Protocol

Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

(80106)

Medical Benefit		**Effective Date**: 01/01/18	**Next Review Date**: 05/21
Preauthorization	No	**Review Dates**: 09/07, 09/08, 09/09, 05/10, 05/11, 05/12, 05/13, 05/14, 05/15, 05/16, 05/17, 11/17, 05/18, 05/19, 05/20	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With obstructing esophageal cancer	Interventions of interest are: • Photodynamic therapy as palliation	Comparators of interest are: • Stenting • Laser therapy • Argon plasma coagulation	Relevant outcomes include: • Change in disease status • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With obstructing endobronchial lesions	Interventions of interest are: • Photodynamic therapy as palliation	Comparators of interest are: • Laser therapy • Brachytherapy • External-beam radiotherapy • Resection	Relevant outcomes include: • Change in disease status • Symptoms • Quality of life • Treatment-related morbidity
Individuals: • With early-stage non-small-cell lung cancer who are not candidates for surgery or radiotherapy	Interventions of interest are: • Photodynamic therapy	Comparators of interest are: • Radiofrequency ablation • Cryotherapy • Brachytherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With Barrett esophagus with high-grade dysplasia	Interventions of interest are: • Photodynamic therapy	Comparators of interest are: • Radiofrequency ablation • Surveillance • Esophagectomy • Cryotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Change in disease status • Quality of life • Treatment-related morbidity
Individuals: • With unresectable cholangiocarcinoma	Interventions of interest are: • Photodynamic therapy plus stenting as palliation	Comparators of interest are: • Stenting alone	Relevant outcomes include: • Change in disease status • Symptoms • Quality of life • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: • With other malignancies	Interventions of interest are: • Photodynamic therapy	Comparators of interest are: • Standard of care	Relevant outcomes include: • Overall survival • Disease-specific survival • Change in disease status • Quality of life • Treatment-related morbidity

DESCRIPTION

Photodynamic therapy (PDT; also called phototherapy, photoradiotherapy, photosensitizing therapy, or photochemotherapy) is an ablative treatment that uses a photosensitizing agent to expose tumor cells to a light source of a specific wavelength for the purpose of damaging the cells. 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. Treatment for tumor cells occurs through selective retention of the photosensitizing agent and the selective delivery of light.

