trials

A search of online site ClinicalTrials.gov in February 2012 identified 2 Phase III trials. A Phase II/III trial will evaluate whether the presence or absence of biomarkers in Barrett’s esophagus influences the outcomes of PDT or radiofrequency ablation treatment. (NCT00587600) A Phase III, randomized controlled study of PDT for inoperable cholangiocarcinoma palliation is scheduled for completion in December 2012. (NCT00907413).

Summary

Photodynamic therapy (PDT) is an ablative treatment consisting of administration of a photosensitizing agent and subsequent exposure of tumor cells to a light source of a specific
wavelength to induce cellular damage. After administration of the photosensitizing agent, the target tissue is exposed to light using a variety of laser techniques.

In general, the evidence to assess the role of PDT in the treatment of malignancies and Barrett’s esophagus is of limited quality but suggests that PDT may be useful for palliative treatment of obstructing esophageal cancer and endobronchial lesions. PDT for treatment of early-stage non-small cell lung cancer has shown benefit and may be used to improve quality of life for patients who are ineligible for surgery and radiation therapy. PDT may also be considered for treatment of high-grade dysplasia in Barrett’s esophagus, as controlled and uncontrolled studies have demonstrated favorable complete response rates with the use of PDT.

Data on use of PDT for other malignancies and Barrett’s esophagus without high-grade dysplasia are limited. The published literature consists of generally small case series without comparator groups. Thus, the use of PDT for other malignancies and Barrett’s esophagus without high-grade dysplasia is considered investigational because the impact on health outcomes is not known.

The policy statements have not been changed due to a lack of any new comparative studies. Radiofrequency ablation and endoscopic mucosal resection appear to be replacing PDT as the preferred methods of ablation for high-grade dysplasia in Barrett’s esophagus. Evidence for efficacy of photodynamic therapy for palliative treatment of unresectable cholangiocarcinoma is accumulating; however, randomized controlled trials are needed to confirm its utility compared to alternative treatments such as chemoradiation.

Practice Guidelines and Position Statements

The Society of Thoracic Surgeons published practice guidelines for the management of Barrett’s esophagus with high-grade dysplasia in June 2009. (33) The guideline states that, based on grade B evidence, “photodynamic therapy (PDT) should be considered for eradication of high-grade dysplasia (HGD) in patients at high risk for undergoing esophagectomy and for those refusing esophagectomy” and that “it is reasonable to use photodynamic therapy (PDT) to ablate residual intestinal metaplasia after endoscopic mucosal resection (EMR) of a small intramucosal carcinoma in high-risk patients.”

The 2011 American Gastroenterological Association’s position statement on Barrett’s esophagus management recommends photodynamic therapy as an option for treatment of confirmed high-grade dysplasia with Barrett’s esophagus. (10)

The National Comprehensive Cancer Network (NCCN) guideline on esophageal cancer lists photodynamic therapy as an ablative method for patients with Barrett’s esophagus with high-grade dysplasia, and for palliation of dysphagia in patients with esophageal cancer. (34) Endoscopic mucosal resection (EMR) and ablation for T1a tumors and EMR or ablation for tumor in situ are listed as treatment options for Barrett’s esophagus and high-grade dysplasia.

The 2007 American College of Chest Physicians (ACCP) practice guidelines on bronchial intraepithelial neoplasia and early central airways lung cancer recommend PDT as a treatment option for superficial squamous cell carcinoma in patients who are not surgical candidates. (35) The ACCP guidelines also note there is limited experience in the use of PDT in patients who are candidates for surgery.
The NCCN guideline on non-small cell lung cancer states that PDT is a treatment option in patients with locoregional recurrence of non-small cell lung cancer with endobronchial obstruction or severe hemoptysis. (36)

NCCN lists ablation (PDT is an ablative technique) as a treatment option in patients with microscopic margins (R1) or residual local disease (R2) post-resection of intrahepatic cholangiocarcinoma. (37) NCCN describes PDT as a relatively new therapy for the local treatment of unresectable cholangiocarcinoma saying that the combination of PDT and biliary stenting “has been shown to significantly improve the overall survival of patients with unresectable cholangiocarcinoma based in 2 small randomized clinical trials.”

The National Institute for Health and Clinical Excellence (NICE) has published guidance on a number of applications of PDT. Guidelines on PDT for palliative treatment of advanced esophageal cancer, (38) treatment of localized inoperable endobronchial cancer, (39) and treatment of advanced bronchial carcinoma (40) state that current evidence on safety and efficacy is sufficient to support the use of PDT for these indications. NICE states that PDT should be used only with special arrangements for clinical governance, consent, and audit for the following 4 indications: interstitial photodynamic therapy for malignant parotid tumors, (41) early stage esophageal cancer, (42) bile duct cancer, (43) and high-grade dysplasia in Barrett’s esophagus. (44) NICE guidance on PDT for brain tumors states that current evidence is limited in quality and quantity, and the procedure should only be used in context of randomized controlled trials with well-defined inclusion criteria and treatment protocols, and collection of both survival and quality-of-life outcomes. (45)

**Medicare National Coverage**

No National Coverage Determination

**References:**


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