SUMMARY OF EVIDENCE

For individuals who have obstructing esophageal cancer who receive PDT as palliation, the evidence includes systematic reviews, randomized controlled trials (RCTs), and uncontrolled single-arm studies. The relevant outcomes are change in disease status, symptoms, quality of life (QOL), and treatment-related morbidity. A meta-analysis comparing PDT with neodymium-doped yttrium aluminum garnet laser suggested that improvements in dysphagia are similar, although estimates are imprecise. Compared with the neodymium-doped yttrium aluminum garnet laser, PDT is associated with a lower risk of perforation and a higher risk of adverse reactions to the light (e.g., photosensitivity). PDT plus argon plasma coagulation appears to prolong the time to recurrence of dysphagia as opposed to argon plasma coagulation alone. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have obstructing endobronchial lesions who receive PDT as palliation, the evidence includes randomized controlled trials (RCTs) and uncontrolled single-arm studies. The relevant outcomes are change in disease status, symptoms, QOL, and treatment-related morbidity. Evidence from RCTs comparing PDT with neodymium-doped yttrium aluminum garnet laser has generally supported reductions in symptoms using PDT similar to those using a laser. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have early-stage non-small-cell lung cancer who are not candidates for surgery or radiotherapy who receive PDT, the evidence includes uncontrolled single-arm studies. The relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, QOL, and treatment-related morbidity. There are few patients with early-stage non-small-cell lung cancer who are not candidates for surgery or radiotherapy. While several treatment methods (e.g., laser, electrocautery, cryotherapy, brachytherapy) are available for this population, studies comparing the treatment methods are not available. Case series of PDT include between 21 and 95 patients and have reported complete response rates ranging from 72% to 100%. Given the small size of this potential population and the ineligibility for standard surgical treatment or radiotherapy, it is unlikely that stronger evidence will become available. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with Barrett esophagus with high-grade dysplasia who receive PDT, the evidence includes two systematic reviews and two RCTs. The relevant outcomes are OS, disease-specific survival, change in disease status, QOL, and treatment-related morbidity. One RCT compared PDT plus a proton pump inhibitor with a proton pump inhibitor alone and demonstrated higher response rates and lower risk of progression with cancer persisting during five years of follow-up for patients in the PDT plus proton inhibitor group. The results of the RCT also revealed that patients treated with PDT had significantly more complications, including a high rate of strictures. Another RCT compared PDT performed with different photosensitizers; results revealed that neither were valuable long-term treatments for dysplastic Barrett esophagus. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have unresectable cholangiocarcinoma who receive PDT plus stenting as palliation, the evidence includes systematic reviews, RCTs, and observational studies. The relevant outcomes are change in disease status, symptoms, QOL, and treatment-related morbidity. Two small RCTs and several observational studies have found that PDT plus stenting is associated with the greater elimination of bile duct stenosis and improved survival benefit compared with stenting alone. One RCT comparing stenting plus chemotherapy and PDT with stenting plus chemotherapy without PDT reported longer progression-free survival, but not OS, with similar adverse event rates. Case series have suggested an improvement in the QOL with PDT. The main complication of PDT in cholangiocarcinoma is cholangitis. Given the small size of this potential population, it is unlikely that stronger evidence will become available. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have other malignancies (e.g., gynecologic, bladder, head and neck, brain, soft tissue) who receive PDT, the evidence includes controlled observational studies and uncontrolled single-arm studies. The relevant outcomes are OS, disease-specific survival, change in disease status, QOL, and treatment-related morbidity. The published literature on PDT for these malignancies is generally comprised of small case series without comparator groups. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 radiotherapy
- treatment of high-grade dysplasia in Barrett esophagus
- palliative treatment of unresectable cholangiocarcinoma when used with stenting

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

BACKGROUND

PHOTODYNAMIC THERAPY

PDT has been investigated for use in a wide variety of tumors, including esophageal, lung, cholangiocarcinoma,

prostate, bladder, breast, brain (administered intraoperatively), skin, and head and neck cancers. Barrett esophagus also has been treated with PDT.

Several photosensitizing agents have been used in PDT: porfimer sodium (Photofrin), administered intravenously 48 hours before light exposure, and 5-aminolevulinic acid, administered orally four to six hours before the procedure. Aminolevulinic acid 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 to 72 hours, but tumor cells retain porfimer for a longer period. Laser treatment of Barrett esophagus may be enhanced by the use of balloons containing a cylindrical diffusing fiber. The balloon compresses the mucosal folds of the esophagus, thus increasing the likelihood that the entire Barrett 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.

REGULATORY STATUS

Labeled indications for porfimer sodium (Photofrin®; Pinnacle Biologics), as approved by the U.S. Food and Drug Administration through a new drug application in 2011, are as follows.[1]

ESOPHAGEAL CANCER

- 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 neodymium-doped yttrium aluminum garnet laser therapy.

ENDOBRONCHIAL CANCER

- Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial non-small-cell lung cancer.
- Treatment of microinvasive endobronchial non-small-cell lung cancer in patients for whom surgery and radiotherapy are not indicated.

HIGH-GRADE DYSPLASIA IN BARRETT ESOPHAGUS

- Treatment of high-grade dysplasia in Barrett esophagus patients who do not undergo esophagectomy.

As of June 2018, oral 5-aminolevulinic acid has not received Food and Drug Administration approval as a photosensitizing agent for PDT. Topical 5-aminolevulinic acid, used for the treatment of actinic keratoses, is addressed separately (Dermatologic Applications of Photodynamic Therapy Protocol).

This evidence review addresses only the non-dermatologic oncology applications of PDT and does not address its use in dermatologic applications, such as actinic keratosis 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 separately.

RELATED PROTOCOLS

Dermatologic Applications of Photodynamic Therapy

Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus

Photodynamic Therapy for Choroidal Neovascularization

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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